Curative efficacy of strengthen transfusion strategy for older patients with hip fracture: A Single-center Retrospective Study

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Abstract

Background: Perioperative transfusion is very common in older patients with hip fracture, but there is still great controversy about whether patients with hemoglobin (Hb) value between 90-100g/L should receive transfusion. The aim of this retrospective study was to observe the curative efficacy of strengthen transfusion strategy for hip fracture patients of age≥65 years.

Methods: A retrospective analysis was made on elderly patients with hip fracture who were treated in a single trauma emergency center from 2015 to 2019. Patients who received surgical treatment and had perioperative transfusion records were selected and were divided into three groups according to the lowest perioperative Hb value of 70-80g/L, 80-90g/L and 90-100g/L. According to whether to continue transfusion when the Hb value is between 90-100g/L, they were divided into strengthen transfusion strategy group or routine transfusion strategy group. The demographic data (gender, age, fracture type, complications, etc.), the Hb value, red blood (RBC)use, and patient outcomes between the two groups were analyzed**.**

Results: In total, 4966 elderly hip fracture patients were identified of whom 22.0% had documented perioperative transfusion. After screening the inclusion and exclusion criteria, a total of 802 patients were included in our study, including 95 in the 70-80g /L group, 264 in the 80-90g /L group and 443 in the 90-100g /L group. There was no significant difference in hospital stay between strengthen and routine transfusion group, however strengthen transfusion strategy can reduce the incidence of perioperative pulmonary infection and cerebral infarction in each group. And it can also reduce the incidence of arrhythmia, urinary tract infection in 80-90g /L group and electrolyte disorder in 90-100g /L group, respectively.

Conclusions: For elderly patients with hip fracture, strengthen transfusion strategy does not increase the risk of perioperative major adverse coronary events (MACE), reduce the incidence of adverse outcomes such as perioperative pulmonary infection, cerebral infarction and shorten the length of hospital stay.

Introduction

Perioperative anemia is very common in patients with Orthopedic surgery hip fractures especially[1]. Elderly patients with hip fractures have varying degrees of preoperative anemia due to trauma, combined malnutrition, chronic hemorrhagic diseases and other reasons. Anemia that cannot be corrected in time and invisible blood loss caused by surgery will aggravate postoperative anemia, prolong hospital stay, affect recovery, and even increase mortality[2]. Therefore, perioperative transfusion is vital for this kind of population.

At present, it is still recommended to adopt the provisions in the technical specifications for clinical transfusion issued by the Ministry of health in 2000 in China: blood transfusion is generally not necessary for Hb > 100g / L, and is required for Hb < 70g / L. But for Hb of 70-10g / L. Whether blood transfusion is needed depends on the patient's age, degree of anemia, cardiopulmonary function and

whether there is an increase in metabolic rate. The clinical effects of transfusion for different populations are also different. The Transfusion Requirements in Critical Care (TRICC) trial found the mortality was similar when patients received transfusion when Hb fell below 70 g/L (keeping Hb between 70 and 90 g/L) compared with more liberal transfusions (keeping Hb > 100 g/L)[3]. But aiming for Hb nearly to 90-100g/L might be better for patients with acute cardiovascular disease(CVD)[4]. However, for elderly hip fracture patients with Hb value between 90-100g /L, the risk-benefit balance of different transfusion strategies is still a controversial topic.

We figured that there is a great reason to adopt strengthen transfusion strategy to elderly hip fracture patients with complex comorbidities. We undertook a retrospective study to assess the feasibility of this strategy by exploring a series of clinically outcomes.

Patients And Methods

Patients and Groups

This retrospective study comparing strengthen transfusion strategy (continue transfusion when the Hb value is between 90-100g/L) with routine strategy (no more transfusion when the Hb value is between 90-100g/L) in anemic elderly hip fracture patients requiring surgery at a single Level I trauma center between 2015 and 2020. This study was approved by the institutional internal review board of the participating institution in compliance with the Declaration of Helsinki and consent were waived because of its retrospective nature. Inclusion criteria were patients who fulfilled all of the following (1): were aged≥65 years old (2): had already definitely diagnosed as femoral neck fracture or femoral intertrochanteric fracture by imaging examination (3): had received transfusion during perioperative period. Exclusion criteria were patients with chronic anemia (Hb value ≤70 g/L), objection to receiving RBC transfusions, appeared with typical hemolytic reaction after blood transfusions during perioperative, combined with gastrointestinal hemorrhage. Patients were divided to three groups according to the minimum Hb value: Hb 70-80g/L were placed in Group A, Hb 80-90g/L were placed in Group B and Hb 90-100g/L were placed in Group C.

Date Collection

The clinical date of patients' demographics included age, gender, type of hip fractures, comorbidities, perioperative Hb values, blood transfusion volume, complications and the length of stay. All the data of patients were evaluated by two orthopedic surgeons and a physician, and a discussion was needed if the consequences differed greatly. Record 1 minimum Hb value and 4 time points Hb value including admission, discharge, pre- and post-transfusion. If multiple but different transfusion strategies were applied to one patient during perioperative, this person would still be divided into strengthen transfusion strategy group.

Statistical Analysis

Statistical analysis was done by using SPSS Statistics software version 26.0 for Windows. Categorical variables such as gender, age groups, fracture types, comorbidities and complications in all groups were expressed as proportions. Continuous variables such as age, Hb value, total volume of transfusion, the length of hospitalization in days were expressed as mean±standard deviation (SD). Differences in the proportion between the two transfusion strategy groups were tested using Pearson Chi-square test or Fisher's exact test. Differences in Hb_{adm}, $Hb_{pre\text{-}transfusion}$, $Hb_{post\text{-}transfusion}$, Hb_{lowest}, $Hb_{pre\text{-}discharge}$ were tested by ANOVA tests on mean. And total volume of blood transfusion was tested by Kruskal-Wallis H-tests on median. $P < 0.05$ was considered statistically significant.

Result

Demographic, the Mean HB Value, RBC Use Data and Comorbidities

In total, 4966 elderly hip fracture patients were identified of whom 22.0% had documented postoperative transfusion. According to the inclusion and exclusion criteria, 294 patients were eliminated (Fig 1). A total of 802 patients, including 95 in Group A (the lowest Hb 70-80g/L), 264 in Group B (the lowest Hb 80-90g/L), and 443 in Group C (the lowest Hb 90-100g/L) met our criteria and then be included in our study.

Demographic, the mean Hb value and RBC use data are showed in Table 1. The most of patients were women (75.3%) , and the average age was 80.5±7.1 years. There were 490 (61.1%) patients with intertrochanteric fractures. After stratification according to the age of 5 years, it was found that the number of patients aged 75-84 was the largest, accounting for 46.9%. The results showed that there was no significant difference in gender, age and fracture type between the two groups ($p>0.05$). More than half of the patients were complicated with hypertension, but there was no significant difference in all complications between strengthen and routine transfusion group.

Table 1 Demographic, Hb values and RBC Use Data

Variables	Transfused	Not Transfused	Total	P value
Patients	406(50.6%)	396(49.4%)	802	
Gender, n (%)				0.548
Male	108(26.6%)	98(24.7%)	206(25.7%)	
Female	298(73.4%)	298(75.3%)	596(74.3%)	
Age, years#	80.6±7.5	80.5±7.1	80.6±7.3	0.854
Age groups, n (%)				0.963
65-74	87(21.4%)	88(22.2%)	175(21.8%)	
75-84	191(47.0%)	185(46.7%)	376(46.9%)	
≥85	128(31.5%)	123(31.1%)	251(31.3%)	
Fracture Types, n (%)				0.568
Femoral neck fractures	154(37.9%)	158(39.9%)	312(38.9%)	
Intertrochanteric fractures	252(62.1%)	238(60.1%)	490(61.1%)	
Comorbidities, n (%)				
Hypertension	193(47.5%)	211(53.3%)	404(50.4%)	0.104
Cerebrovascular disease	147(36.2%)	138(34.8%)	285(35.5%)	0.688
Coronary heart disease (CHD)	107(26.4%)	118(29.8%)	225(28.1%)	0.278
Diabetes	100(24.6%)	88(22.2%)	188(23.4%)	0.421
COPD	12(3.0%)	14(3.5%)	26(3.2%)	0.643
Hb values, g/L				
Hb_{adm}	103.8±16.9	107.4±15.7	105.5±16.4	0.002*
$Hb_{pre\text{-}transfusion}$	88.5±7.5	92.3±6.4	90.3±7.2	<0.001*
$Hb_{post\text{-}transfusion}$	108.5±6.4	98.7±5.9	103.6±7.9	<0.001*
Hb_{lowest}	88.1±7.5	91.4±6.7	89.7±7.3	<0.001*
$Hb_{pre\text{-}discharge}$	107.7±9.2	101.1±8.0	104.3±9.2	<0.001*
Total volume of blood transfusion, g/L	4(2,6)	2(0,4)	4(2,6)	<0.001*

Notes: Plus-minus values are means ± SD. * P<0.05, statistical significance. Gender, age, age group, fracture types and comorbidities are presented as number (%). Hb values are presented as means ± SD.

Total volume of blood transfusion is presented as the median (interquartile range). In gender, age, age group, fracture types and comorbidities, p values are the results of Pearson chi-square tests. In Hb_{adm}, $Hb_{pre\text{-}transfusion}$, $Hb_{post\text{-}transfusion}$, Hb_{lowest}, $Hb_{pre\text{-}discharge}$, p values are the results of ANOVA tests on mean. In total volume of blood transfusion, p value is the result of Kruskal-Wallis H-tests on median.

During all the intervention period, there was a statistically significant difference in the severity of anemia occurred between strengthen and routine transfusion groups, which continued during subsequent hospitalization until hospital discharge. Strengthen transfusion strategy not only corrected the more severe anemia, but also made the Hb value of this group higher post-transfusion and at discharge.

Complications and the Length of Hospitalization

Table 2-4 shows the clinical outcomes of patients with different minimum Hb value. Strengthen transfusion could reduce the incidence of perioperative pneumonia and cerebral infarction in the three subgroups ($P < 0.05$). There was no significant difference in the incidence of CVD between the two transfusion groups. However, after classifying CVD, it was found that in group B, the incidence of arrhythmia in strengthen strategy was lower than that with routine transfusion strategy, and the difference was statistically significant ($P <0.001$). At the same time, patients in group B with routine transfusion had a higher risk of urinary tract infection ($P = 0.006$). In group C, the risk of electrolyte disorder with routine transfusion strategy was significantly higher ($P = 0.001$).

Table 2 Complications and the Length of Hospitalization of Group A

Variables	Transfused (N=68)	Not Transfused(N-27)	Total (N=95)	P value
Cardiac Perioperative Complications, n (%)	30(44.1%)	13(48.1%)	43	0.722
Heart failure	22(32.4%)	13(48.1%)	35	0.150
Arrhythmia	12(17.6%)	6(22.2%)	18	0.608
Other Perioperative Complications, n (%)				
Electrolyte disturbance	29(42.6%)	9(33.3%)	38	0.403
Deep vein thrombosis in lower limbs	45(66.2%)	15(55.6%)	60	0.333
Lung infection	5(7.4%)	9(33.3%)	14	0.001*
Acute cerebral infarction	1(1.5%)	6(22.2%)	7	<0.001*
Gastrointestinal dysfunction	1(1.5(%)	0	1	1.000
Urinary tract infection	7(10.3%)	2(7.4%)	9	0.964
Hospital outcomes				
Length of hospital stay	13(10,14)	12(9,16)	12(10,15)	0.577

Notes: Complications are presented as number (%), p value is the result of Pearson chi-square tests. Length of hospital stay is presented as the median (interquartile range), p value is the result of Kruskal-Wallis H-tests on median. * P<0.05, statistical significance.

Table 3 Complications and the Length of Hospitalization of Group B

Variables	Transfused (N=171)	Not Transfused(N-93)	Total (N=264)	P value
Cardiac Perioperative Complications, n (%)	100(58.5%)	55(59.1%)	155	0.917
Heart failure	92(53.8%)	48(51.6%)	140	0.734
Arrhythmia	23(13.5%)	30(32.3%)	53	<0.001*
Angina Pectoris	4(2.3%)	5(5.4%)	9	0.345
Myocardial Infarction	0	1(1.1%)	1	0.757
Other Perioperative Complications, n (%)				
Electrolyte disturbance	122(71.3)	71(76.3%)	193	0.382
Deep vein thrombosis in lower limbs	76(44.4%)	44(47.3%)	120	0.655
Lung infection	43(25.1%)	42(45.2%)	85	0.001*
Acute cerebral infarction	28(16.4%)	35(37.6%)	63	<0.001*
Gastrointestinal dysfunction	6(3.5%)	7(7.5%)	13	0.149
Urinary tract infection	10(14.1%)	15(16.1%)	25	0.006*
Hospital outcomes				
Length of hospital stay	13(11,17)	14(10.19)	13.9±6.0	0.515

Notes: Complications are presented as number (%), p value is the result of Pearson chi-square tests. Length of hospital stay is presented as the median (interquartile range), p value is the result of Kruskal-Wallis H-tests on median. * P<0.05, statistical significance.

Table 4 Complications and the Length of Hospitalization of Group C

Variables	Transfused (N=250)	Not Transfused(N-193)	Total (N=443)	P value
Cardiac Perioperative Complications, n (%)	68(27.2%)	65(33.7%)	133	0.140
Heart failure	59(23.6%)	49(25.4%)	108	0.664
Arrhythmia	21(8.4%)	26(13.5%)	47	0.086
Angina Pectoris	1(0.4%)	5(2.6%)	6	0.118
Myocardial Infarction	1(0.4%)	1(0.5%)	2	1.000
Other Perioperative Complications, n (%)				
Electrolyte disturbance	73(29.2%)	99(51.3%)	172	0.001*
Deep vein thrombosis in lower limbs	123(49.2%)	111(57.5%)	234	0.082
Lung infection	20(8.0%)	32(16.6%)	52	0.005*
Acute cerebral infarction	1(0.4%)	12(6.2%)	13	0.001*
Gastrointestinal dysfunction	1(0.4%)	1(0.5%)	2	1.000
Urinary tract infection	6(2.4%)	2(1.0%)	8	0.478
Hospital outcomes				
Length of hospital stay	14.3±6.4	13.5±5.5	13.9±6.0	0.170

Notes: Complications are presented as number (%), p value is the result of Pearson chi-square tests. Length of hospital stay is presented as the median (interquartile range), p value is the result of Kruskal-Wallis H-tests on median. * P<0.05, statistical significance.

Discussion

Currently, perioperative Hb value of hip fracture has always been a topic of debate. Previous studies has found that hidden blood level(HBL) in patients with hip fractures decreased by an average of 16 g/L between admission and discharge, 6-fold higher than that recorded during the Orthopedic operation[5]. And for old hip fracture patients with intertrochanteric fractures, the cumulative total blood loss from admission to the second day after operation was 863.8 ± 429.9 ml, of which the average Hb value was 772.3 ± 424.7 (89.4%), and the average Hb value before operation was 375.5 ± 242.0 ml[6]. At the same time, evidence suggests that total blood loss during hip fracture operation may be much greater than that observed intraoperatively whose different value can up to 1473 mL[7].

More and more articles focus on Hb value. Although there are several clinical practice guidelines regarding transfusion[8,9], none specific strategy for elderly hip fracture patients when Hb 70-90g/L. Here we present an entirely new approach to transfuse—strengthen transfusion strategy, that is, transfusion is still carried out when Hb value reaches 90-100g/L. This article compared the clinical outcomes of elderly hip fracture patients with strengthen or routine transfusion strategy, clarified the advantages and disadvantages of this transfusion strategy.

Age and anemia were recognized as independent risk factors of postoperative pneumonia[10,11]. Due to the massive blood loss caused by hip fracture and the debilitating state of elderly patients, our subjects have a greatly increased risk of perioperative pneumonia. Therefore, timely correction of anemia is very important to these patients. At the same time, long-term inflammation can lead to delayed healing and even potential non-union progression, which has been observed in up to 10% of fracture patients[12]. Bedfast patients due to delayed fracture healing can also bring a higher risk of hypostatic pneumonia. In addition, Marianne et al. found that blood age also has a certain impact on pneumonia in trauma patients [13]. Due to the turn in the cell's surface-to-volume ratio caused by impaired oxygen delivery, ATP depletion and decreased microvascular perfusion, stored blood can have adverse effects, such as reduced erythrocyte survival in the post-transfusion 24h[14]. Moreover, cytokines, released by stored cells, can affect patients through a variety of adverse reactions, such as changing the sensitivity and expression of inflammatory factors[15]. Since all patients were infused with fresh RBC during our study, this may also have a positive impact on the results. Therefore, we can reduce the incidence of perioperative pneumonia through timely and effective strengthen transfusion strategy for elderly hip fracture patients.

About 40% to 50% of hip fracture patients were reported to develop delirium during perioperative[16]. A great deal of strokes are resulted from tissue ischemia caused by sever inadequate cerebral perfusion[17], which resulted directly from the low Hb value and reduced cerebral oxygenation. In the early stage of anemia, there will be typical responses to anemia such as an increase in cardiac output, additional cerebral vasodilation in an attempt to maintain adequate cerebral blood flow and oxygen transport[18]. While ischemia can result if these compensations fail. As the second most common type of stroke, intracerebral hemorrhage (ICH), can also be benefited by transfusion. Kumar et al. showed that anemia on admission was independently associated with increase hemorrhage volume[19]. Therefore, compared with routine blood transfusion, strengthen transfusion strategy can reduce the incidence of perioperative cerebral infarction by improving cerebral vascular hypoperfusion and reducing the risk of bleeding.

Anemia was suggested to be an independent risk factor for CVD [20]. The decrease of Hb value may affect the oxygen supply of infarcted or ischemic myocardium, which may lead to arrhythmia[21]. Previous analysis pointed that in patients hospitalized for non-cardiac indications, liberal transfusion strategy (Hb 80-90g/L) are associated with a decreased risk of MACE [22,23]. However, there are still some articles reported that improper perioperative transfusion may increase cardiac pressure, aggravate cardiac injury, and eventually lead to perioperative MACE[24,25]. Our results suggest that strengthen transfusion strategy

can increase the incidence rate of MACE, even perioperative arrhythmias in some patients. However, this positive effect was only reflected in group B. The reason may be that patients in group A can improve cardiovascular blood perfusion through timely transfusion due to severe symptoms, while patients in group C can tolerate the injury of low blood volume to cardiomyocytes to a certain extent due to their relatively mild degree of anemia.

Unlike previous studies[26], strengthen transfusion strategies did not prolong hospital stay in our study. This may be related to the fact that transfusion reduces the incidence of perioperative complications and accelerates rehabilitation.

In conclusion, our results show that for different subgroups of elderly hip fracture patients, strengthen transfusion strategy can bring a more positive prognosis without risk of worse outcome. More researches are needed to further understand the impact of this transfusion strategy

Conclusion

Strengthen transfusion strategy can reduce the incidence of perioperative pneumonia and cerebral infarction in elderly patients who occurred hip fracture. At the same time, it can also improve other complications of some patients. It may be a better transfusion strategy worthy of promotion in elderly patients with hip fracture.

Limitations And Strengths

This study has some limitations. As a single-center, retrospective study, selection bias due to the lack of randomization is unavoidably. All the variables are limited to previously collected data in our study. Furthermore, we may have missed a small increase in some perioperative complications because the small sample size. Another limitation of our study is the lack of standardization of anemia drugs taken by elderly patients with hip fractures during perioperative. In spite of these limitations, our study provides clues on a new perioperative transfusion strategy for elderly patients with hip fractures.

Declarations

Availability of data and materials

All the data during the current study are available from the corresponding author on reasonable request.

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Contributions

Yuqi Zhao and Junfei Guo contributed equally to this work. Zhiqian Wang and Yingze Zhang designed the study. Yuqi Zhao and Junfei Guo searched relevant studies and collected data on variables of interest. Mingming Fu and Yaqian Zhang analyzed and interpreted the data. Yuqi Zhao and Junfei Guo wrote the manuscript, and Zhiqian Wang approved the final version of the manuscript. The authors read and approved the final manuscript.

Ethics declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of the 3rd Hospital of Hebei Medical University. For this retrospective analysis, informed consent is not required.

Consent for publication

Not application.

Competing interests

The authors have no conflict of interest.

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Figures

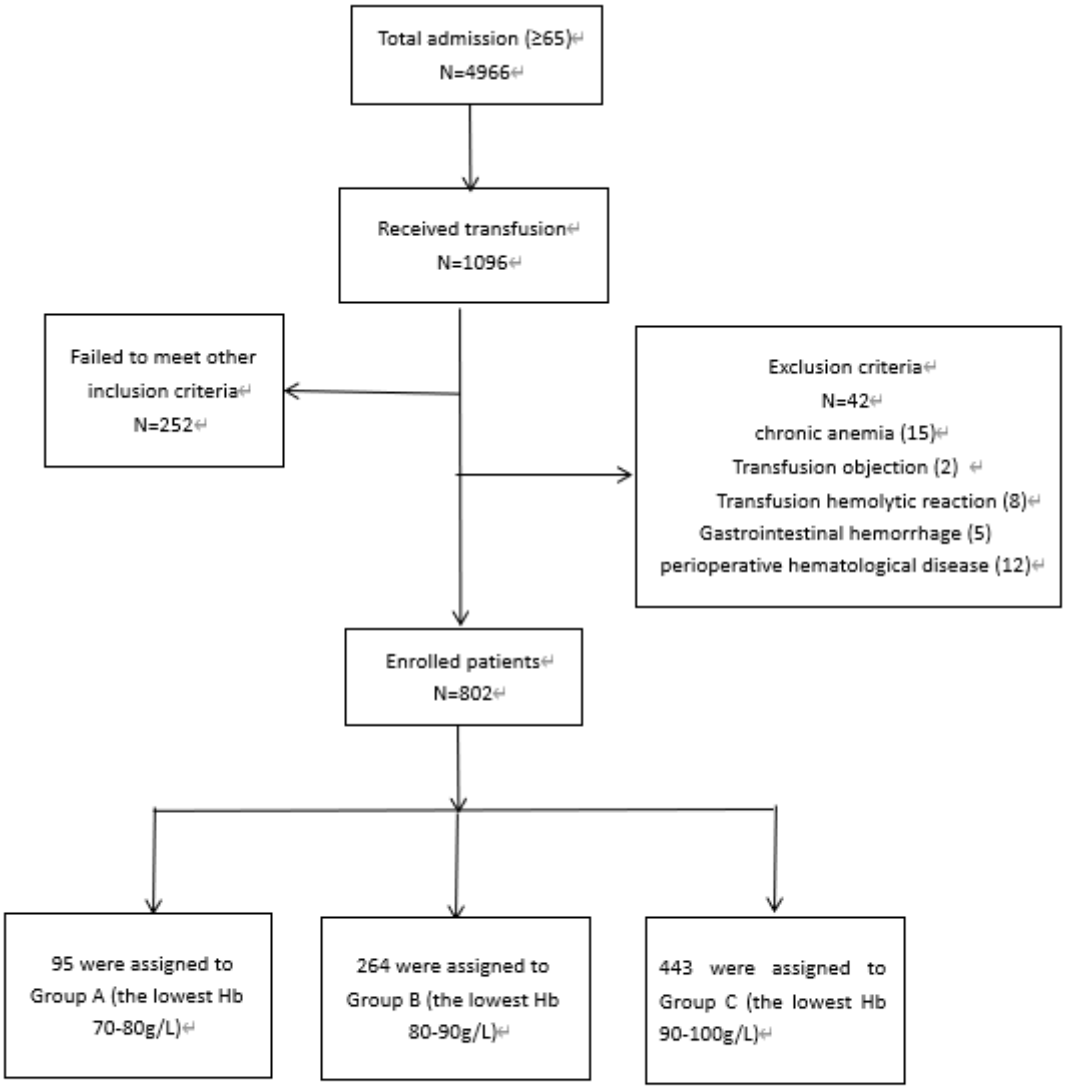

Figure 1 Flow diagram of included patients

Figure 1

See image above for figure legend.