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Development of a Nomogram for Predicting Blood Transfusion Risk After Hemiarthroplasty for Femoral Neck Fractures in Elderly Patients

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: The aim of this study was to determine the risk factors and develop a nomogram for blood transfusions after hemiarthroplasty (HA) in patients with femoral neck fractures (FNFs).

Material/Methods: We performed a retrospective study including consecutive elderly FNF patients treated by HA between January 2015 and December 2017. Perioperative information was obtained retrospectively, uni- and multivariate regression analyses were conducted to determine risk factors for blood transfusion, and a nomogram model was constructed to predict the risk of blood transfusion. The predictive performance and consistency of the model were evaluated by the consistency coefficient (C-index) and the calibration curve, respectively.

Results: Of 178 patients, 151 were finally enrolled in the study and 21 received blood transfusion. Binary logistic regression analysis showed the low preoperative hemoglobin (Hb), longer time to surgery, general anesthesia, longer surgery duration, and higher intraoperative blood loss (IBL) were risk factors for blood transfusion. The accuracy of the contour map for predicting transfusion risk was 0.940.

Conclusions: We found a correlation between blood transfusion requirement and low preoperative Hb, longer time to surgery, general anesthesia, longer surgery duration, and higher IBL, and we then developed a nomogram. Our nomogram model can be used to evaluate the transfusion risk for FNF patients after HA, and provides better guidance for clinicians to intervene perioperatively, so as to reduce the incidence of blood transfusion.

MeSH Keywords: Blood Transfusion • Femoral Neck Fractures • Hemiarthroplasty • Nomograms • Risk Factors

Abbreviations: **HA** – hemiarthroplasty; **FNF** – femoral neck fractures; **BMI** – body mass index; **Hb** – hemoglobin; **IBL** – intraoperative blood loss; **DBL** – the amount of drainage blood loss; **TV** – transfusion volume; **GA** – general anesthesia; **CSEA** – combined spinal-epidural anesthesia; **ASA** – American Society of Anesthesiologists; **PLOS** – postoperative length of stay; **DVT** – deep vein thrombosis

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Background

Hemiarthroplasty (HA) is currently accepted as an appropriate treatment method for femoral neck fractures (FNFs) in elderly patients with low functional requirements and an intact acetabulum [1]. Compared to total hip arthroplasty, HA has a lower dislocation rate, shorter operating time, and lower initial cost [2]. However, it still has many short- and long-term disadvantages, such as the need for blood transfusion, risk of infection, groin pain caused by acetabular wear, and a potential need for revision surgery [3–5]. Of these, blood transfusion is most common and troublesome, particularly for the elderly; the blood transfusion requirements for hip fractures ranges from 19% to 69% postoperatively [6–8]. Blood transfusions are costly and can cause complications, such as transfusion reactions, surgical site infections, and thrombotic and cardiac events, and can increase hospital stay [9–11]. Due to the poor tolerance of the elderly to blood transfusions, they are more likely to have transfusion-related complications. Consequently, it is necessary to improve blood management perioperatively. While risk factors for blood transfusion after hemiarthroplasty have been reported, no study has presented these risk factors visually in a nomogram. Therefore, identifying predictors of transfusion after hemiarthroplasty and establishing an effective prediction model can help clinicians identify high-risk patients and to perform early postoperative interventions to decrease the transfusion rate. A nomogram can integrate more clinical parameters to achieve individualized prediction. It is a computational chart that replaces complex mathematical formulas for accurate, individualized prediction.

Therefore, our study aimed to determine the risk factors and develop a nomogram for blood transfusions after HA in elderly FNFs patients.

Material and Methods

Patients

This study was approved by the Ethics Committee of our hospital. The inclusion criteria were FNF caused by a low-energy injury (e.g., falls from standing height and osteoporosis), and no history of bone tumor, blood or hemorrhagic disease, nonsteroidal anti-inflammatory or antiplatelet drugs within 1 week preoperatively, or chronic liver disease. From January 2015 to December 2017, 178 consecutive FNF patients underwent HA in our hospital. Of these, 27 were excluded: 10 used oral nonsteroidal anti-inflammatory drugs or antiplatelet drugs within 1 week preoperatively, 6 were lost to follow-up, 5 died, and 2 each had a history of hematological diseases, a history of chronic liver disease, and bone tumor. Ultimately, 151 patients met our inclusion criteria and were enrolled. All patients underwent a standard HA in our hospital. Although the indications for blood transfusion for hip fracture patients have not been clearly evaluated [12], due to the restrictive transfusion policy of our institution, we transfuse only patients with a hemoglobin lower than 80 g/L or 100 g/L with unstable vital signs or obvious symptoms (heart rate >100 bpm, systolic blood pressure <90 mmHg, chest pain, major

Bleeding, or extreme weakness). Low-molecular-weight heparin was used for anticoagulant therapy perioperatively, and all patients took rivaroxaban 10 mg orally at least 35 days postoperatively.

Potential risk factors

The risk factors evaluated were sex, age, body mass index (BMI), comorbid diseases (e.g., hypertension and diabetes), preoperative hemoglobin (Hb) levels, time to surgery, type of anesthesia (General anesthesia [GA] or combined spinal-epidural anesthesia [CSEA]), American Society of Anesthesiologists (ASA) scores, surgical approach (lateral or posterior), intraoperative blood loss, and surgery duration. Perioperative information was obtained through our electronic medical record system, and type of anesthesia and ASA scores were obtained from anesthesia records.

Statistical analysis

The statistical analyses were performed using SPSS for Windows (ver. 19.0; SPSS, Chicago, IL, USA). Means were compared using the independent samples *t* test for normally distributed variables; otherwise, group comparisons were compared using the Mann-Whitney *U* test, and qualitative variables were compared using the chi-square test. Univariate analyses were used to evaluate the relationship between different factors and the blood transfusion. Then, confounding effects were controlled for by binary logistic regression analyses. Predictor exclusion was continued until all predictors had *p*-values less than 0.10 [13], which then was defined as the final prediction model. The final independent risk factors were incorporated into R3.6.1 software (R Foundation for Statistical Computing, Vienna, Austria) to establish a nomogram prediction model. The prediction performance of the model was evaluated by the consistency index (C-index), and the calibration curve was used to judge the predictive consistency. The range of C-index value was 0.5–1.0. When C-index value equals 0.5, the model has no prediction ability; 0.5–0.7 indicates low accuracy, 0.70–0.9 indicates high accuracy, and >0.9 is extremely accurate. The calibration curve was the image comparison of predicting risk and a patients' real risk. The closer the predicted risk to the standard curve, the better the conformity of the model is. In all analyses, $p<0.05$ was taken to indicate statistical significance.

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Table 1. Patient demographics and preoperative characteristics.

Characteristics	Normal patients	Transfusion patients	*p* Value
Number of patients	130	21	
Sex			0.820
Male	34 (26.15%)	5 (23.81%)	
Female	94 (73.85%)	16 (76.19%)	
Age (year)	80.82±5.23	78.95±5.26	0.130
BMI (Kg/m²)	22.52±2.49	21.80±2.72	0.186
Hypertension			0.181
No	54 (41.54%)	12 (57.14%)	
Yes	76 (58.46%)	9 (42.86%)	
Diabetes			0.097
No	96 (73.85%)	19 (90.48%)	
Yes	34 (26.15%)	2 (9.52%)	
Hb (g/L)	121.20±13.87	110.43±7.47	***<0.001***
Time to surgery (d)	4.15±1.65	6.43±1.91	***<0.001***
ASA score			0.867
2	82 (63.08%)	12 (57.14%)	
3	42 (32.31%)	8 (38.10%)	
4	6 (4.62%)	1 (4.76%)	
Type of anesthesia			***0.001***
CSEA	85 (65.39%)	6 (28.57%)	
GA	45 (34.61%)	15 (71.43%)	
Surgical approach			0.587
Posterior	98 (75.39%)	17 (80.95%)	
Lateral	32 (34.61%)	4 (19.05%)	
Surgery duration (min)	62.62±18.87	79.76±17.14	***<0.001***
IBL (ml)	175.08±75.64	271.43±112.44	***<0.001***
DBL (ml)	160.54±111.46	331.90±198.69	***<0.001***
TV (ml)	–	457.14±150.24	–
PLOS (d)	8.12±3.11	10.91±2.83	***<0.001***
DVT	1	2	***0.008***
Superficial infection	2	3	***0.002***
Urinary tract infection	7	2	0.457
Pneumonia	2	2	***0.034***

BMI – body mass index; Hb – hemoglobin; ASA score – American Society of Anesthesiologists score; CSEA – combined spinal and epidural anesthesia; GA – general anesthesia; IBL – intraoperative blood loss; DBL – the amount of drainage blood loss; TV – transfusion volume; PLOS – postoperative length of stay; DVT – deep venous thrombosis.

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Table 2. Univariate association for each risk factor and blood transfusion.

Characteristics	RR (95% CI)	*p* Value
Sex		
Female	Ref.	
Male	0.88 (0.30, 2.59)	0.820
Age (year)	0.93 (0.85, 1.02)	0.132
BMI (Kg/m^2)	1.15 (0.93, 1.43)	0.187
Hypertension		
No	Ref.	
Yes	0.53 (0.21, 1.35)	0.186
Diabetes		
No	Ref.	
Yes	0.30 (0.07, 1.34)	0.115
Hb (g/L)	0.93 (0.89, 0.97)	***0.001***
Time to surgery (d)	1.81 (1.39, 2.36)	***<0.001***
ASA score		
2	Ref.	
3	1.30 (0.49, 3.43)	0.594
4	1.14 (0.13, 10.30)	0.908
Type of anesthesia		
CSEA	Ref.	
GA	4.72 (1.71, 13.01)	***0.003***
Surgical approach		
Posterior	Ref.	
Lateral	0.72 (0.23, 2.30)	0.580
Surgery duration (min)	1.06 (1.03, 1.09)	***<0.001***
IBL (ml)	1.02 (1.01, 1.03)	***<0.001***

BMI – body mass index; Hb – hemoglobin; ASA score – American Society of Anesthesiologists score; CSEA – combined spinal and epidural anesthesia; GA – general anesthesia; IBL – intraoperative blood loss.

Results

The study enrolled 151 patients, of whom 21 (13.9%) required blood transfusion. Table 1 shows the preoperative baseline characteristics. There were no statistically significant differences according to sex, age, BMI, comorbid diseases, ASA scores, or surgical approach. The preoperative Hb was significantly lower, while the time to surgery, surgery duration, intraoperative blood loss, postoperative drainage blood loss, and postoperative length of stay (PLOS) were significantly higher, in transfused patients than in non-transfused patients. In addition, transfused patients were at higher risk for complications, such as thrombotic events, superficial infection, and pneumonia. No transfusion reactions occurred after blood transfusion. All superficial infections healed after debridement and wound dressing; urinary tract infections and pneumonia were cured after the appropriate antibiotic treatment. Patients with preoperative deep vein thrombosis underwent inferior vena cava filter implantation and all patients received perioperative anti-fibrinolytics.

Table 3. Risk factors for blood transfusion (binary logistic regression model).

Characteristics	RR (95% CI)	*p* Value
Hb (g/L)	0.86 (0.79, 0.94)	***0.001***
Time to surgery (d)	1.95 (1.23, 3.11)	***0.005***
Type of anesthesia	0.22 (0.05,0.91)	***0.036***
Surgery duration (min)	1.07 (1.02,1.12)	***0.005***
IBL (ml)	1.01 (1.00, 1.02)	***0.034***

Hb – hemoglobin; CSEA – combined spinal and epidural anesthesia; GA – general anesthesia; IBL – intraoperative blood loss.

In univariate analyses, the following were significantly associated with blood transfusion: the preoperative Hb level, time to surgery, general anesthesia, surgery duration, and intraoperative blood loss (IBL) (Table 2). Binary logistic regression analyses indicated that all 5 candidate variables were independent risk factors for transfusion and constituted the final model (Table 3).

A nomogram was established to predict the risk for needing a blood transfusion. The preoperative Hb value had the highest score, which suggested that this parameter had the greatest impact on the model (Figure 1). The total score of prognostic indicators was obtained by summing the individual scores, and the transfusion probability was obtained using the total score. For example, 1 patient underwent surgery 4 days after injury; his preoperative Hb was 90 g/L, he received general anesthesia during the operation, the IBL was 300 ml, and the surgery lasted was 70 min. The patient's time-to-surgery score was 20, the preoperative Hb score was 100, the type of anesthesia score was 15, the IBL score was 20, and the surgery duration score was 25. The total score was 20+100+15+20+25=180, which corresponds to an 80% risk for blood transfusion.

The C-index of the model was 0.940 after 1000 bootstrap self-sampling replicates, which indicated that the consistency

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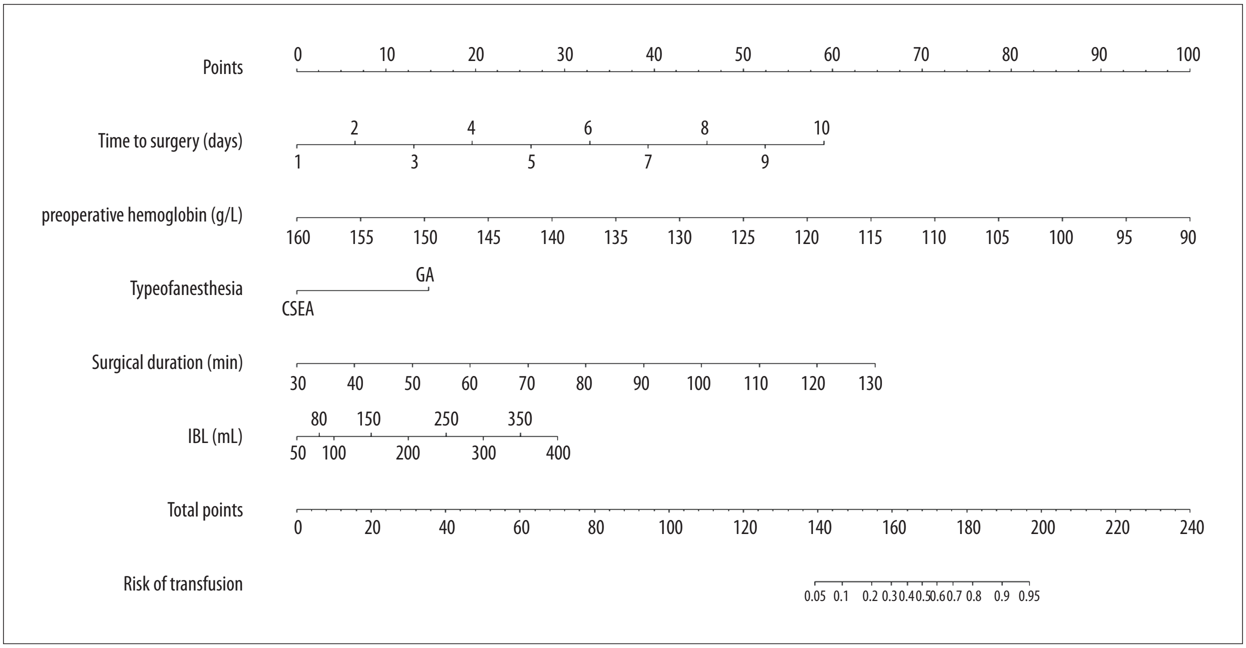

Figure 1. A nomogram to predict the incidence of blood transfusions after hemiarthroplasty in patients with femoral neck fractures. CSEA – combined spinal and epidural anesthesia; GA – general anesthesia; IBL – intraoperative blood loss.

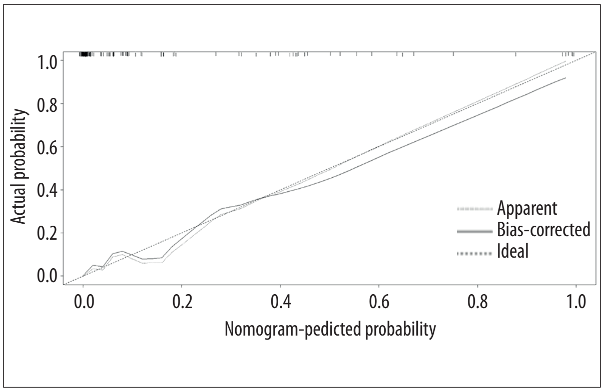

Figure 2. Calibration curve for nomogram prediction of blood transfusions after hemiarthroplasty in patients with femoral neck fractures.

between the predictions and the actual observations obtained from this chart is in line with the standard and that the chart has a standard resolution. Figure 2 shows the calibration curve. The average absolute error of the coincidence between the predicted value and real value was 0.020. The predicted risk was close to the actual risk, and the coincidence was good.

Discussion

The morbidity, mortality, and financial cost associated with FNF is a major public health problem, which creates a serious social burden [14]. Generally, for elderly FNF patients with lower functional demands and more comorbidities, HA is widely used because it is a less complex surgery and is quicker than total hip arthroplasty [1,5]. However, it is associated with risk of needing a blood transfusion. Elderly patients tolerate blood transfusion less well and have a higher incidence of related complications than younger patients. Therefore, it is necessary to strengthen the perioperative blood management in such patients to reduce the blood transfusion requirement. This study identified risk factors and developed a nomogram for blood transfusions after HA in FNF patients.

Binary logistic regression analyses showed that a low preoperative Hb level, longer time to surgery, general anesthesia, longer surgery duration, and IBL were independently associated with blood transfusion. The preoperative Hb was 110.43±7.47 g/L in the transfused group and 121.20±13.87 g/L in those who were not transfused ($p<0.001$). These results are in line with Dillon et al. [15] who reviewed 124 hip fractures patient and reported that a low preoperative Hb was a risk factor for blood transfusion. Furthermore, they suggested that the use of restrictive cross-matching policies during the perioperative period reduced the cost of healthcare delivery. Adunsky et al. [16] reported that a Hb <120 g/L and increased the transfusion risk by 5-fold, likely due to the poor immune response and low compensative ability to stresses, such as surgical stress and blood loss, in patients with a low preoperative Hb.

Previous studies reported that the delay from admission to surgery increases mortality [17], postoperative infections [18], and the length of postoperative stay [19]. Our results confirmed these conclusions; transfusion patients had longer

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postoperative stays and higher risk of postoperative infections. The mean time to surgery was 6.43±1.95 days in transfused patients compared to 4.15±1.65 days in patients who were not transfused ($p<0.001$). We believe that while the patients are waiting for surgery, the fracture site continues to lose blood, leading to greater blood loss and a higher risk for blood transfusion. We also found that the IBL was an independent risk factor for blood transfusion requirement: the mean IBL was 271.43±112.44 ml in transfusion patients, significantly higher than in normal patients (175.08±75.64, $p<0.001$). Generally, large perioperative blood loss leads to increased blood transfusion risk.

Our preliminary data showed patients with general anesthesia were at increased risk for requiring a blood transfusion. Compared to combined spinal and epidural anesthesia, there was a 3.90 times greater risk for blood transfusion in patients who received general anesthesia ($p=0.035$). These results are consistent with those of Basques et al. [20], who found that general anesthesia was a risk factor for blood transfusion. We consider that this may be partly related to the following. First, the hemodynamic differences between GA and CSEA and GA with higher blood pressures during surgery can increase the blood loss and risk for transfusion [21]. The anesthetic gases used in GA, mixed with nitrous oxide, can hinder erythropoiesis during endogenous recovery of red blood cells [22]. Finally, hypothermia during GA can lead to coagulation disorders and increase the transfusion demand [23]. Moreover, longer surgery also means greater IBL.

Blood transfusion increases the incidence of complications and prolongs the hospital stay. These problems should not be ignored when treating elderly FNF patients with HA. In addition, for elderly patients with potential risk factors, particularly when combined with multiple injuries or serious comorbidities, it is necessary to improve blood management, such as with controlled hypotension, intravenous iron, intraoperative blood salvage, and the administration of antifibrinolytic agents [24,25].

Various predictors of blood transfusions after hemiarthroplasty in patients with FNF have been reported. However, no study has examined the visual presentation of these risk factors in a nomogram. Compared to traditional multiple regression models, the advantage of a nomogram is that all key predictors can be displayed graphically. Our nomogram can evaluate the incidence of blood transfusions after HA in patients with FNF and provide better guidance for clinicians to intervene in patients during the perioperative period, so as to reduce the incidence of blood transfusion.

Limitations to this study should be considered. First, this study was based on retrospective data and the sample size was relatively small, which is inevitably affected by the inherent data. The demographic and preoperative data of the 2 groups were not truly homogenous. Thus, a prospective study is necessary to validate our results. Furthermore, our nomogram model has only been validated internally, and still needs to be validated externally.

Conclusions

We found correlations between blood transfusion requirement and low preoperative Hb, longer time to surgery, general anesthesia, longer surgery duration, and higher IBL, and then developed a nomogram. Our nomogram model can be used to evaluate the transfusion risk for FNF patient after hemiarthroplasty, and provide better guidance for clinicians to intervene perioperatively, so as to reduce the incidence of blood transfusion.

Availability of data and materials

The datasets analyzed in the study are available from the corresponding author on reasonable request.

Conflict of interest

None.

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