Preoperative Blood Management in Elderly Patients with Delayed Intertrochanteric Fracture Surgery as a Necessary Measure: A Review Data Collection

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Abstract

Research on preoperative blood management in the elderly with delayed intertrochanteric fractures surgery is scarce, especially in hematopoiesis and hemostasis. We aimed to assess the effectiveness of the optimized blood management program in elderly patients with delayed intertrochanteric fractures surgery. This retrospective study included 833 patients with intertrochanteric fractures after delayed surgery. According to the actual optimized blood management plan, they were divided into four groups: Group A was the control group; Group B received 1 g of IV TXA at admission; group C underwent sequential TXA treatment after admission until 1 d before surgery (1 g/d); group D received iron supplements (200 mg/d) in addition to the treatment administered to group C, with or without recombinant human erythropoietin (rHuEPO; 40,000 IU). The primary outcomes were preoperative hidden blood loss (HBL), preoperative allogeneic blood transfusion (ABT) rate, hemoglobin (Hb) change, and actual Hb drop. The Hb reduction, calculated HBL, and hospitalization duration in groups C and D were significantly lower than those in groups A and B. The preoperative ABT rates in groups C and D were significantly lower than those in groups A and B, but there was no statistical difference between groups C and D. In conclusion, this study suggested that the iron supplement (with or without rHuEPO) combined with sequential intravenous tranexamic acid (IV TXA) scheme did not show a better clinical effect than sequential IV TXA scheme in management of patients with delayed intertrochanteric fractures surgery. Therefore, before recommending iron supplements and rHuEPO in elderly patients, further evaluation is needed.

Introduction

China has a huge population, and it is aging rapidly, making China the country with the largest number of elderly people in the world. Hip fractures have become a public health concern because of poor prognosis, and China is currently facing great challenges due to an increasing number of hip fractures^{1,2}. According to a systematic analysis, the 1-year mortality rate after hip fracture in China is 13.96%, while that of intertrochanteric fracture (IF) is 17.47%³. Perioperative anemia is an important factor of mortality after hip fracture surgery and is closely related to the type of fracture, such as intracapsular or extracapsular^{4,5}.

Acute post-traumatic anemia and the need for transfusion in elderly patients with intertrochanteric fractures are the major concerns of orthopedic surgeons. Pre-anemia increases the severity and incidence of postoperative anemia and increases the need for blood transfusion⁶. Therefore, an ideal blood management program should include an attempt to minimize preoperative blood loss and correct preoperative anemia⁷. Post-traumatic hyperfibrinolysis is one of the most important causes of preoperative blood loss, and the administration of anti-fibrinolytic drugs seems to be an effective treatment to reduce hidden blood loss⁸. Previous studies have focused on tranexamic acid (TXA) to reduce intraoperative and postoperative hemorrhage in intertrochanteric fractures^{9–11}, while studies on occult hemorrhage before the operation are limited¹². Intravenous iron supplementation, with or without

recombinant human erythropoietin (rHuEPO) therapy, has been proposed as an intervention to correct preoperative anemia¹³. However, actual clinical effects remain controversial^{14,15}. There is currently a lack of strong evidence to prove the preoperative clinical benefit of iron supplements and rHuEPO in elderly patients with intertrochanteric fractures.

Over the past 8 years, we have been committed to perioperative blood management for elderly patients with hip fractures. Among them, the management of patients with delayed intertrochanteric fracture surgery is the focus of our study. We have adopted a variety of intervention programs, focusing on the application of TXA, iron, and rHuEPO, but the actual clinical effects of their different application programs have not been effectively summarized. Therefore, we summarized the original data to evaluate the following: (1) whether the optimized blood management plan was effective and safe; (2) compared with the early intravenous single injection of TXA, whether sequential TXA can effectively reduce post-traumatic blood loss and allogeneic blood transfusion (ABT) rate; and (3) whether adding iron supplements, with or without rHuEPO, can further maintain Hb levels.

Results

Patients Demographics

A total of 833 consecutive patients with intertrochanteric fractures were screened between January 2013 and October 2020, and their eligibility for participation was assessed in this study. A total of 377 patients were excluded according to the exclusion criteria, including 38 patients under 65 years of age, 124 patients with injury time > 12 h, 73 patients with Hb < 110 g/L upon admission, 11 patients with polytrauma, 27 patients with long-term oral anticoagulants before injury, 4 patients with pathological fractures, 37 patients with waiting time for post-traumatic to surgery exceeding 5 days, 26 patients who received other hemostatic or hematopoietic medications after trauma, 18 patients lost to follow-up, and 19 patients who received non-proximal femoral nail anti-rotation (PFNA) fixation. Finally, a total of 456 patients with intertrochanteric fractures were enrolled in the present study (Fig. 1). No significant differences in demographic data upon admission were found between the groups, and the baseline characteristics of the four groups were comparable (Table 1).

Table 1. Baseline characteristics

Patient characteristics	Group A (N=126)	Group B (N=96)	Group C (N=116)	Group D (N=118)	P value
Age (yr) ^a	77.31±6.77	78.77±7.06	77.35±7.32	77.69±7.02	0.416
Gender (male/female) ^b	41/85	36/60	46/70	43/75	0.707
BMI (kg/m ²) ^a	23.52±3.41	23.12±2.04	23.06±1.94	22.47±2.78	0.150
PBV (L) ^a	3.85±0.47	3.93±0.49	3.80±0.37	3.89±0.47	0.181
Injury side (Left/Right) ^a	72/54	48/48	63/53	67/51	0.713
Length of trauma to admission (h) ^a	9.17±1.73	8.77±2.49	9.26±2.01	9.09±2.67	0.425
Time to operation (days) ^a	3.98±0.75	4.40±0.79	4.00±0.81	3.96±0.76	0.338
ASA classification ^b					
	5	7	10	5	0.843
	86	71	82	73	
	72	57	62	55	
AO fracture classification ^b					
A1	57	44	42	53	0.597
A2	40	36	46	39	
A3	29	16	28	26	

Abbreviations: BMI, body mass index; PBV, preoperative blood volume; ASA, American Society of Anesthesiologists.

Intergroup comparisons were performed using the ANOVA, chi-square test, or Fisher's test (^aANOVA; ^bChi-square test or Fisher).

Primary Outcome

Figure 2-A presents a line graph showing mean hemoglobin concentration of the four groups, from PTA to POD 1, and the drop trend in each group. The comparison between groups showed that there was a significant statistical difference in the mean Hb values preoperatively and POD 1 ($P < 0.001$).

The preoperative recorded mean Hb values were 105.06 ± 8.52 g/L, 106.59 ± 9.04 g/L, 111.47 ± 10.01 g/L, and 112.86 ± 8.79 g/L in groups A, B, C, and D, respectively. Groups C and D, compared with groups A and B, had significant statistical differences between groups, but group A vs. group B and group C vs. group D

comparisons did not reach statistical significance (Fig. 2-B). The mean Hb values recorded on POD 1 were 97.24 ± 8.66 , 99.29 ± 9.58 , 100.23 ± 10.07 , and 102.67 ± 8.89 g/L in groups A, B, C, and D, respectively. In terms of mean Hb values on POD1, groups C and D were significantly different from group A ($P = 0.014$ and $P < 0.001$, respectively). Group D was also statistically significant compared with group B ($P = 0.008$); however, there is no statistically significant difference between groups B and C ($P = 0.490$) (Fig. 2-C). The average preoperative drop in Hb in the four groups was 21.48 g/L, 21.02 g/L, 17.36 g/L, and 16.55 g/L, respectively, and the difference was statistically significant ($P < 0.001$). Groups C and D, compared with groups A and B, had significant inter-group statistical differences (all $P < 0.001$); however, pairwise comparisons between the groups showed that the differences between groups D and C and between groups B and A did not reach statistical significance (Fig. 2-D).

Figure 3 shows that the average preoperative HBL was 526 ± 159 mL (range: 292 mL – 1063 mL) in group A, 531 ± 154 mL (range: 221 mL – 955 mL) in group B, 466 ± 115 mL (range 276 mL – 997 mL) in group C, and 449 ± 117 mL (range: 242 mL – 1168 mL) in group D, and the difference between the groups was significant ($P < 0.001$). Pairwise comparisons between groups showed that groups C and D, compared with groups A and B, were significantly different, with $P < 0.001$, but there was no statistically significant difference between groups A and B, and groups C and D ($P > 0.05$). The preoperative transfusion rates in groups B, C, and D were lower than those in group A, but the difference between the groups was not statistically significant ($P > 0.05$).

Secondary outcomes

Compared with group A ($n = 21$) and group B ($n = 17$), group C ($n = 12$) and group D ($n = 10$) had fewer people who needed ABT during the operation ($P = 0.104$). The intraoperative blood loss and operation duration of the four groups of patients were similar, and there was no statistical difference between the groups (all $P > 0.05$). Similarly, fewer patients in groups C and D needed ABT on postoperative day 1 than those in groups A and B, but the difference was not statistically significant ($P = 0.353$). Intermuscular vein thrombosis is the most common preoperatively, with 22 cases in group A. Among the patients (17.40%), there were 15 cases (15.63%) in group B, 19 cases (16.37%) in group C, and 20 cases (16.95%) in group D. The incidence was similar ($P = 0.986$). No symptomatic PE occurred in the four groups of patients. Compared with patients in groups A and B, patients in groups C and D had a good effect in shortening the hospitalization duration ($P < 0.001$). No difference was detected between groups C and D ($P > 0.05$). According to the existing medical data of our department, 16 patients had been hospitalized within 30 days. Among them, four were admitted to the hospital due to poor blood sugar control, four with hypoproteinemia, two with redness and swelling, four with DVT, and two with stroke (Table 2).

Table 2. Comparison of the primary and secondary outcomes among the groups

Variable	Group A	Group B	Group C	Group D	<i>P</i> value
Intraoperative ABT rate (n,%) ^b	21(16.67%)	17(17.71%)	12(10.34%)	10(8.47%)	0.104
Intraoperative blood loss (mL) ^a	262.70±191.72	250.00±178.30	266.38±176.28	267.37±221.04	0.914
Operative time (min) ^a	90.08±40.65	96.26±33.37	96.58±45.70	95.20±42.87	0.579
POD 1 ABT rate (n,%) ^b	11(8.73%)	8(8.33%)	8(6.90%)	4(3.39%)	0.353
Intramuscular venous thrombosis (n,%) ^b	22(17.40%)	15(15.63%)	19(16.37%)	20(16.95%)	0.986
DVT (n,%) ^b	6(4.76%)	3(3.13%)	3(2.58%)	4(3.39%)	0.820
Symptomatic PE (n,%) ^b	0	0	0	0	-
Hospitalization duration (d) ^a	9.14±1.44	8.79±1.62	7.38±2.78	7.47±2.38	<0.001
All-cause 30-day readmission (n,%) ^b	4(3.17%)	5(5.21%)	4(3.45%)	3(2.54%)	0.756
30-day mortality (n,%) ^b	0	0	0	0	-

Abbreviations: ABT, allogeneic blood transfusion; POD 1, postoperative day 1; DVT, deep venous thrombosis; PE, pulmonary embolism.

Intergroup comparisons are performed using the ANOVA, chi-square test, or Fisher's test (^aANOVA; ^bChi-square test or Fisher).

Discussion

The most important findings of the current study are as follows. First, post-traumatic sequential IV TXA can reduce the preoperative waiting period of HBL and maintain Hb levels, without increasing the incidence of preoperative DVT. It also has certain benefits in reducing transfusion rates. Second, the patients did not receive additional benefits from the combined supplementary treatment plan (iron supplementation, with or without rHuEPO). Finally, the early blood management intervention of patients

should follow the conclusions of the CRASH-2 trial, in which the first IV single-dose TXA should be used within 8 h post-trauma.

Intertrochanteric fractures cause substantial blood loss in elderly and frail patients, exposing them to preoperative anemia, which negatively impacts clinical outcomes and mortality^{16,17}. In addition, studies have shown that patients with IF have obvious HBL during the perioperative period, and the volume of HBL after injury gradually increases as the operation time is delayed. Wu et al.¹⁸ reported that blood loss occurring between the time of fracture time and operation is the main reason underlying the decrease in Hb level, and the Hb decrease before operation is significantly higher than that after operation. Li et al.¹⁹ conducted a prospective analysis of perioperative hidden blood loss in 123 elderly patients with femoral intertrochanteric fractures and found that the HBL in the preoperative waiting period was approximately 375.6 mL, which was 62.4% of the total HBL on the first postoperative day (602 mL) and 48.6% (772 mL) of total HBL on the third postoperative day. Therefore, blood management during the preoperative waiting period for elderly patients with delayed surgery is particularly important.

With the popularization of TXA in China, an increasing number of orthopedic surgeons have started using TXA, with satisfactory results in clinical practice. Based on this background, our department confirmed the effectiveness and safety of TXA in IF¹¹, complex tibial plateau fractures²⁰, femoral shaft nonunion revision surgery²¹, and high tibia osteotomy²². However, these studies focused on the effectiveness and safety of intraoperative and postoperative IV use. Two consecutive global multicenter studies have shown that the early application of TXA effectively reduces the incidence of mortality due to traumatic bleeding^{8,23}. However, we have not summarized the effect of TXA in the early post-traumatic period and sequential IV TXA before surgery, although some orthopedic surgeons at our department have begun an empirical IV intervention. A prospective randomized controlled study by Ma et al.¹² confirmed that a single-dose IV TXA (1 g, 200 mL) interventional treatment in the early post-traumatic period of elderly patients with IF can effectively reduce hidden blood loss. The pharmacokinetic study of TXA showed that its half-life is approximately 3 h. However, the high fibrinolytic state of the body caused by trauma is persistent, and for severe trauma patients, red blood cells (RBCs) and plasma need to be used for more blood transfusion support within 6 h²⁴. In addition, the use of anticoagulants, such as enoxaparin or rivaroxaban, after trauma, may cause new bleeding. These facts indicate that a single dose of TXA in the early post-traumatic period cannot sufficiently inhibit hyperfibrinolysis; therefore, this provides a theoretical basis for multiple doses and sequential IV TXA to inhibit fibrinolysis and reduction in invisible blood loss after trauma.

Intravenous iron supplementation, with or without rHuEPO, before surgery, is considered a compelling potential intervention to increase Hb levels and reduce perioperative transfusion exposure. Yoon et al.²⁵ applied a restrictive transfusion strategy combined with intravenous iron supplementation in 859 patients with hip fracture before surgery, resulting in less total blood loss and blood transfusion rate, and higher Hb levels, 6 weeks after surgery. Muñoz et al.²⁶ conducted a pooled observational analysis of 2,547 patients undergoing major orthopedic surgery (lower-limb arthroplasty and hip fracture repair) and

confirmed that very-short-term perioperative intravenous iron supplementation, with or without rHuEPO, is closely related to reduced transfusion rates and length of hospital stay. García-Erce et al.²⁷ found that, in patients with anemia due to hip fracture managed with perioperative intravenous iron and a restrictive transfusion protocol, preoperative administration of rHuEPO is associated with reduced transfusion requirements. However, some scholars are skeptical about the clinical effects of intravenous iron supplementation. Jeong et al.²⁸ found that among patients who underwent primary staged bilateral total knee arthroplasty (TKA) during a single hospitalization, although the serum iron profile of patients with intravenous iron supplementation improved, it could not increase the Hb level or reduce the transfusion rates. All of the above studies were observational. To date, there is no broad consensus or established clinical practice guideline to support the routine use of preventive intravenous iron supplementation, with or without rHuEPO, to treat anemia before major elective surgery; further, the best treatment timing, specific doses, and whether patients with anemia need additional nutritional supplements remain unclear.

The present study is the first to investigate the effectiveness and safety of different preoperative blood optimization management programs for elderly patients with delayed intertrochanteric fracture surgery. The results showed that with sequential IV TXA (Group C) and iron supplementation treatment (with or without rHuEPO, Group D) in the preoperative waiting period, the HBL volumes were lower than those in the single-dose TXA (Group B) and control group (Group A); however, there was no statistically significant difference between groups C and D (466.25 ± 114.82 mL vs. 448.66 ± 116.83 mL, $P = 0.247$). In the last laboratory results prior to surgery, the Hb levels of groups C and D were higher than those of groups A and B, but there was still no significant statistical difference between groups C and D, with Hb drop also showing the same trend. This indicates that when we extended the use of TXA, with or without iron and rHuEPO, the HBL and actual Hb loss after admission could be reduced. The results of the preoperative transfusion rate also confirmed the advantages of long-term use of TXA, with the rates for groups A, B, C, and D being 22.22%, 19.79%, 14.66%, and 14.41%, respectively. Another important finding is that, theoretically, TXA intervention in the early post-traumatic period can reduce HBL, but in this study, there was no statistical difference between groups A and B in terms of the HBL and Hb levels. According to our analysis, the mean time from trauma to admission in the single-dose group was 8.77 h, which was higher than that of 8 h in the CRASH-II trial⁸ and 2 h in the study by Ma et al.¹² Therefore, when choosing an early single-dose intervention, the time should be controlled within 8 h after trauma.

Preoperative sequential IV TXA (12 patients, 10.34%) and supplementation treatment (10 patients, 8.47%) program also had certain benefits in reducing the requirement for transfusion during the operation compared to the programs for the single-dose TXA group (17 patients, 17.71%) and control group (21 patients, 16.67%) ($P = 0.104$). In addition, on the first day after surgery, transfusion was required for 11 patients (8.73%) in the control group, 8 patients (8.33%) in the single-dose group, 8 patients (6.90%) in the sequential IV TXA group, and 4 patients (3.39%) in the supplementation treatment group. The reason why groups C and D experienced reduced blood transfusion rate during surgery and on the first day after surgery is that good blood preservation before surgery can increase the tolerance of elderly patients to surgical trauma. The reduction in blood transfusion rate not only reduces the risk of infection in the

blood, but also contributes to a substantial reduction in healthcare costs and resource utilization for these patients²⁹. In addition, in this study, there was a significant statistical difference in the length of stay between the four groups ($P < 0.001$), with the length for groups C and D being significantly less than that for groups A and B. Therefore, good preoperative blood management can reduce the post-trauma hidden blood loss and transfusion requirement caused by elderly IF, reduce the incidence of anemia, maintain high Hb levels during hospitalization, and shorten hospitalization duration, which is closely related to postoperative physical function recovery and the concept of enhanced recovery after surgery (ERAS)³⁰.

Studies have confirmed that delaying the operation time increases the probability of postoperative complications and mortality of elderly patients with hip fracture³¹, but other studies have shown that there is no significant difference in the mortality of patients whose surgery is delayed by up to 3 days³². Our research results showed that there was no mortality or serious adverse events within 30 days after the operation in the four groups. Surgeons have always focused on whether intravenous TXA is safe. Although many studies have reported administering the routine dose without increasing the risk of venous thromboembolism, there is still no consensus on the safety of higher doses or prolonged use^{33,34}. Conservation of blood products, reduced laboratory costs, and shorter hospital stays are likely the major factors driving the cost savings associated with TXA use³⁵. Our department has accumulated rich experience in the prevention and treatment of venous thromboembolism associated with postoperative prolongation IV TXA, but the safety of preoperative prolongation is still unknown^{21,22}. Similarly, the use of erythropoiesis agents results in thrombotic events³⁶. In this study, there was no significant difference in the incidence of venous thrombosis in the lower extremities of the three groups, and the incidence of venous thrombosis was comparable to that in a previous study. Intravenous iron supplementation can cause life-threatening hypersensitivity reactions, cardiovascular events, and infections³⁷. In the present study, we did not encounter such adverse events. These results are consistent with the results of a previous systematic review that included 10,390 patients participating in 103 trials, which concluded that intravenous iron supplementation is not associated with adverse drug reactions or increased risk of infection³⁸.

Although this study was not a prospective randomized controlled study, it still has some advantages. Our study employed strict inclusion criteria; for elderly patients with Hb > 110 g/L, it is difficult for doctors to pay attention to preoperative anemia and blood transfusion requirement in the clinic. However, this study confirmed that, with delay in surgery, the Hb level of patients showed a declining trend. Further, the time from injury to admission was strictly controlled to reduce potential interference. This study has some limitations. First, the study only focused on hospitalization and a short follow-up period, which may not be sufficient to evaluate the clinical efficacy and safety of the treatment. Second, the coagulation index was easily missed by the doctor during the post-trauma admission examination; thus, it was excluded from this study. Third, when the Gross formula was obtained, taking into account the impact of dehydration on the Hb level upon admission, the Hb level upon admission was corrected to 0.9 to simulate 10% dehydration for all patients; however, rehydration following admission may interfere with

the accuracy of Hb measurements. Finally, a prospective study might better verify the effectiveness and safety of an optimized blood management program with the application of TXA, iron supplement, and rHuEPO in the elderly population with hip fractures.

Conclusion

We found that elderly patients with delayed intertrochanteric fracture surgery who received sequential IV TXA combined with iron supplementation, with or without rHuEPO, in the preoperative waiting period did not show better effects than those who underwent the sequential IV TXA program. Therefore, further evaluation is required before recommending iron supplementation to patients. In addition, if the patient undergoes early TXA intervention, the first IV time should be guaranteed within 8 hours post-trauma.

Materials And Methods

Patients

We conducted this retrospective large-scale self-censorship study at the Department of Orthopedics and Trauma, Hong Hui Hospital (level-1 trauma center), with elderly patients who were diagnosed with an intertrochanteric fracture and an operative delay of greater than 72 hours, between January 2013 and October 2020. All the data in this study were derived from two randomized controlled studies in our department, which have been registered in the Chinese Clinical Trial Registry (ChiCTR-TRC-1800017754 and ChiCTR-INR-16008134). This study was approved by the ethics committee of the hospital (No. 201606008), and proceeded in accordance with the Declaration of Helsinki. All participating patients provided written informed consent.

The inclusion criteria were elderly patients with intertrochanteric fractures, age ≥ 65 years, injury time ≤ 12 h, and Hb ≥ 110 g/L on post-trauma admission (PTA). The exclusion criteria were as follows: (1) polytrauma; (2) open fractures or continuous bleeding from other parts of the body, such as spleen rupture or gastrointestinal bleeding; (3) recent or continuous thromboembolic events and long-term consumption of oral anticoagulants before injury; (4) known allergies to TXA, rHuEPO, or iron supplements; (5) coagulation dysfunction caused by diffuse intravascular coagulation or liver and kidney dysfunction; (6) severe brain, heart, liver, or kidney dysfunction, and patients who could not tolerate surgery; (7) patients with pathological fractures or tumors; (8) waiting time for post-traumatic to surgery exceeding 5 days; (9) American Society of Anesthesiologists (ASA) score of V; and (10) administration of any drugs, other than TXA, iron, and rHuEPO that are conducive to hemostasis and hematopoiesis.

Study design and blood management

The patients were divided into four groups according to the actual optimized blood management plan that they received at post-traumatic (Table 3). The details of each strategy are described below.

Table 3. Optimized blood management program of the four groups

Blood management program	Group A	Group B	Group C	Group D
Single-dose IV TXA		✓		
Sequential IV TXA			✓	✓
Iron supplements, with or without rHuEPO				✓

Abbreviations: IV, intravenous; TXA, tranexamic acid; rHuEPO, recombinant human erythropoietin.

Single-dose intravenous (IV) TXA: Patients received IV TXA (0.5 g; Tiancheng Pharmaceutical Co., Ltd., Changchun, China) 1 g (200 mL) immediately at PTA.

Sequential IV TXA: sequential TXA treatment after admission until 1 day before surgery (1 g/day).

Iron supplements, with or without rHuEPO: received additional IV iron supplements (200 mg/d, Hengsheng Pharmaceutical Co., Ltd., Nanjing, China), with or without rHuEPO (the first dose was 40,000 IU, and the following dose was 10,000 IU; Shenyang 3SBio Inc., Shenyang, China). The indications for discontinuation of iron supplementation and rHuEPO are as follows: male Hb > 130 g/L and female Hb > 120 g/L.

Preoperative management

All patients were managed according to the standardized IF pathway protocol after admission, including blood pressure control, blood glucose monitoring, and standardized fluid and blood transfusion procedures³⁹. The only difference was in the above three main preoperative blood optimization management programs. In addition, according to the recommendations of the China Orthopedic Major Surgery Venous Thromboembolism Prevention Guidelines, all patients were treated with anticoagulants (Enoxaparin, 1H 20 mg qd) and intermittent compression boots as a preventive treatment for lower extremity venous thrombosis during hospitalization. If a positive result was observed on lower extremity vein ultrasound, the enoxaparin (1H) regimen was changed to Bid. According to the agreement signed upon admission, the patient would undergo intravenous ultrasound examination for both lower extremities at the bedside every day during hospitalization, and would be examined at the outpatient clinic, 14 and 30 days after discharge.

Data collection

The hospital records contained data on age, sex, body mass index (BMI), patient's blood volume (PBV), injury side, time from injury to operation, duration of operation, the American Society of Anesthesiologists (ASA) classification, and AO fracture classification (A1/A2/A3). We noted the Hb and hematocrit (Hct) levels at PTA, day 2 of PTA (PTA 2), preoperatively, and on postoperative day 1 (POD 1).

Outcome Measurements

Primary outcome

Preoperative hidden blood loss (HBL), preoperative allogeneic blood transfusion (ABT) rate, Hb change, and actual Hb drop were the primary outcomes in the present study. HBL was calculated using the Gross formula, as follows⁴⁰:

$$\text{HBL} = \text{PBV} \times (\text{Hct}_1 - \text{Hct}_2) + \text{Hb}_{\text{trans}}$$

Hct₁ = the initial Hct level upon admission

Hct₂ = the lowest Hct level detected before surgery

The PBV was calculated using Nadler's equation, as follows⁴¹:

$$\text{PBV} = K_1 \times h^3 + K_2 \times w + K_3, [\text{h: height (m), w: weight (kg)}]$$

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 $K_3 = 0.1833$

The ABT indications, formulated according to the guidelines of the Chinese Ministry of Health, were as follows: (1) Hb level < 70 g/L; (2) 70 g/L < Hb level < 100 g/L; and (2) when the patient had symptoms of dizziness, tachycardia, asthma, and fatigue. Because most elderly people are in a frail state before injury, our department and the anesthesiology department jointly developed a new blood transfusion strategy if patients with hemoglobin levels < 90 g/L preoperatively received ABT.¹¹

Secondary outcomes

The secondary outcomes included intraoperative and postoperative day 1 blood transfusion rates and hospitalization duration. Complications, such as intramuscular venous thrombosis, deep vein thrombosis (DVT) and symptomatic pulmonary embolism (PE), were recorded preoperatively. In addition, through the existing medical data of the department, the incidence of 30-day mortality and 30-day all-cause re-admission were recorded. Clinically suspected PE was diagnosed based on clinical symptoms and using an enhanced chest computed tomography scan.

Statistical Analysis

Statistical analyses were computed using the SPSS 22.0, and GraphPad Prism 8.0. The one-way analysis of variance and Tukey's post-hoc tests were performed to analyze the parametric samples, while the Kruskal–Wallis H test and Mann–Whitney U test were used for nonparametric data. The chi-square or Fisher's test were used for the analysis of qualitative variables. Statistical significance was set at $P < 0.05$.

Declarations

Acknowledgment

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Author contributions

ZK and HZX were responsible for the study design, the revision for intellectual content, and literature research. ZMW, CY, and YL analyzed and interpreted the data. TM and QW performed the statistical analyses. ZMW, QH, and ZCM drafted the manuscript. ZL, HZX, and RC revised the manuscript. All authors have read and approved the final manuscript.

Competing Interest

The authors declare no competing interests.

Additional information

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Figures

Figure 1

Flow diagram of patient selection

Figure 2

Trends of mean Hb changes in the four groups of patients with delayed surgery.

Group C and Group D vs Group A: *p<0.05; ***P < 0.001.;

Group C and Group D vs. Group B: ## p<0.01; ###P < 0.001.

Figure 3

Bar graph shows the four groups in preoperative HBL and preoperative ABT rates

Group C and Group D vs Group A: ***P < 0.001;

Group C and Group D vs Group B: ###P < 0.001