Journal of Orthopaedic Translation 34 (2022) 85–90

Contents lists available at ScienceDirect

Journal of Orthopaedic Translation

journal homepage: www.journals.elsevier.com/journal-of-orthopaedic-translation

Oral versus intravenous tranexamic acid in elderly patients with intertrochanteric fracture undergoing proximal femur intramedullary nailing: A prospective cohort study

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ARTICLE INFO

Keywords:
Intertrochanteric fracture
Tranexamic acid
Blood loss
Blood transfusion
Economic benefits

ABSTRACT

Objective: To investigate and compare the efficacy and safety of intravenous and oral application of tranexamic acid (TXA) in geriatric patients undergoing intertrochanteric fracture surgeries.

Methods: All patients with intertrochanteric fracture admitted to the trauma center of the Zhongda hospital were selected after January 1st, 2020. The final patients were divided into three groups. Oral group: 2 g oral TXA 2 h preoperatively; intravenous group: 15 mg/kg intravenous TXA before incision; control group: no intervention. The main outcome measures were blood transfusion rate and total blood loss. Secondary outcomes include intraoperative blood loss, postoperative blood loss, perioperative blood transfusion volumes, length of hospital stay, thromboembolism events and other adverse events.

Results: From January 1, 2020 to December 31, 2020, 124 patients with intertrochanteric fracture were enrolled. According to the inclusion and exclusion criteria, 105 patients were included, including 32 patients in the oral group, 36 patients in the intravenous group and 37 patients in the control group. The demographic characteristics of each group were similar. The blood transfusion rate in the control group was significantly more than that in the experimental group (64.9% vs 40.6% vs 36.1%, $P = 0.041$). There was no significant difference between the oral group and the intravenous group ($P = 0.704$). The total blood loss of the oral group and the intravenous group were less than the control group (990.29 ± 250.19 ml vs 997.47 ± 452.34 ml vs 1408.54 ± 461.74 ml), the difference was statistically significant ($P = 0.001$), and there was no significant difference between the intravenous group and the oral group ($P = 0.459$). The perioperative blood transfusion volumes of the oral group and the intravenous group were less than the control group (250.00 ± 198.62 ml vs 227.78 ± 179.27 ml vs 367.57 ± 323.90 ml), the difference was statistically significant ($P = 0.001$), and there was no significant difference between the intravenous group and the oral group ($P = 0.832$). During hospitalization and follow-up, there were no thromboembolism events such as deep vein thrombosis and pulmonary embolism.

Conclusion: It is safe and effective to use TXA intravenously and orally in elderly patients with intertrochanteric fracture. The results of the two methods are similar in safety and effectiveness. Oral TXA is recommended because of its cost-benefit superiority and its ease of administration.

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https://doi.org/10.1016/j.jot.2022.05.012
Received 28 December 2021; Received in revised form 23 May 2022; Accepted 27 May 2022

The translational potential of this article: The result of this prospective cohort study shows that the utilization of oral TXA in elderly patients with intertrochanteric fracture undergoing proximal femur intramedullary nailing possesses great potential in reducing blood loss and cost-benefit superiority.

1. Introduction

With the aging of the world population, the incidence of hip fractures has increased year by year [1,2]. Intertrochanteric fracture is one of the common types of hip fractures, accounting for about half of hip fractures, which are often caused by low-energy injury mechanisms such as falling in standing position [3]. For elderly patients, early surgical treatment is the preferred choice because it might allow initial full weight-bearing and rehabilitation [4,5].

It is reported that the mortality of elderly patients with intertrochanteric fracture during hospitalization is as high as 15% [6], which is related to a variety of complications in elderly patients. Anemia is the most common complication associated with increased perioperative mortality [7]. Approximately 30–45% of patients with hip fracture have varying degrees of anemia during perioperative period, and 10% of patients will have severe anemia [8]. Perioperative blood loss frequently leads to anemia and aggravates it. The stronger the degree of anemia, the higher the risk of postoperative death. Intertrochanteric fractures are extracapsular fractures, with more blood loss after fracture than intracapsular fractures, and elderly intertrochanteric fractures are usually treated with intramedullary nail internal fixation, increasing intraoperative and postoperative blood loss. Therefore, elderly patients with intertrochanteric fractures have more perioperative blood loss and more serious anemia, so clinicians should pay more attention to perioperative blood management.

The main measures of perioperative blood management of elderly intertrochanteric fractures include minimally invasive surgery, application of hemostatic drugs, blood transfusion, etc [9]. Blood transfusion is the most common way. The perioperative blood transfusion rate of elderly patients with hip fracture is as high as 84% [10]. Blood products are rare and costly, facing the risks of transfusion related infection, immune response, cardiovascular dysfunction and even death [11]. At present, medical policies all over the world recommend limited use of blood products [12].

In recent years, as a common hemostatic drug, tranexamic acid (TXA) has been proved to be effective and safe in many surgical operations, especially in hip and knee arthroplasty surgery [13] and spinal surgery, and gradually began to be used in orthopaedic trauma surgery, especially in hip fracture surgery. In the application of elderly intertrochanteric fractures, a few numbers of existing studies [14–17] have preliminarily confirmed the effectiveness and safety of intravenous and local use of TXA, but there is no study on oral application.

Therefore, we designed a prospective cohort study to collect and analyze the relevant data of elderly patients with intertrochanteric fracture treated surgically in our hospital to compare the effectiveness and safety of intravenous and oral TXA, and provide evidence-based medical evidence for its feasibility in clinical application.

2. Materials and methods

2.1. Ethical approval

This study was approved by the Ethics Committee of Zhongda Hospital Southeast University (2019ZDSYLL202-P01) and performed in line with the Declaration of Helsinki international ethical guidelines for studies involving human subjects. Written informed consent was obtained prospectively from all patients before they were enrolled.

2.2. Inclusion criteria

The inclusion criteria were

1. age ≥65 years at the time of injury;
2. a confirmed diagnosis of intertrochanteric fractures
3. the time from fracture to operation less than 2 weeks;
4. the patients agreed to receive surgical treatment with proximal femur intramedullary nail.

2.3. Exclusion criteria

The exclusion criteria were:

1. receiving anticoagulant therapy before the operation;
2. combined with other fractures requiring surgery;
3. pathological fracture;
4. allergy to TXA
5. recent or ongoing thromboembolic events such as deep vein thrombosis or pulmonary embolism;
6. liver or renal insufficiency;
7. refuse to receive surgical treatment.

2.4. Methods

All patients with intertrochanteric fractures admitted to the trauma center of Zhongda Hospital Southeast University from January 1, 2020 to December 31, 2020 were selected.

According to the order of admission and the patient's own requirements, patients were divided into oral group, intravenous group and control group. Different preoperative interventions were taken for different groups of patients:

1. Oral group: take oral TXA 2 g 2 h before operation.
2. Intravenous group: give intravenous drip (15 mg/kg) of TXA 30 min before operation.
3. Control group: receive no special intervention.

The operation was completed by the same group of surgeons in the same operating room. All patients were treated with proximal femur intramedullary nail fixation. No drainage tubes were placed in all patients during the operation. All patients received standard thrombo prophylaxis with low-molecular-weight heparin from the second day after admission to 24 h prior to the operation and for 12 h after the operation. Allogeneic blood transfusion was performed when the patient's hemoglobin (HB) concentration was<70 g/L. Routine follow-up visits were scheduled at 1, 2, 3, 6, and 12 months postoperatively.

2.5. Outcome measurements

The main outcome measures were blood transfusion rate and total blood loss. Secondary outcomes include intraoperative blood loss, postoperative blood loss, perioperative blood transfusion volumes, length of hospital stay, thromboembolism events and other adverse events. Collect the hemoglobin level and hematocrit on the day of admission, the morning of the operation day, the first and third day after operation, and collect whether blood transfusion and blood transfusion volume (in red blood cells) during and after operation. The postoperative recovery was recorded. The incidence of adverse events during hospitalization was recorded, including wound infection, hematoma formation and allergic

symptoms. The incidence of related thromboembolic events was recorded, including lower extremity deep venous thrombosis and pulmonary embolism. Outpatients were followed up 1 year after discharge.

Blood volume was predicted using the method of Nadler [18], and the total blood loss was calculated with the method of Gross [19].

2.6. Statistical methods

The normality of measurement data is evaluated. The measurement data with normal distribution are analyzed by t-test, and the measurement data with non normal distribution are analyzed by Wilcoxon rank sum test; for the comparison of counting data rate, chi square test is selected according to the theoretical frequency and sample size.

Spss23.0 was used for statistical analysis, and the difference was statistically significant ($P < 0.05$).

3. Results

3.1. Patient demography

Between January 1, 2020 and December 31, 2020, 124 patients with intertrochanteric fracture were enrolled, and 106 patients were included according to the inclusion and exclusion criteria. Among the excluded patients, 9 refused to participate in the study, 4 were younger than 65 years old, 2 were not treated with surgery, and 3 had fracture for more than 2 weeks. After 106 patients communicated and obtained informed consent, perioperative intervention was carried out. One case had serious complications during the operation and discontinued the study. The remaining 105 patients continued the study, including 32 cases in the oral group, 36 cases in the intravenous group and 37 cases in the control group. No patients were lost during follow-up (Fig. 1).

The patient demographic characteristics, baseline data and preoperative laboratory results are shown in Table 1. There were 80 female patients and 25 male patients. The mean age of the patients (standard deviation) was 83.12 ± 6.41 years. No significant differences were observed between the groups regarding preoperative laboratory values.

3.2. Primary outcomes

Table 2 shows the results of perioperative blood transfusion. The difference among the groups was statistically significant ($P = 0.041$), but there was no significant difference between the oral group and the intravenous group ($P = 0.704$).

The total perioperative blood loss of the oral group and the

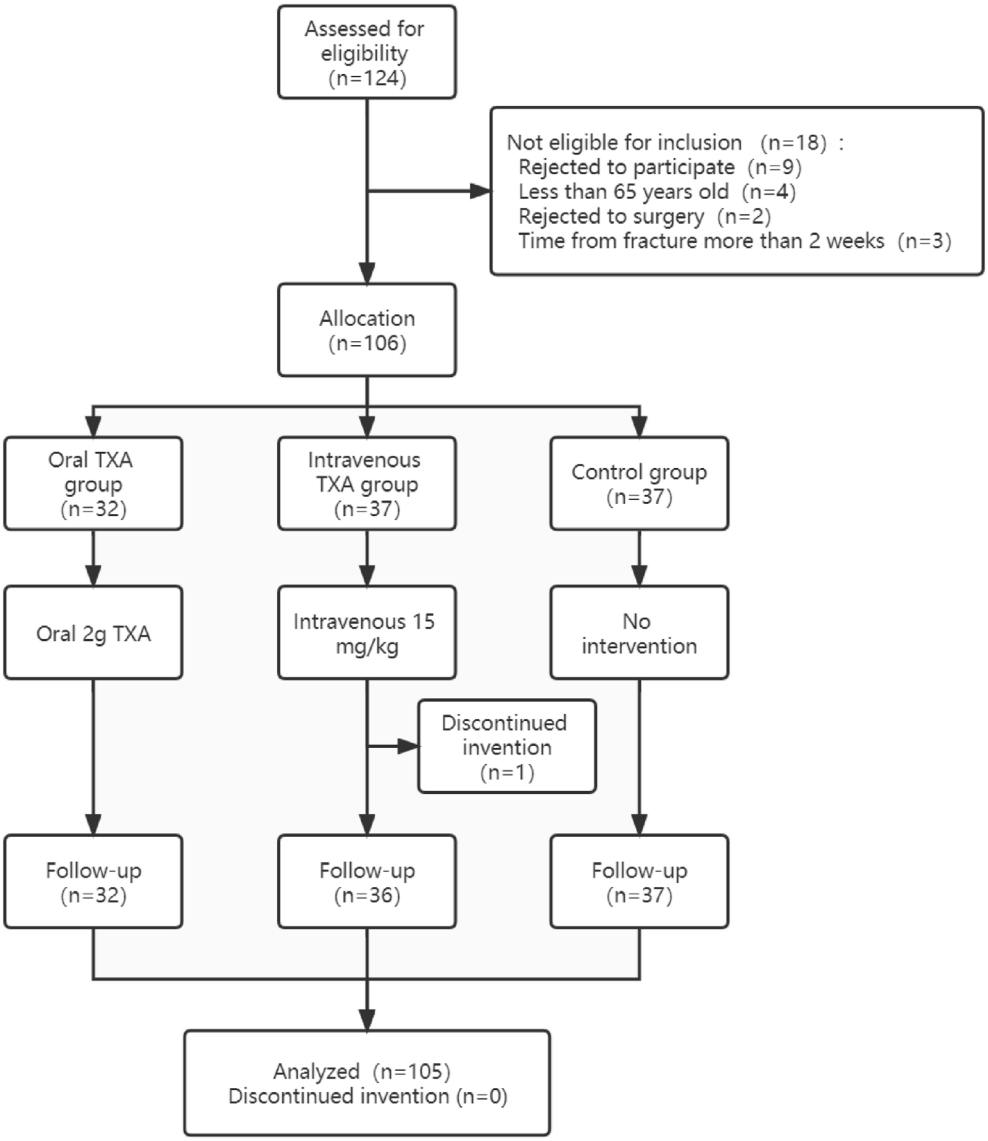

Fig. 1. Flow diagram of patients eligible for this study.

Table 1
Baseline characteristics and perioperative demographics.

Variable	Oral Group (n = 32)	Intravenous Group (n = 36)	Control Group (n = 37)	P Value
Demographic characteristics				
Female	25	28	27	0.657[b]
Age	83.19 ± 6.31	83.98 ± 5.41	82.20 ± 7.50	0.608[a]
Height (m)	1.60 ± 0.08	1.60 ± 0.08	1.61 ± 0.07	0.886[a]
Weight (kg)	57.03 ± 10.52	58.30 ± 11.401	57.35 ± 9.64	0.903[a]
BMI(kg/m^2)	22.46 ± 4.09	22.67 ± 3.73	22.21 ± 3.35	0.878[a]
Predicted blood volume (L)	3.612 ± 0.54	3.70 ± 0.67	3.72 ± 0.54	0.868[a]
Operated side				0.807[b]
Left ([%] of patients)	21 (67%)	24 (67%)	22 (59%)	
Right	11	12	15	
ASA grade	2.47 ± 1.02	2.56 ± 1.27	2.41 ± 1.07	0.825[a]
I	7	7	9	
II	8	9	11	
III	12	13	10	
IV	5	7	7	
Preoperative laboratory values				
Hemoglobin (g/dL)	11.77 ± 1.67	11.18 ± 1.80	11.68 ± 1.82	0.427[a]
Hematocrit (%)	35.33 ± 4.76	33.83 ± 4.98	34.79 ± 4.98	0.579[a]
Platelet count (*10^9/L)	183.45 ± 57.98	189.08 ± 61.51	184.76 ± 65.72	0.338[a]
INR	1.02 ± 0.05	1.01 ± 0.06	0.99 ± 0.08	0.440[a]
Prothrombin time (s)	11.48 ± 0.71	11.51 ± 0.70	11.58 ± 0.98	0.958[a]
Surgical duration (min)	106.45 ± 23.96	101.67 ± 25.81	108.33 ± 31.47	0.502[a]

BMI, body mass index; INR, international normalized ratio; ASA, American Society of Anesthesiologists.
[a] The P value represents the result of one-way analysis of variance for independent means for continuous variables.
[b] The p value represents the results of chi square test for categorical variables among the 3 groups

intravenous group was lower than that of the control group (P = 0.001). No significant difference was observed between the intravenous group and the oral group (P = 0.459).

3.3. Secondary outcomes

The intraoperative blood loss and postoperative blood loss of the oral group and the intravenous group were lower than that of the control group with significant difference, while no significant difference was observed between the intravenous group and the oral group (Table 2).

The perioperative blood transfusion volumes of the oral group and the intravenous group were less than the control group (250.00 ± 198.62 ml vs 227.78 ± 179.27 ml vs 367.57 ± 323.90 ml), the difference was statistically significant (P = 0.001), and there was no significant difference between the intravenous group and the oral group (P = 0.832).

Regarding adverse events, 1 patient in the IV group experienced wound infection during hospitalization. During 1-year follow-up, 3 patients died of basic diseases. No other adverse events such as deep venous thrombosis, pulmonary embolism, myocardial infarction, stroke, or acute renal failure occurred during the follow-up period (Table 3).

4. Discussion

The most common hemostatic drug used in perioperative period of intertrochanteric fracture is TXA. Previous study [20] has proved that the application of TXA in intertrochanteric fracture could achieve good clinical results. Similarly, in our study, we found that the total blood loss in the intravenous group was 997.47 ± 452.34 ml and that in the oral group was 990.29 ± 250.19 ml (P = 0.459), which was lower than that in the control group (1408.54 ± 461.74 ml, P = 0.002). Compared with the

Table 3
Secondary outcomes regarding adverse events.

Variable	Oral Group (n = 32)	Intravenous Group (n = 36)	Control Group (n = 37)
Adverse events			
Wound Infection	0	1	0
Wound Hematoma	0	0	0
PE	0	0	0
DVT	0	0	0
Myocardial Infarction	0	0	0
Stroke	0	0	0
Acute Renal Failure	0	0	0
Death	0	2	1

Table 2
Primary outcomes, secondary outcomes, and postoperative laboratory values.

Variable	Oral Group (n = 32)	Intravenous Group (n = 36)	Control Group (n = 37)	P Value	P_1	P_2	P_3
Primary outcome							
Transfusion, n (n of units)	13 (40)	13 (41)	24 (68)	0.041[a]	0.015	0.046	0.704
Total blood loss (mL)	990.29 ± 250.19	997.47 ± 452.34	1408.54 ± 461.74	0.001[b]	0.002	0.000	0.459
Secondary outcomes							
Intraoperative blood loss (mL)	96.00 ± 24.13	110.86 ± 54.90	149.03 ± 70.73	0.010[b]	0.037	0.000	0.154
Postoperative blood loss (mL)	637.34 ± 174.06	656.77 ± 346.98	1003.73 ± 379.91	0.000[b]	0.001	0.000	0.350
Perioperative blood transfusion volumes (mL)	250.00 ± 198.62	227.78 ± 179.27	367.57 ± 323.90	0.001[b]	0.000	0.001	0.832
Length of stay (d)	10.67 ± 3.29	10.15 ± 4.20	9.93 ± 3.55	0.785[b]			
Postoperative laboratory values							
Hemoglobin (g/dL)							
POD1	8.42 ± 1.28	8.67 ± 1.55	8.18 ± 1.36	0.552[b]			
POD3	8.26 ± 1.33	8.39 ± 1.72	7.71 ± 1.28	0.433[b]			
Reduction in Hemoglobin	2.42 ± 1.61	2.33 ± 1.72	3.25 ± 1.74	0.047[b]	0.038	0.045	0.407
Hematocrit (%)							
POD1	25.61 ± 3.906	26.43 ± 4.82	23.93 ± 4.02	0.540[b]			
POD3	25.16 ± 4.74	25.82 ± 5.54	22.91 ± 5.28	0.555[b]			
Reduction in Hematocrit	11.53 ± 6.17	13.40 ± 9.71	17.75 ± 9.24	0.010[b]	0.049	0.023	0.085

POD, postoperative day
P_1: Intravenous Group vs Control Group; P_2: Oral Group vs Control Group; P_3: Intravenous Group vs Oral Group.
[a] The P value represents the result of chi square test for categorical variables among the 3 groups.
[b] The p value represents the results of one-way analysis of variance for independent means for continuous variables.

control group, the total blood loss with TXA was reduced by about 40%. Reducing blood loss not only means reducing the cost, but also means reducing the risk of clinical deterioration of elderly patients, which is conducive to postoperative recovery and improving the prognosis.

Previous studies have indicated that the blood transfusion rate of hip fracture patients was up to 80% [10], and the use of TXA could reduce the blood transfusion demand by about half [3]. In our study, we observed that 24 people in the control group received blood transfusion, and the blood transfusion rate was 64.9%. After using TXA, the blood transfusion rate decreased to 38.2%, about half, and the difference was statistically significant ($P = 0.041$). There were 13 patients receiving blood transfusions in the oral group and the intravenous group, and the blood transfusion rates were 40.6% and 36.1% respectively, with no significant difference ($P = 0.704$). It is demonstrated that both intravenous and oral use of TXA can reduce the blood transfusion demand.

Some studies have also shown that the application of TXA in elderly patients with intertrochanteric fracture could not reduce the demand for blood transfusion [21]. Malnutrition or chronic diseases can lead to anemia in elderly patients [22], those with intertrochanteric fractures more vulnerable. Perioperative blood loss and anemia increase the demand for clinical blood transfusion. The perioperative blood transfusion indication of elderly patients is 8–10 g/L, which is broader. In addition, the personal preference of the attending doctor will affect the blood transfusion demand. These can explain why the perioperative blood transfusion rate of elderly intertrochanteric fracture patients remains high and the demand for blood transfusions is large. We observed that the number of postoperative blood transfusion in the oral group and the intravenous group after the use of TXA was less than that in the control group (18.7% vs 11.1% vs 37.8%, $P = 0.025$). Therefore, both intravenous and oral use of TXA can reduce the postoperative blood transfusion rate and blood transfusion demand of elderly patients with intertrochanteric fracture, but they still lack the ability to improve the postoperative anemia of elderly patients. Other blood management methods need to be supplemented to help patients improve postoperative anemia.

The safety of TXA has been confirmed in previous studies. The use of TXA will neither increase the probability of postoperative thrombosis events nor increase the incidence of postoperative related complications [1,3]. During the long-term follow-up of 1 year, no thrombosis event was observed and no patient died. Its security has also been verified.

2 h after oral administration of TXA, the blood concentration reached the peak level [23]. According to its pharmacokinetics, oral TXA 2 h before operation is a very suitable way. The efficacy and safety of oral TXA has been verified in the treatment of total knee arthroplasty and total hip arthroplasty [24,25]. Oral administration of TXA 2 g 2 h before operation can effectively reduce blood loss and blood transfusion rate. In the perioperative period of thoracolumbar fusion, the perioperative blood loss of patients with intravenous and oral TXA is the same [26]. Compared with intravenous TXA, the cost of oral TXA is reduced by 3.4–7.7 times, which is cost-effective [27]. These conclusions prove that oral application of TXA is equivalent to intravenous application, and is more convenient and cheaper. Therefore, there is great clinical and economic significance to studying the safety and effectiveness of oral TXA in the perioperative period of elderly intertrochanteric fracture patients.

Our study confirmed that preoperative use of TXA can obtain good economic benefits, and the benefits of oral application are greater than intravenous application. In this study, the average blood transfusion volumes per patient in the control group was 367.57 ± 323.90 ml. While after the use of TXA, it decreased to 227.78 ± 179.27 ml in the intravenous group and 250.00 ± 198.62 ml in the oral group, which means it could reduce about 35% the volume of blood transfusion of every patient undergoing surgery. In our hospital, the cost of one dose of intravenous TXA was 10 times that of oral 2 g TXA. Therefore, the use of oral TXA can save more costs. Although cost saving is not the ultimate goal of medical treatment and research, and comprehensive rehabilitation is the ultimate goal of medical treatment, the saving of blood transfusion for patients has economic and social value. Therefore, oral use of TXA has more economic benefits and is worth promotion.

To the best of our knowledge, this is the first study on the oral application of TXA in elderly patients with intertrochanteric fracture. We verified the effectiveness of oral administration of TXA by comparing the efficacy among the control group, the intravenous group and the oral group. According to the postoperative results and long-term follow-up results, oral application is as safe and effective as intravenous application. In addition, we found that oral TXA has more economic benefits than intravenous applications, reduces the demand for blood transfusion, and can save 2–3 times the cost related to blood transfusion.

Although this study was carefully designed, several limitations exist. First, this study could have included a fourth group in which local application was administered. Second, the international standardized ratio or prothrombin time after anticoagulant therapy was not monitored and collected after operation. Third, the sample size is small. Therefore, further prospective randomized controlled trials with larger sample sizes and different doses and times of TXA administration are warranted to confirm our findings.

5. Conclusion

Perioperative intravenous and oral administration of TXA in elderly patients with intertrochanteric fracture undergoing proximal femur intramedullary nailing are safe and effective, and the safety and effectiveness of the two methods are similar. Compared with intravenous applications, oral TXA has more economic benefits and is worthy of clinical application.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors, and no material support of any kind was received.

Declaration of competing interest

The authors have no conflict of interest relevant to this article.

Acknowledgments

We are grateful to all participants and their families enrolled in this study. We thank for the support of the nursing staffs from the trauma center of Zhongda Hospital.

References

[1] Qi YM, Wang HP, Li YJ, Ma BB, Xie T, Wang C, et al. The efficacy and safety of intravenous tranexamic acid in hip fracture surgery: a systematic review and meta-analysis[J]. J Orthop Trans 2019;19:1–11.
[2] Sy A, Yl B, Qin SA, Jz A, Hy A. Characteristics of bone biochemical indices in predicting secondary osteoporotic fracture after intertrochanteric fracture in elderly women[J]. J Orthop Trans 2018;12:1–5.
[3] Xing F, Chen W, Long C, Huang F, Wang G, Xiang Z. Postoperative outcomes of tranexamic acid use in geriatric trauma patients treated with proximal femoral intramedullary nails: a systematic review and meta-analysis[J]. Orthop Traumatol Surg Res 2020;106(1):117–26.
[4] Wu K, Xu Y, Zhang L, Zhang Y, Guo JJ. Which implant is better for beginners to learn to treat geriatric intertrochanteric femur fractures: a randomised controlled trial of surgeons, metalwork, and patients[J]. J Orthop Trans 2020;21:18–23.
[5] Zhang R, Wang L, Lin Y, Yang M, Guo Z, Xia W, et al. A novel method for estimating nail-tract bone density for intertrochanteric fractures[J]. J Orthop Trans 2019;18:40–7.
[6] Alzahrani K, Gandhi R, Davis A, Mahomed N, et al. In-hospital mortality following hip fracture care in southern Ontario[J]. Can J Surg 2010;53(5):294–8.
[7] Malafarina V, Reginster JY, Cabrerizo S, Olivier Bruyère, Zulet MA, et al. Nutritional status and nutritional treatment are related to outcomes and mortality in older adults with hip fracture[J]. Nutrients 2018;10(5).
[8] Chatterton BD, Moores TS, Ahmad S, Cattell A, Roberts PJ, et al. Cause of death and factors associated with early in-hospital mortality after hip fracture[J]. Bone Joint Lett J 2015;97-B(2):246–51.

[9] Socci AR, Casemyr NE, Leslie MP, Baumgaertner MR, Baumgaertner MR. Implant options for the treatment of intertrochanteric fractures of the hip: rationale, evidence, and recommendations[J]. Bone Joint Lett J 2017;99-B(1):128–33.
[10] Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature[J]. Anesthesiology 2010;113(2):482–95.
[11] Huang F, Zhao Q, Guo C, Ma G, Wang Q, Yin Y, et al. Use of aprotinin to reduce blood loss and transfusion in major orthopedic surgery: a meta-analysis[J]. Transfus Apher Sci 2014;51(2):152–61.
[12] Carson JL, Stanworth SJ, Roubinian N, Fergusson DA, Hebert PC. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion[J]. Cochrane Database Syst Rev 2016;10:D2042.
[13] Georgiev GP, Tanchev PP, Zheleva Z, Kinov P. Comparison of topical and intravenous administration of tranexamic acid for blood loss control during total joint replacement: review of literature[J]. J Orthop Trans 2018;13:7–12.
[14] Tengberg PT, Foss NB, Palm H, Kallemose T, Troelsen A. Tranexamic acid reduces blood loss in patients with extracapsular fractures of the hip: results of a randomised controlled trial[J]. Bone Joint Lett J 2016;98-B(6):747–53.
[15] Drakos A, Raoulis V, Karatzios K, Doxariotis N, Kontogeorgakos V, Malizos K, et al. Efficacy of local administration of tranexamic acid for blood salvage in patients undergoing intertrochanteric fracture surgery[J]. J Orthop Trauma 2016;30(8):409–14.
[16] Lei J, Zhang B, Cong Y, Zhuang Y, Wei X, Fu Y, et al. Tranexamic acid reduces hidden blood loss in the treatment of intertrochanteric fractures with PFNA: a single-center randomized controlled trial[J]. J Orthop Surg Res 2017;12(1):124.
[17] Wang W, Yu J. Tranexamic acid reduces blood loss in intertrochanteric fractures: a meta-analysis from randomized controlled trials[J]. Medicine (Baltim) 2017;96(52):e9396.
[18] Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults [J]. J Surg 1962;51(2):224–32.
[19] Gross JB. Estimating allowable blood loss: corrected for dilution[J]. Anesthesiology 1983;58(3):277–80.
[20] Zhou XD, Li J, Fan GM, et al. Efficacy and safety of tranexamic acid in elderly patients with intertrochanteric fracture: an updated meta-analysis[J]. World J Clin Cases 2019;7(11):1302–14.
[21] Qianzheng Z, Caixia Y, Xingzuo C, Xiaodong X, Ying C, Chenggang L, et al. Efficacy and safety of tranexamic acid for blood salvage in intertrochanteric fracture surgery: a meta-analysis[J]. Clin Appl Thromb Hemost 2018;24(8):1189–98.
[22] Bross MH, Soch K, Smith-Knuppel T. Anemia in older persons[J]. Am Fam Physician 2010;82(5):480–7.
[23] Irwin A, Khan SK, Jameson SS, Tate RC, Copeland C, Reed MR, et al. Oral versus intravenous tranexamic acid in enhanced-recovery primary total hip and knee replacement: results of 3000 procedures[J]. Bone Joint Lett J 2013;95-B(11):1556–61.
[24] Luo ZY, Wang HY, Wang D, Zhou K, Zhou ZK. Oral vs intravenous vs topical tranexamic acid in primary hip arthroplasty: a prospective, randomized, double-blind, controlled study[J]. J Arthroplasty 2018;33(3):786–93.
[25] Qi Y, Li Y, Wang C, Chen H, Rui Y. Comparison of oral and intravenous tranexamic acid in total hip arthroplasty: a systematic review and meta-analysis[J]. Arthroplasty 2020;2(1):2–9.
[26] Yu CC, Kadri O, Kadado A, Buraimoh M, Pawloski J, Bartol S, et al. Intravenous and oral tranexamic acid are equivalent at reducing blood loss in thoracolumbar spinal fusion: a prospective randomized trial[J]. Spine (Phila Pa 1976) 2019;44(11):755–61.
[27] Kayupov E, Fillingham YA, Okroj K, Plummer DR, Valle C. Oral and intravenous tranexamic acid are equivalent at reducing blood loss following total hip arthroplasty: a randomized controlled trial[J]. J Bone Joint Surg Am 2017;99(5):373–8.