Feasibility of Hip Fracture Surgery Using a No Transfusion Protocol in Elderly Patients: A Propensity Score-Matched Cohort Study

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Objectives: To determine whether hip fracture surgery (HFS) without transfusion affects postoperative mortality and complications in elderly patients.

Design: Retrospective comparative study.

Patients: Three hundred fourteen patients ≥65 years of age who underwent HFS between May 2003 and December 2014. Patients were divided into 2 groups: those who consented to blood transfusion if needed and those who did not. One-to-one propensity score matching generated 50 matched pairs of patients.

Intervention: Patients underwent HFS with or without blood transfusion. In the no transfusion group, simultaneous administration of erythropoietin and iron was used as an alternative.

Main Outcome Measurements: The primary outcome was postoperative mortality (90-day, 1-year, overall). The secondary outcomes were hemoglobin change and the incidence of postoperative complications.

Results: HFS using a no transfusion protocol was not associated with increased mortality at any time point. Mean hemoglobin levels were significantly different between the 2 groups on postoperative day 1 (11.0 ± 1.3 vs. 10.5 ± 1.6, $P = 0.002$) but levels completely recovered within 2 weeks in both groups. There was also no difference in postoperative complication rates between the 2 groups, and overall hospital stays and charges were similar.

Conclusions: An HFS protocol without blood transfusion was not associated with increased mortality or complications in elderly patients.

Key Words: hip fracture, allogeneic blood transfusion, mortality, complication, propensity score matching

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

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INTRODUCTION

The prevalence of hip fracture surgery (HFS) is increasing worldwide, in line with the increase in osteoporotic fractures among elderly patients.[1] Despite preoperative and postoperative improvements in HFS, allogeneic blood transfusion (ABT) is commonly required (38%–65%) in elderly patients undergoing the procedure.[2–4] ABT is performed for several reasons in hip fracture patients, including low hemoglobin (Hb) on admission, blood loss caused by the fracture itself, or blood loss during and after surgery.[5]

However, some patient groups refuse to receive blood transfusions because of religious or other reasons, even in life-threatening situations.[6] Although several strategies can compensate for blood loss and prevent the need for transfusions in these patients, surgery without ABT is concerning because of high mortality and morbidity rates among patients with hip fractures.[7,8]

The purpose of this study was to evaluate patients who underwent HFS with or without ABT to investigate the following: (1) mortality rates (90-day, 1-year, and overall), (2) the difference in Hb changes between the 2 groups, and (3) postoperative complication rates, hospital stay durations, and costs of medical care. Propensity score matching was performed to adjust for different characteristics between the 2 groups.

PATIENTS AND METHODS

Subject Selection

This retrospective study was approved by the institutional review board at our hospital (IRB: IIT-2016-230). A total of 395 consecutive patients with proximal femur fractures were admitted and treated from May 2003 to December 2014 in our hospital. The exclusion criteria were age <65 years (n = 32), pathologic fracture (n = 8), periprosthetic fracture (n = 7), and revision surgery (n = 7). Among the remaining 341 patients, those with incomplete records (n = 16) or patients who were lost to follow-up with a minimum of 1 year follow-up after index operation (n = 11) were also excluded. Therefore, the records of 314 patients were

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included in the analysis. There were 55 patients (17.5%) who had refused blood transfusion (RBT) in the patient cohort, and these patients were matched by applying one-to-one propensity score matching.[9]

One-To-One Propensity Score Analysis

The comparative group was selected from the remaining pool of patients in whom hip fracture had been managed. Confounding factors included age, sex, body mass index, Charlson comorbidity index, primary diagnosis, surgery type, Hb on admission, and time from admission to surgery. Based on these variables, propensity scores were estimated on the scale of the log odds using a logistic regression model. We selected the patient group with a cutoff value of delta (the difference of propensity) > 0.01. Finally, 50 patients in each group were selected after propensity score matching (see **Figure**, **Supplemental Digital Content 1**, http://links.lww.com/BOT/A979).[10] Patient demographics between the 2 groups are described in Table 1.

Protocol for Hip Fracture Patients Who Accepted or Refused Allogeneic Blood Transfusion

The treatments for proximal femoral fracture were selected based on fracture configuration and preoperative function state. All surgeries were performed by a single senior surgeon. We defined anemia as a blood Hb concentration <12 g/dL for women and <13 g/dL for men, according to World Health Organization criteria. Our transfusion thresholds were Hb level <10 g/dL preoperatively and <8 g/dL postoperatively; transfusion was also considered necessary postoperatively if patients complained of symptoms, including dizziness or headache, even if the Hb level was above 8 g/dL.

In patients who refused to receive transfusions, as soon as they were admitted to the emergency department, pharmacological treatment was started using the following protocol. If the patient was considered anemic, daily simultaneous injection of 30,000 units of recombinant erythropoietin (EPO) (Darbepoetin; Aranesp, CA) and 100 mg of iron supplements (Venoferrom; Venofer, Glattbrugg, Switzerland) were given for 3 days. Subsequently, if the Hb level was <8 g/dL, 10,000 daily units of EPO and 100 mg iron supplements were administered. When the Hb level was >8 g/dL, we administered 10,000 units of EPO every other day and 100 mg iron every day until the Hb level reached 10 g/dL. In nonanemic patients, we administered 10,000 units EPO and iron supplements, just once before the operation and same manner of anemic patients postoperatively.

We did not use tranexamic acid, autonomous normovolemic hemodilution, or reinfusion of blood through CellSave. No medical thromboprophylaxis was used in all patients.

Outcomes

Our primary outcome was postoperative mortality. We had identified patient's death and the date of death by matching their information with the Korean National Health Insurance Program claims data.[11] Mortality rates were evaluated at 90 days, 1 year, and overall to extrapolate accurate values.

Secondary outcomes were Hb change, postoperative complications, which were subcategorized according to Parvizi et al.[12] We compared Hb levels at 4 time points: on admission, immediate after surgery, 7 days after surgery, and 14 days after surgery. Postoperative in-hospital medical complications included deep vein thrombosis, pulmonary embolism, pneumonia, urinary tract infection, cardiac arrest, and stroke. Postoperative complications after discharge from the

TABLE 1. Demographic Data of Patients Between 2 Groups Before and After Matching With the Propensity Score

	Before Matching				After Matching			
Variable	RBTG (n = 55)	CBTG (n = 259)	*P*	*D*	RBTG (n = 50)	CBTG (n = 50)	*P*	*D*
Age at index operation, y	84.3 ± 9.6	81.9 ± 8.4	0.080	0.278	83.1 ± 9.1	81.5 ± 8.4	0.322	0.182
Sex (men/women)	9/46	72/187	0.169	0.373	11/39	11/39	1.000	0.000
BMI, kg/m^2	21.6 ± 4.3	21.7 ± 3.5	0.913	0.027	21.9 ± 4.2	22.6 ± 3.1	0.505	0.018
CCI	1.43 ± 1.0	1.51 ± 1.2	0.676	0.069	1.44 ± 1.0	1.40 ± 1.2	0.843	0.036
Hb on admission	11.5 ± 1.7	11.7 ± 1.9	0.409	0.107	11.5 ± 1.8	11.6 ± 2.0	0.753	0.052
Time to surgery, d	3.6 ± 3.2	3.9 ± 2.7	0.723	0.108	3.6 ± 3.2	3.9 ± 2.6	0.723	0.101
Primary diagnosis			0.275	0.174			0.616	0.167
Femur neck fracture	16	91			14	11		
Intertrochanteric fracture	39	168			36	39		
Type of surgery			0.314				0.738	
Bipolar hemiarthroplasty	16	89		0.134	14	16		0.105
CR/IF using MCS	0	2		—	0	0		—
OR/IF using IM nail	16	75		0.004	14	15		0.053
OR/IF using DHS	23	93		0.134	22	19		0.127

Data are expressed as mean ± SD.

BMI, body mass index; CBTG, consent to blood transfusion group; CCI, Charlson comorbidity index; CR/IF, closed reduction and internal fixation; D, standardized difference, expressed as log odds ratios by multiplying by 1.814; DHS, dynamic hip screw; Hb, hemoglobin; IM, intramedullary; MCS, multiple cannulated screws; OR/IF, open reduction and internal fixation; RBTG, refuse blood transfusion group.

TABLE 2. Comparison of Mortality Rates Between 2 Groups Using Log-rank Test

Variable	RBT Group (n = 50)	CBT Group (n = 50)	*P*
90 d	4.0 ± 0.4%	4.0 ± 0.4%	1.000
1 y	13.4 ± 0.8%	15.1 ± 0.9%	0.671
Overall, 8 y	72.1 ± 1.8%	85.0 ± 1.5%	0.079

Data are expressed as mortality rate ±95% confidence interval.
CBT, consent to blood transfusion.

hospital included periprosthetic joint infection, periprosthetic fracture, and secondary hip fracture.

Last, we compared operation time, surgical blood loss, postoperative drainage, change in Hb level, length of stay, and hospital charges between the 2 groups.

Statistical Analysis

The Kaplan–Meier method was used to estimate survival rates, with the date of HFS as the starting point.[13] If patients who were lost to follow-up, the data were regarded as censored. Survival curves between the 2 groups were compared by log-rank test. We compared 3 points: 30 day, 120 day, and overall mortality rates. The Kolmogorov–Smirnov test was first used to estimate the normality, and all continuous variables showed normal distribution. The χ^2 test or Fisher exact test was used to analyze categorical data. *t* tests were used to compare continuous data, including demographic and clinical variables, between the 2 groups. Statistical analysis was performed using SPSS, version 20 (SPSS, Chicago, IL). For all other tests, a 2-sided *P* value <0.05 was considered significant.

RESULTS

Among all patients, 56 patients (56%) were considered anemic on admission. In patients who consented to ABT, 34 patients (68%) received a total mean of 2.2 units of packed red blood cells, before surgery (8 patients) and after surgery (31 patients including 5 who received transfusion preoperatively). During the follow-up period (mean, 4.2 years; range, 0.2–10 years), 42 patients (42%) died.

Primary Outcome—Postoperative Mortality

Based on the Kaplan–Meier survival curves, there was no significant difference in 90-day, 1-year, or overall mortality rates between the 2 groups (Table 2, Fig. 1).

Secondary Outcomes—Hb Change, Postoperative Complications, and Operation-related Data

The mean Hb level of all patients was 11.5 ± 1.7 g/dL preoperatively and 10.5 ± 1.6 g/dL on postoperative day 1 and completely recovered within 2 weeks in both groups (Fig. 2). In transfusion refusing group, the lowest Hb level was 8.9 g/dL, and no medical emergencies related to low Hb were observed. There were no significant differences between the 2 groups with regard to postoperative medical or clinical complications (see **Table**, **Supplemental Digital Content 2**, http://links.lww.com/BOT/A980). The average hospitalization time was 25.5 days, and the average cost of medical care was 8573 US dollars. Overall hospital stays and total charges were similar between the 2 groups (Table 3).

DISCUSSION

Surgery is the main treatment for hip fracture, with over 98% of patients undergoing operative fixation, and urgent surgical treatment is crucial in elderly patients.[14] However, the urgent and unplanned nature of surgery limits the time necessary to attain safe Hb levels before surgery in patients who refuse to receive blood transfusions. To our knowledge, there are no sufficient studies that compare HFS performed with or without ABT in elderly patients. Our study shows that HFS can be performed with no negative impact on

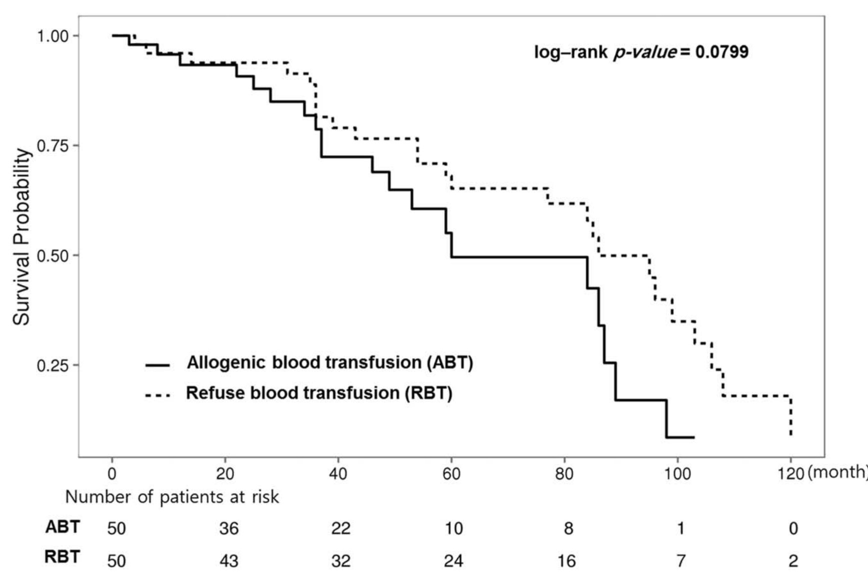

FIGURE 1. Kaplan–Meier survival curves revealed similar overall mortality rates between the 2 groups.

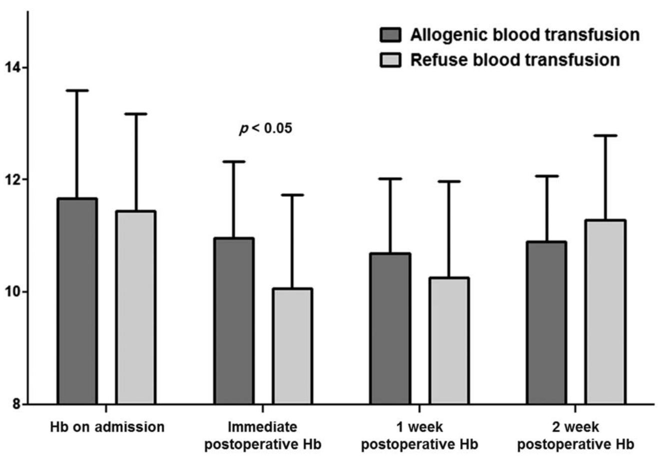

FIGURE 2. Hemodynamic changes based on hemoglobin level between the 2 groups after HFS. The mean hemoglobin level difference between the 2 groups was significant only on postoperative day 1 and had completely recovered 2 weeks postoperatively in the refusing blood transfusion group. Data are presented as mean ± SDs.

postoperative mortality and complications using EPO and iron as an alternative to transfusion.

HFS is a common procedure, and mean transfusion rates range from 38% to 65%, whereas mean blood transfusion volume ranges from 1.4 to 1.7 units.[3,4,15–17] The observed transfusion rate (68%) in our cohort was relatively higher than that in previous reports.[18,19] We have adopted a liberal strategy (transfusions indicated when Hb < 10 g/dL preoperatively) with regard to our transfusion threshold. The slight high rate of preoperative anemia (56%) compared with previous reports[18,19] and transfusion strategy in our study could lead to a relatively high transfusion rate.[2]

In our hospital, a protocol for surgery without transfusion was established to enhance the health of the RBT community. Effective preoperative evaluation and preparation of the patient, as well as surgeon factors, including meticulous coagulation and bone bleeding control, are essential to the success of hip surgery without transfusion.[20] Several previous studies reported the use of EPO and iron as a blood-saving program effectively decreased transfusion rates in HFS without increasing morbidity.[21–24] Some studies reported the usefulness of intra-arterial occlusive balloons as a regional tourniquet when treating complex procedures with risks of excessive bleeding, such as total hip arthroplasty revision or pelvic fracture surgery in patients with RBT.[25,26]

The Hb level completely recovered within 2 weeks after surgery, although the physiological response to decreased Hb level is generally slower and less effective in elderly patients. In our study, the mean Hb decrease after surgery was 1.54 g/dL (0.94–2.51) in the RBT group. Red blood cell expansion with EPO therapy is evidenced by an increase in reticulocyte count by day 3 of treatment, with the equivalent of 1 blood unit produced by day 7 of EPO treatment.[27] The total average period EPO was used in our patients was 14.4 days (mean time from admission to surgery was 3.8 days; mean duration of EPO and iron supplement after surgery was 10.6 days), and this duration is similar to the amount of time EPO administration that is required to treat blood loss. In one study, the use of 10 daily doses of 20,000 IU EPO in intertrochanteric fractures reduced mean transfusion units from 2.5 units to 1.5 units.[28] The Hb level was even higher in the RBT group than the transfusion group at 2 weeks after surgery (Table 3). The enhanced hematopoietic response induced by EPO and iron availability would result in much faster Hb recovery after blood loss.[29]

When performing elective orthopaedic surgery in patients with RBT, the duration and dose of EPO supplementation have not been consistent between studies.[30–34] One study used 600 units EPO per kilogram before 21 days before total hip replacement.[34] In revision total hip replacement, a dose of 100 units EPO per kilogram of body weight 3 times a week for 2 to 4 weeks had been administered.[30] In other reports, EPO was administered only when Hb was not easily recovered with iron and folate supplement in primary and revision total knee arthroplasty.[33] Although there was no established optimal use for EPO, simultaneous intravenous iron administration to maximize the efficacy of EPO nearly equals a daily dosage of 100 mg.[30–33]

TABLE 3. Operation Details and Medical Costs Between 2 Groups

Variable	All	RBT Group (n = 50)	CBT Group (n = 50)	*P*
Operation time, min	78.8 ± 29.5	77.5 ± 33.2	80.16 ± 25.6	0.695
Mean intraoperative blood loss, mL	613.8 ± 339.3	603.5 ± 362.4	624.6 ± 318.2	0.787
Mean postoperative drainage, mL	301.7 ± 178.3	330.2 ± 165.1	380.1 ± 203.0	0.734
Hb on admission	11.5 ± 1.9	11.5 ± 1.7	11.7 ± 1.9	0.753
Immediate postoperative Hb	10.5 ± 1.6	10.0 ± 1.8	11.0 ± 1.3	0.002
1-wk postoperative Hb	10.4 ± 1.5	10.3 ± 1.7	10.7 ± 1.1	0.215
2-wk postoperative Hb	11.0 ± 1.3	11.2 ± 1.5	10.8 ± 1.0	0.170
Red blood cell transfusion (unit)	2.2 ± 2.1	0	2.2 ± 2.1	—
Length of hospital stay, d	25.5 ± 22.8	26.3 ± 22.2	24.5 ± 21.2	0.322
Period of iron and EPO use, d	10.6 ± 7.3	10.6 ± 7.3	0	—
Total cost of hospitalization (US dollars)	8573 ± 3445	8522 ± 3245	8615 ± 3915	0.535

Data are expressed as mean ± SD. Cost was calculated using the following conversion: 1 US dollar = 1150 won.
CBT, consent to blood transfusion; Hb, hemoglobin.

With the increasing recognition of transfusion-related adverse effects, surgery without transfusion has become of interest among the elderly, who often have multiple comorbidities.[35,36] Most strategies used in our hospital are easy to apply, and surgery without transfusion is feasible in the geriatric population as long as it is performed in specialized centers where a multidisciplinary team is prepared to specifically manage this scenario.[37] Therefore, we believe this strategy of surgery without transfusion could feasibly be implemented for other surgery types and may lead to a high level of satisfaction and potentially improved care for elderly patients.[38]

This study has some limitations. First, as a retrospective study, this study was limited by the accuracy of the medical records and potential information bias. Second, although previous studies have not examined patients who had RBT specifically, the patient number is still small, which can lead to statistical bias. Third, dementia or preoperative mobility can be important covariant factors, but these could not be included in propensity score matching because of the lack of medical records.

In summary, EPO and iron supplements in elderly HFS used as transfusion alternatives have demonstrated complete recovery of Hb levels within 2 weeks without increasing the risk of postoperative mortality and complications. Thus, in elderly hip fracture patients who refuse to receive ABT, EPO and iron supplements can be an alternative to transfusions because transfusions do not affect patient's outcome and can accelerate the recovery of blood loss.

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