



# Hip Fracture Surgery without Transfusion in Patients with Hemoglobin Less Than 10 g/dL

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**Background:** Hip fracture surgery is associated with blood loss, which may lead to adverse patient outcomes. The hemoglobin level declines gradually in most hip fracture cases involving femoral neck fractures and intertrochanteric fractures. It decreases further after hip fracture surgery due to perioperative bleeding. We developed a protocol, which avoids transfusion in hip fracture surgery, and reviewed the hemodynamic outcomes of patients with hemoglobin less than 10 g/dL without transfusion.

**Methods:** From 2014 to 2019, we retrospectively recruited 34 patients with hip fractures and a hemoglobin level less than 10 g/dL, who refused to undergo transfusion. There were 19 patients with femoral neck fractures and 15 patients with intertrochanteric fractures. Our patient blood management (PBM) protocol involving 4,000 U erythropoietin (3 times a week) and 100 mg iron supplement (every day) was applied to all included patients. Intraoperatively, a cell saver and tranexamic acid were used. Postoperatively, the protocol was maintained until the patients' hemoglobin level reached 10 g/dL. We evaluated the feasibility of our protocol, perioperative complications, and hemodynamic changes.

**Results:** Nineteen patients with femoral neck fractures underwent bipolar hemiarthroplasty and 15 patients with intertrochanteric fractures underwent internal fixation with a cephalomedullary nail. The mean hemoglobin level was 8.9 g/dL (range, 7.3–9.9 g/dL) preoperatively, 7.9 g/dL (range, 6.5–9.3 g/dL) immediately postoperatively, 7.7 g/dL (range, 4.3–9.5 g/dL) on postoperative day 1, 7.4 g/dL (range, 4.2–9.4 g/dL) on postoperative day 3, 8.1 g/dL (range, 4.4–9.7 g/dL) on postoperative day 5, 8.5 g/dL (range, 4.5–9.9 g/dL) on postoperative day 7, and 9.9 g/dL (range, 5.7–11.1 g/dL) on postoperative day 14. The average intraoperative bleeding was  $206.2 \pm 78.7$  mL. There was no case associated with complications of anemia.

**Conclusions:** Hip fracture surgery in patients with hemoglobin less than 10 g/dL was feasible without the need for transfusion using our PBM protocol in 34 patients. Using this protocol, the operation was conducted safely despite the anemic condition of patients with fractures whose hemoglobin was less than 10 g/dL.

**Keywords:** Patient blood management, Transfusion, Hip fracture, Femoral neck fracture, Intertrochanteric fracture

A hip fracture may be associated with blood loss, warranting transfusion. Older patients with hip fractures represent an important, large group of inpatients in acute care hos-

pitals, along with elderly patients with osteoporotic fractures.<sup>1-3)</sup>

Hip fracture surgery is associated with blood loss, which may lead to adverse patient outcomes, for example, hemodynamic stress, increased cardiac demand, and potential tissue hypoxia in the elderly population, so anemia might contribute to the high morbidity and mortality rates after hip fracture surgery.<sup>4)</sup> In most cases of hip fracture including femoral neck and intertrochanteric fractures, hemoglobin decreases gradually following the fracture.

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After fracture surgery, hemoglobin decreases further due to perioperative bleeding. In general, perioperative bleeding ranges from 500 to 1,500 mL in hip fracture surgery.<sup>2,5)</sup> Despite perioperative advances in hip fracture surgery, anemia is highly prevalent (39%–69%) in patients undergoing surgery for acute hip fractures.<sup>4)</sup> Therefore, allogeneic blood transfusion is generally required in elderly patients undergoing hip fracture surgery.<sup>1,6)</sup>

The level of preoperative hemoglobin is a major predictor of the need for transfusion following orthopedic surgery.<sup>2,6)</sup> A few studies reported that elective surgery could be done safely in patients with a preoperative hemoglobin level above 10 g/dL if the estimated blood loss was greater than 500 mL.<sup>2,7,8)</sup> Thus, we determined the target hemoglobin level before surgery as 10 g/dL. We developed a protocol to avoid the need for transfusion in hip fracture surgery and reviewed the hemodynamic outcomes of hip fracture surgery without transfusion in patients with hemoglobin less than 10 g/dL.<sup>2,6)</sup>

The purpose of this study was to determine the feasibility and safety of our protocol and to analyze hematologic changes and complications during the perioperative period of hip fracture surgery without transfusion.

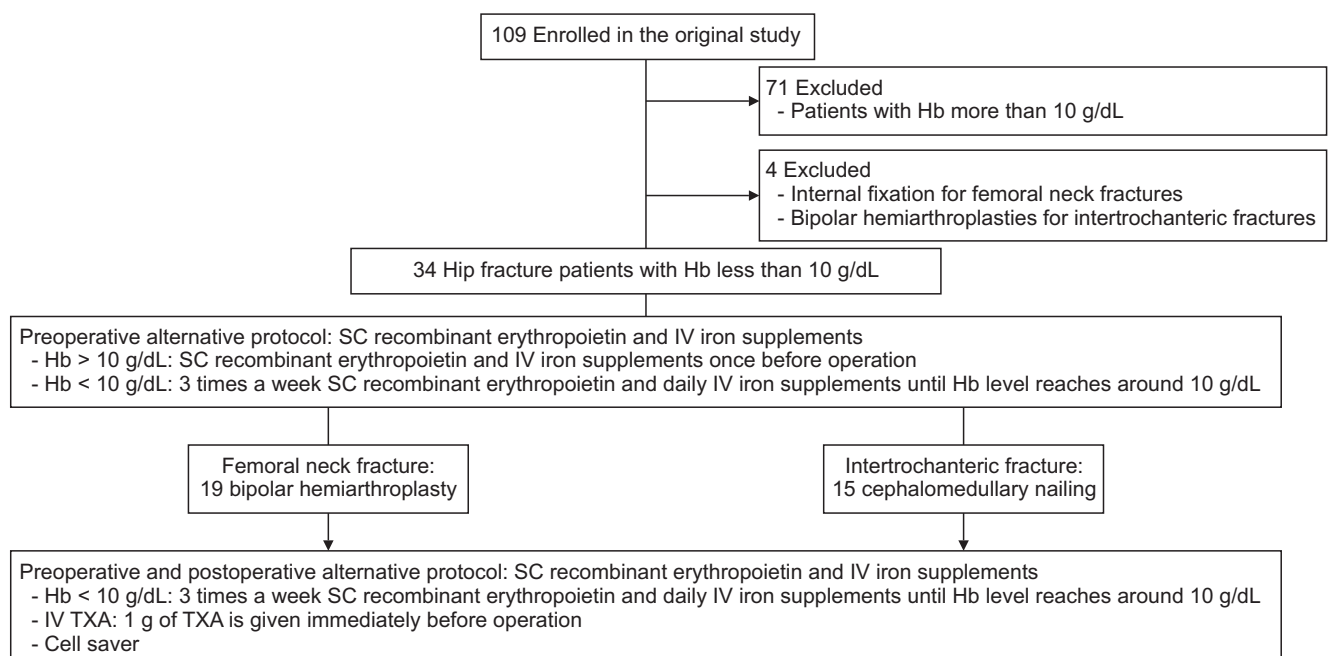
## METHODS

### Developing a Patient Blood Management Protocol for Fracture Surgery without Transfusion

We conducted this study in compliance with the principles

of the Declaration of Helsinki. The study design and protocol were approved by the Institutional Review Board of Soonchunhyang University Hospital Seoul (IRB No. 2019-04-010-001) and all patients provided written informed consent after the risk of fracture surgery without transfusion was explained.

According to our patient blood management (PBM) protocol for hip fracture surgery without transfusion, when the preoperative hemoglobin level was higher than 10 g/dL, we administered recombinant erythropoietin and iron supplements just once before the operation. However, when the preoperative hemoglobin level was lower than 10 g/dL, we administered the recombinant erythropoietin every other day (3 times a week) and iron supplements every day until the hemoglobin level reached 10 g/dL. Immediately before the operation, 1 g of intravenous tranexamic acid was given, except for high-risk patients with venous thromboembolism. During the operation, reinfusion of drainage blood using a cell saver and plasma expanders was performed. The cell saver device (Haemonetics Corporation, Braintree, MA, USA) filtered and washed the collected blood to remove hemolyzed cells, free hemoglobin, and other impurities, which was followed by administration of 1 g of tranexamic acid immediately before the operation, except in high-risk patients for venous thromboembolism. Postoperatively, recombinant erythropoietin and iron supplements were administered similarly using the preoperative protocol, which was continued until the hemoglobin level reached 10 g/dL (Fig. 1).<sup>2,6)</sup>



**Fig. 1.** Flowchart showing inclusion and exclusion criteria of the study. Hb: hemoglobin, SC: subcutaneous, IV: intravenous, TXA: tranexamic acid.

### Demographic Characteristics

From January 2014 until December 2019, we performed 109 hip fracture operations in patients who refused transfusion during the perioperative period due to religious beliefs or personal preferences. All of them provided written informed consent regarding the risk and protocol for transfusion-free arthroplasty without allogeneic transfusion. They agreed with the risk of surgery without transfusion, including death due to massive bleeding.

In 71 of the 109 patients, the preoperative hemoglobin level was higher than 10 g/dL, and thus the operation as performed without transfusion immediately after admission according to the above protocol. However, in 34 patients with a hemoglobin level 10 g/dL or below, the changing pattern of hemoglobin level was evaluated by monitoring the daily levels of hemoglobin. The demographic characteristics of these 34 patients are summarized in Table 1. We evaluated only 2 fracture types: femoral neck fractures and intertrochanteric fractures. Nineteen patients had fractures of the femoral neck: 3 men and 16 women with a mean age of 83.1 years (standard deviation [SD], 6.5 years; range, 65–94 years). Fifteen patients had intertrochanteric fractures: 5 men and 10 women with a mean age of 78.3 years (SD, 12.9 years; range, 65–91 years). Patients who underwent internal fixation for femoral neck fracture (1 patient) and bipolar hemiarthroplasty for in-

tertrochanteric fractures (3 patients) were not included in this study due to scarcity of data. (Fig. 1).

### Performing Arthroplasty without Transfusion When Hemoglobin Is Less Than 10 g/dL

In older patients, a delay in fracture operation can lead to poor outcomes with worsening of the general condition, such as pneumonia, sores, infection, and various unexpected illnesses, and mortality caused by loss of mobility.<sup>9-14)</sup> We performed the operation immediately after the rebound of preoperative hemoglobin level according to the above protocol.

When hemoglobin levels continued to decrease due to fractures, the operations were delayed until the hemoglobin level reached the nadir. When the hemoglobin level started increasing gradually by maintaining the above protocol, hip fracture operations were performed even when the hemoglobin level was 10 g/dL or less to prevent the complications associated with delayed operation. The average number of days from the date of fracture to the date of operation was 4.8 days (SD, 1.54; range, 1–7 days).

All operations were performed by a single senior surgeon (YSS) with the patient under spinal anesthesia and/or epidural anesthesia. On the fracture table, bipolar hemiarthroplasty was performed via the conventional posterior approach in patients with femoral neck fractures

**Table 1.** Demographic Characteristics

Variable	Femoral neck fracture	Intertrochanteric fracture	Overall
Number of patients	19	15	34
Male	3	5	8
Female	16	10	26
Age (yr)	83.1 ± 10.3 (65–94)	78.3 ± 12.9 (65–91)	81.5 ± 10.9 (65–94)
Operation	Bipolar hemiarthroplasty	Cephalomedullary nailing	
Comorbidity			
Hypertension	14	12	
Diabetes	11	4	
Stroke	5	4	
Cardiovascular disease	6	3	
Pulmonary disease	3	2	
Chronic kidney disease	5	4	
Antithrombotic drugs	4	4	
None	2	1	

Values are presented as number or mean ± standard deviation (range).

and osteosynthesis by intramedullary nailing in patients with intertrochanteric fractures. The prosthesis for bipolar hemiarthroplasty was the Bencox stem and the Coren bipolar cup (Corentec, Seoul, Korea). Osteosynthesis was performed using cephalomedullary nailing (Compression hip nail, TDM, Seongnam, Korea). Suction drainage was routinely inserted after the operation and removed on the postoperative day 1 to 2. After removal of the suction drainage, patients started ambulation. Gradual weight-bearing was initiated with a crutch or walker.

### Hemodynamic Evaluation

We measured the levels of intraoperative bleeding, blood infused by the cell saver, and postoperative drainage. The hemoglobin and hematocrit levels were measured immediately before and after the operation and on postoperative days 1, 3, 5, 7, and 14. We monitored the changing pattern of hemoglobin after fracture operation and evaluated the feasibility of our protocol, perioperative complications, hematological changes, mortality, and infection associated with the protocol.

### Statistical Analysis

Baseline characteristics and perioperative clinical data were analyzed for all patients and by gender and operation type with descriptive statistics. Bivariate tests of association were based on either Pearson's chi-square or Fisher's exact tests for categorical variables. Next, the least significant difference method of post hoc multiple comparisons with Tamhane T2 was used to compare each group of operations to determine significant differences before and immediately after the operation, and on postoperative days 1, 3, 5, 7, and 14. All hemoglobin and hematocrit levels measured in this study were analyzed as continuous variables. All tests were two-sided, and statistical significance was accepted for a  $p$ -value of  $< 0.05$ , and statistical analysis was performed using IBM SPSS ver. 21.0 (IBM Corp., Armonk, NY, USA).

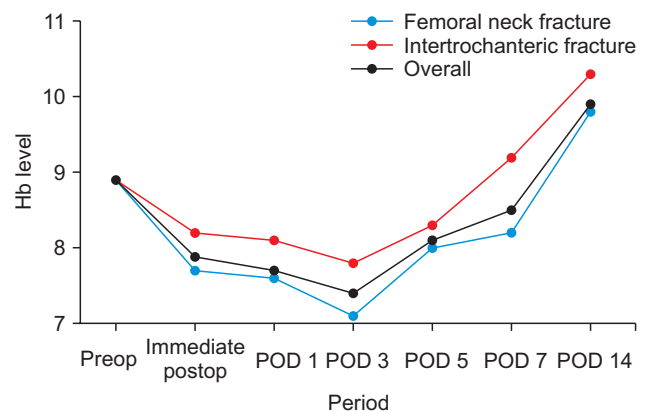
## RESULTS

Thirty-four patients manifested 19 femoral neck fractures and 15 intertrochanteric fractures, with a hemoglobin level less than 10 g/dL. Bipolar hemiarthroplasty was performed in 19 patients with femoral neck fractures; 15 patients with intertrochanteric fractures underwent internal fixation with cephalomedullary nails. In these 34 patients, the preoperative protocol was applied: if the hemoglobin level was  $< 10$  g/dL, subcutaneous recombinant erythropoietin administration (3 times a week) and intravenous iron sup-

plementation (every day) were performed until the hemoglobin level of 10 g/dL was reached. The mean hemoglobin level of overall patients was 8.9 g/dL (range, 7.3–9.9 g/dL) preoperatively, 7.9 g/dL (range, 6.5–9.3 g/dL) immediately postoperatively, 7.7 g/dL (range, 4.3–9.5 g/dL) on postoperative day 1, 7.4 g/dL (range, 4.2–9.4 g/dL) on postoperative day 3, 8.1 g/dL (range, 4.4–9.7 g/dL) on postoperative day 5, 8.5 g/dL (range, 4.5–9.9 g/dL) on postoperative day 7, and 9.9 g/dL (range, 5.7–11.1 g/dL) on postoperative day 14. The lowest mean hemoglobin level was observed on postoperative day 3. After postoperative day 3, the hemoglobin level recovered gradually, and by postoperative day 14, the hemoglobin level increased to around 10 g/dL (Fig. 2, Table 2).

The average intraoperative bleeding was  $225 \pm 81$  mL in patients with femoral neck fractures who underwent bipolar hemiarthroplasty and  $75 \pm 56$  mL in those with intertrochanteric fractures treated with cephalomedullary nails. The mean volume of reinfused blood by the cell saver was  $152 \pm 62$  mL in the femoral neck fracture group and  $124 \pm 68$  mL in the intertrochanteric fracture group. The average amount of postoperative drainage was  $338 \pm 142$  mL in the femoral neck fracture group and  $103 \pm 59$  mL in the intertrochanteric fracture group (Table 3).

The average duration from admission to surgery was  $5.0 \pm 1.5$  days in patients treated with bipolar hemiarthroplasty for femoral neck fractures and  $4.6 \pm 2.1$  days in patients treated with cephalomedullary nails for intertrochanteric fractures. During hospitalization, 1 patient had deep vein thrombosis and recovered after treatment with anticoagulatory medication. Five patients had postoperative delirium (3 after bipolar hemiarthroplasty and



**Fig. 2.** Hemoglobin (Hb) changes after bipolar hemiarthroplasty for femoral neck fractures and cephalomedullary nailing for intertrochanteric fractures in patients with our blood management protocol. Preop: preoperative, Postop: postoperative, POD: postoperative day.

**Table 2.** Hemodynamic Changes from before Surgery to 14 Days after Surgery in the FNF Group and ITF Group

Variable	FNF (19 cases)	ITF (15 cases)	Overall (34 cases)	Significance
Preoperative hemoglobin (g/dL)	8.9 ± 0.7 (7.3–9.9)	8.9 ± 1.4 (8.0–9.9)	8.9 ± 0.9 (7.3–9.9)	0.000
Immediate postoperative hemoglobin (g/dL)	7.7 ± 1.5 (6.5–9.3)	8.2 ± 1.1 (7.6–9.2)	7.9 ± 1.2 (6.5–9.3)	0.000
POD 1 hemoglobin (g/dL)	7.6 ± 1.3 (4.3–9.2)	8.1 ± 1.2 (7.1–9.2)	7.7 ± 1.5 (4.3–9.2)	0.000
POD 3 hemoglobin (g/dL)	7.1 ± 1.9 (4.2–9.4)	7.8 ± 1.2 (7.2–9.4)	7.4 ± 1.6 (4.2–9.4)	0.000
POD 5 hemoglobin (g/dL)	8.0 ± 1.7 (4.4–9.5)	8.3 ± 1.6 (7.5–9.7)	8.1 ± 1.5 (4.4–9.7)	0.000
POD 7 hemoglobin (g/dL)	8.2 ± 1.5 (4.5–9.9)	9.2 ± 1.7 (8.1–9.9)	8.5 ± 1.6 (4.5–9.9)	0.000
POD 14 hemoglobin (g/dL)	9.8 ± 1.8 (5.7–11.1)	10.3 ± 1.3 (9.3–10.9)	9.9 ± 1.6 (5.7–11.1)	0.000

Values are presented as mean ± standard deviation (range).

FNF: femoral neck fracture with bipolar hemiarthroplasty, ITF: intertrochanteric fracture with cephalomedullary nailing, POD: postoperative day.

**Table 3.** Comparison of Perioperative Hemodynamic Data and Operative Delay between the FNF Group and ITF Group

Variable	FNF	ITF	Significance
Intraoperative blood loss (mL)	225 ± 81	75 ± 56	0.000
Cell saver (mL)	152 ± 63	64 ± 68	0.000
Postoperative drainage (mL)	338 ± 72	103 ± 59	0.000
Operation delay (from admission to operation)	5.0 ± 3.1	4.6 ± 2.2	0.000

Values are presented as mean ± standard deviation.

FNF: femoral neck fracture, ITF: intertrochanteric fracture.

2 after cephalomedullary nailing). No medical emergency occurred, and the direct cause of death was not related to postoperative anemic symptoms or complications associated with the PBM protocol during 3 months postoperatively.

## DISCUSSION

Hip fracture surgery is associated with blood loss, which may lead to adverse patient outcomes.<sup>15-17)</sup> Older patients with hip fractures represent an important, large group of in-patients in acute hospitals.<sup>3)</sup> In most cases of hip fracture including femoral neck and intertrochanteric fractures, the hemoglobin level decreases gradually following the fracture. Postoperatively, the hemoglobin level declines further due to perioperative bleeding. Jehovah's Witnesses do not accept transfusion for religious reasons even in life-threatening situations.<sup>2,18)</sup> Performing hip fracture surgery in patients who do not accept transfusion has been a matter of concern. It is very difficult and challenging to oper-

ate on a patient with hip fracture and anemia when the hemoglobin level is 10 mg/dL or less.

Fracture operations differ from elective arthroplasties including total hip arthroplasty and total knee arthroplasty. Patients with anemia do not need to undergo these elective arthroplasties. However, in the case of acute hip fractures, if fracture operations are postponed until after correction of anemia and other unexpected complications, the risk of mortality increases.<sup>9-14,17)</sup> A delayed operation may lead to worsening of systemic conditions and unexpected progression. Whether to correct anemia or perform a rapid fracture operation is a difficult decision.

More than 98% of the patients with hip fractures undergo an operation, and urgent surgical treatment is very important in elderly patients.<sup>19)</sup> Preoperative allogeneic blood transfusions have often been performed to maintain hemoglobin levels before and after fracture operations.<sup>1,20)</sup> However, orthopedic surgeons and their patients have been plagued by transfusion in the perioperative period.<sup>2,15,21-23)</sup> Hence, surgery without transfusion is of interest, especially for the elderly who often carry multiple comorbidities.<sup>24,25)</sup>

Complications associated with allogeneic blood transfusion in patients undergoing surgery for hip fractures are an increasing cause for concern and allogeneic blood transfusions are associated with increased long-term mortality after hip fracture surgery.<sup>4,9,26)</sup> In addition, an increased risk of postoperative illness including pneumonia, delirium, short-term mortality, length of hospital stay, and systemic inflammatory response syndrome in patients receiving blood transfusion was reported.<sup>4)</sup> Furthermore, perioperative allogeneic transfusions were associated with a higher rate of reoperation for suspected acute infection.<sup>27)</sup> Therefore, prompt surgical intervention

without transfusion and perioperative PBM are imperative for fracture patients with anemia with a hemoglobin level of 10 mg/dL or less.

In this study, we obtained successful results with our programmed PBM protocol using the combination of recombinant erythropoietin, iron supplements, tranexamic acid, and a cell saver without allogeneic transfusion. Our protocol was not associated with any notable complications related to anemic symptoms. Our study showed that it can be safe to perform hip fracture surgery without allogeneic transfusion in anemic patients whose hemoglobin level is less than 10 g/dL with use of our protocol. We used a variety of methods including bleeding reduction, erythropoietin therapy, iron supplements, and a cell saver in this study. Treatment with tranexamic acid has been used to reduce blood loss and transfusion rates in orthopedic surgery.<sup>28-30)</sup> However, our protocol focused not only on blood conservation management but also on reproduction by inducing erythropoiesis.<sup>2,6)</sup>

Despite the PBM protocol, in the fracture patients, the hemoglobin level declined until the postoperative day 3, which was followed by a gradual increase. The hemoglobin nadir was observed on postoperative day 3. A similar hemodynamic pattern was reported in previous studies of patients with hemoglobin less than 10 g/dL.<sup>2)</sup> Understanding of these altered hemoglobin patterns is very important in maintaining the protocol.

There are several limitations to our study. First, it was not a randomized trial and it was a retrospective study including 2 different operations: bipolar hemiarthroplasty for femoral neck fractures and cephalomedullary nailing for intertrochanteric fractures in a small number of patients. In addition, patients who underwent internal fixation

for femoral neck fractures and bipolar hemiarthroplasty for intertrochanteric fractures were not included in this study because of scarcity of the data. We have a plan for further research including these cases, as the volume increases. However, patients with anemic fractures who refused transfusion because of religious beliefs or personal preference were rare. Second, all arthroplasties were done by a single high-volume surgeon. Low-volume surgeons may not be able to reproduce our results. Third, the protocol was used mostly in Jehovah's Witness patients who did not accept transfusion due to their religious beliefs. However, transfusion is a serious issue for patients regardless of their religion, and our protocol would be applicable to patients who are not Jehovah's Witnesses. Finally, we could not evaluate postoperative clinical outcomes such as ambulatory status and functional scores.

Despite these limitations, hip fracture operations in patients with a hemoglobin level less than 10 g/dL could be done without transfusion using the programmed PBM protocol. In patients who refused to undergo allogeneic transfusion, the hemodynamic pattern was similar to that reported previously. Our protocol can be a safe alternative to hip fracture operation without transfusion. Using this protocol, it can be possible to reduce overall blood transfusion levels and rates during the perioperative period in hip fracture surgery, even in cases of fractures in patients with anemia, who are considering allogeneic transfusion.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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