ORIGINAL ARTICLE

Irrationality of Allogeneic Red Blood Cell Transfusion in Intraoperative Cell Salvage Patients: a Retrospective Analysis

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Key words: intraoperative cell salvage; rational transfusion; patient blood management; preoperative anemia

Objective Although intraoperative cell salvage (ICS) has been widely used to reduce the demand for allogeneic blood transfusion, patients who use ICS approach still have not completely avoided chances of blood transfusion. This study aims to investigate the rate of allogeneic red blood cell(RBC) transfusion in patients receiving ICS, and to evaluate irrationality of allogeneic RBC transfusion and its risk factors.

Methods Medical records of all patients associated with ICS approach from January 2013 to July 2014 were retrospectively reviewed. Theoretical hemoglobin level after reinfusion of salvaged RBC at the end of operations was estimated. Irrational transfusion was defined as initiating allogeneic transfusion with theoretical hemoglobin above 100 g/L. The clinical variables, including the surgical department, gender, age, body weight, ratio of blood loss to estimated blood volume(EBV), salvaged blood volume and preoperative hemoglobin level were subsequently compared between patients who received rational transfusion and those did not. Logistic regression was performed to identify the risk factors for irrationality of allogeneic RBC transfusion in these patients.

Results Of 1487 patients with ICS approach in this study, the rate of allogeneic RBC transfusion was 31.4%(467/1487), and the rate of irrational allogeneic RBC transfusion was 26.0% (341/1313). Patients with irrational transfusion were younger ($t=4.656$, $P<0.001$), with lower body weight ($t=3.910$, $P<0.001$) and slightly lower preoperative HGB level ($t=2.822$, $P=0.005$) than those with rational transfusion, but had significantly larger salvaged blood volume ($U=-10.926$, $P<0.001$) and higher ratio of blood loss to EBV ($U=-17.067$, $P<0.001$), disregarding whether they preoperatively met anemia criteria or not ($U=-1.396$, $P=0.163$). Preoperative hemoglobin level ($OR=1.975$, $P=0.005$) and the ratio of blood loss/EBV ($OR=5.392$,

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$P<0.001$) were independent risk factors leading to the irrational allogeneic RBC transfusion.

Conclusions The irrationality of allogeneic RBC transfusion existed in ICS patients, which may be associated with the preoperative hemoglobin level and the ratio of blood loss to EBV. Determining the HGB levels before transfusion is required to avoid unnecessary blood administration. Doctors should keep their knowledge in blood management updated and improve their awareness of rational transfusion for a better patients care.

A LLOGENEIC transfusion has been regarded to be associated with increased risks of hemolytic and allergic reactions, acute lung injury, infectious diseases, and immunomodulation.¹ In addition to these transfusion-associated diseases, the shortage of allogeneic blood has posed an increasingly important issue in China. Therefore, intraoperative cell salvage (ICS) has been widely used to mitigate the demand for allogeneic blood transfusion and its related complications.

However, many patients who use ICS still receive allogeneic blood transfusion in their clinical management. A systematic review on perioperative allogeneic blood transfusion reported that ICS did not reduce the demand of allogeneic red blood cell (RBC) transfusion and its intraoperative transfusion rate was $38.3\% \pm 0.17\%$ in over half (53.7%, 36/67) of the randomized controlled trials analyzed.² The reasons may lie in the individual factors of patients, including preoperative anemia,^{3,4} children or the elderly,⁵ serious comorbidities or high risk score of anesthesia according to the American Society of Anesthesiologists (ASA), disease severity (such as long-segment spinal diseases),⁵ and operative factors (such as significant blood loss, long surgical duration,^{3,5-7} excessive postoperative drainage).³ Additionally, physician's personal preference of the trigger level of HGB for transfusion also plays an important role in clinical patients care. For instance, it was reported that some surgeons or anesthesiologists rejected the relatively low trigger level of HGB for transfusion,⁸ and were not likely to change their decision-making habits.⁹

A large prospective randomized trial, Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS) study, confirmed that compared with the restrictive strategy for transfusion (symptomatic anemia or the triggering HGB level of 80 g/L), the liberal strategy for blood transfusion (the triggering HGB level of 100 g/L) did not minimize the patients' mortality, the inability to walk independently on 60-day follow-up, and the in-hospital morbidity in the elderly patients with cardiovascular disease risks.¹⁰

Therefore, doctors are supposed to transfuse allogeneic blood to patients with $HGB < 100 \text{ g/L}$ according to the Technical Specifications of Clinical Blood Transfusion of China, and had better to adopt the strict transfusion strategy, which is to transfuse only when HGB level is under 70 g/L.

This retrospective study investigated the rate of allogeneic RBC transfusion in ICS patients, aiming at evaluating reasonableness of allogeneic RBC transfusion and identifying the risk factors for the irrationality of allogeneic RBC transfusion, for the purpose to provide clues to improve the patient blood management (PBM).

MATERIALS AND METHODS

Patients selection and data collection

This retrospective study was approved by the institutional ethic committee and the informed consent from the patients were waived. We reviewed the medical records of inpatients who were associated with ICS approach in Peking Union Medical College Hospital from January 2013 to July 2014. The patients were from the departments of orthopedics, neurosurgery, vascular surgery, obstetrics and gynecology, hepatic surgery, general surgery, urology, thoracic surgery, stomatology, otorhinolaryngology, and cardiac surgery. Cases were excluded because of incomplete medical records, or cardiopulmonary bypass cardiac surgeries in which blood loss and salvaged blood volume cannot be evaluated accurately due to the washing of bypass blood by cell saver. The clinical medical records we collected included patient age, gender, body weight, preoperative hemoglobin (HGB), intraoperative estimated blood loss, salvaged blood volume, intraoperative allogeneic RBC transfusion or not, and the volume of transfusion.

Transfusion performance and decision making

All patients received autotransfusion with Haemonetics Cell Saver 5+ system (Haemonetics Corporation, Braintree, MA, USA) throughout surgeries. Clinically, the decision whether patients receive allogeneic RBC

transfusion after reinfusion of salvaged blood was made by consensus of discussion between the anesthesiologist and the surgeon based on their personal judgments. For example, some physicians made decision of transfusion when the estimated blood loss was greater than 500 mL.

Variable estimations

The theoretical HGB level at the end of the operation was estimated by the following formula:

$$\text{HGB}_{\text{post-operative}} (\text{g/L}) = [\text{HGB}_{\text{pre-operative}} (\text{g}) - \text{HGB}_{\text{intra-operative blood loss}} (\text{g}) + \text{HGB}_{\text{salvaged blood}} (\text{g})] / \text{estimated blood volume (EBV, L)}.$$

The variables in above formula were estimated as followed:

$$\text{HGB}_{\text{pre-operative}} (\text{g}) = \text{HGB}_{\text{pre-operative blood concentration}} (\text{g/L}) \times \text{EBV(L)}, \text{ where the EBV(L) = body weight(kg)} \times 0.07 \text{ L/kg}.$$

$$\text{HGB}_{\text{intra-operative blood loss}} (\text{g}) = \text{HGB}_{\text{Pre-operative blood concentration}} (\text{g/L}) \times \text{Volume}_{\text{estimated blood loss}} (\text{L}), \text{ where the Volume}_{\text{estimated blood loss}} = \text{Volume}_{\text{blood in negative pressure aspirators (including the volume collected by cell saver)}} + \text{Volume}_{\text{blood in gauzes}} + \text{Volume}_{\text{blood in drainage bag}} - \text{Volume}_{\text{irrigating saline on the operating table}} - \text{Volume}_{\text{heparinized and washing saline used by cell saver}}.$$

The volume of blood in gauzes was estimated by the weight of blood-soaked gauzes minus the net weight of gauzes, then divided by the density of blood which was represented by the density of water (1000 g/L).

$$\text{HGB}_{\text{salvaged blood}} (\text{g}) = \text{Volume}_{\text{salvaged blood}} (\text{L}) \times 10 \times 50 / 3 (\text{g/L}).$$

Since the hematocrit (HCT) is commonly 50% in washed salvaged blood and HCT (%) is approximately twice bigger than HGB (g/dL),¹¹ namely HGB level of salvaged blood = 10 × 50 / 3 (g/L).

Patients grouping and data management

According to whether the enrolled patients received allogeneic RBC transfusion in the medical records, we divided them into non-transfusion group and transfusion group, and compared the clinical characteristics between the two groups. Based on the theoretical HGB, all the patients was assigned into two groups: group A, patients with theoretical HGB < 100 g/L, group B, patients with theoretical HGB ≥ 100 g/L. For patients in group B, the clinical variables were compared between who received allogeneic RBC transfusion and who did not. Specifically, variables of patient age, ratio of blood loss/EBV and preoperative HGB were analyzed as both continuous and categorical variables in order to thoroughly check the clinical significance: ①age: stratified into children (<14 years), adults (14 ≤ age < 65 years) and

the elderly (≥65 years); ②ratio of blood loss to EBV: low(<20%), medium(20%-50%) and massive bleeding(>50%); ③preoperative HGB level: anemia(HGB <120 g/L in male and HGB <110 g/L in female) and non-anemia according to the diagnostic criteria of China.

Statistical analysis

Statistical analysis was conducted by SPSS 18.0 software. Continuous variables were described as means and standard deviations if normally distributed, or as medians if abnormally distributed. Clinical characteristics of different groups were compared by independent *t* test for normally distributed continuous variables, or independent Mann-Whitney *U* test for non-parametric test. Logistic regression was performed to identify risk factors for irrationality of allogeneic RBC transfusion. The differences were considered statistically significant if *P* value was less than 0.05.

RESULTS

Demographic and clinical data

Of 1631 patients who were associated with ICS approach in the medical records, 144 cases were excluded according to exclusion criteria, and 1487 patients were enrolled in this study. There were 467 (31.4%) patients who received intraoperative transfusion, and the mean allogeneic RBC was 736.19 ± 534.11 mL. Comparing to those who did not, patients with transfusions were significantly younger with lower body weight, lower preoperative HGB, significant higher ratio of blood loss to EBV, and higher salvaged blood volume (**Table 1**). There was no significant difference in the surgical departments and gender between the two groups of patients.

Rates of allogeneic RBC transfusion in patients with different theoretical HGB levels

Of 1487 patients in this study, there were 174 (11.7%) cases whose theoretical HGB < 100 g/L (group A) and 1313 (88.3%) cases whose theoretical HGB ≥ 100 g/L (group B). Of 174 cases in the group A, 126 (72.4%) cases received transfusion and 48 (27.6%) cases did not. Of 1313 cases in the group B, 341 (26.0%) cases received transfusion, the mean transfusion volume was 611.7 ± 400.4 mL, and 972 (74.0%) cases did not receive transfusion. The difference of transfusion rates between two groups was found to be significant ($\chi^2 = 153.8$, $P < 0.001$).

Table 1. Demographic and clinical characteristics of enrolled patients ($n=1487$)[§]

Characteristics	Non-transfusion ($n=1020$)	Transfusion ($n=467$)	t or U value	P value
Surgical department, n (%)			-0.836	0.178
Orthopedics	715(70.1)	356(76.2)		
Neurosurgery	146(14.3)	25(5.4)		
Vascular	62(6.1)	36(7.7)		
Obstetrics and gynecology	52(5.1)	3(0.6)		
Hepatic	29(2.8)	11(2.4)		
General	10(1.0)	19(4.1)		
Urology	6(0.6)	11(2.4)		
Thoracic	0(0)	3(0.6)		
Stomatology	0(0)	2(0.4)		
Otorhinolaryngology	0(0)	1(0.2)		
Gender, n (%)			-1.674	0.094
Male	403(39.5)	206(44.1)		
Female	617(60.5)	261(55.9)		
Age, years	43.1 $\pm$ 21.5	37.6 $\pm$ 22.3	4.528	<0.001
Body weight, kg	62.9 $\pm$ 15.9	57.8 $\pm$ 19.6	4.944	<0.001
Preoperative HGB, g/L	136.7 $\pm$ 16.6	127.8 $\pm$ 22.8	7.571	<0.001
Blood loss, mL	579.1 $\pm$ 348.00	1323.6 $\pm$ 1178.2	-13.389	<0.001
Blood loss /EBV, %	12.1 $\pm$ 7.7	30.3 $\pm$ 27.0	-14.345	<0.001
Salvaged blood volume, mL	291.5 $\pm$ 174.6	553.0 $\pm$ 445.3	-12.266	<0.001

§: Plus and minus values are means $\pm$ standard deviation. EBV: estimated blood volume; HGB: hemoglobin.

Differences in clinical characteristics between non-transfusion patients and transfusion patients in group B

Compared to patients who did not receive transfusion in group B, those who received transfusion were younger, with lower body weight and slightly lower preoperative HGB, but had significantly larger salvaged blood volume and higher ratio of blood loss to EBV when analyzed in terms of continuous variables (**Table 2**). When compared in terms of categorical variable, preoperative anemia, which is based on preoperative HGB, was not significantly different between the patients who received transfusion and those did not ($U=-1.396$, $P=0.163$). The age and ratio of blood loss to EBV were significantly different between the two subgroups (both $P<0.001$). The surgical departments where patients received therapy were not different significantly between the transfusion and non-transfusion patients ($P>0.05$).

Risk factor analysis of irrational allogeneic RBC transfusion in group B

For patients with theoretical HGB $\geq$ 100 g/L, among variables that was significantly different between patients received transfusion and those did not, the

logistic regression analysis showed that preoperative HGB (continuous variable, $OR=1.975$, 95% CI : 1.23-3.8, $P=0.005$) and ratio of blood loss/EBV (category variable, $OR=5.392$, 95% CI : 3.57-8.14, $P<0.001$) were the independent risk factors for irrationality of allogeneic RBC transfusion (**Table 3**). The body weight ($OR=0.989$, 95% CI : 0.979-1.000, $P=0.048$) and the salvaged blood volume ($OR=1.002$, 95% CI : 1.001-1.003, $P<0.001$) were also statistically significant, but their OR values approximated 1, indicating their small clinical significances.

DISCUSSION

It has been reported that the risk of allogeneic RBC transfusion can be reduced by 38% (RR 0.61, 95% CI 0.55~0.77) with 204mL volume reduction of allogeneic RBC transfusion by using ICS.² The efficacy of ICS in some orthopedics or cardiac surgeries was getting more definite. ICS can reduce patients' risks of blood-borne infection, postoperative infection, tumor recurrence and immune modulation, and relieve blood shortages.¹²

In this observational study, the intraoperative allogeneic RBC transfusion rate was 31.4% (467 out of

Table 2. Comparison of clinical variables between subgroups of non-transfusion and transfusion patients in group B ($n=1313$)[§]

Clinical characteristics	Theoretical HGB >100g/L		<i>t</i> or <i>U</i> value	<i>P</i> value
	Non-transfusion ($n=972$)	Transfusion ($n=341$)		
Gender, <i>n</i> (%)			-0.614	0.539
Male	392(40.3)	144(42.2)		
Female	580(59.7)	197(57.8)		
Age, years	43.2±21.7	36.8±22.5	4.656	<0.001
Body weight, Kg	63.2±16.0	58.3±20.8	3.910	<0.001
Blood loss/EBV, %	11.7±6.6	22.8±11.4	-17.067	<0.001
Salvaged blood volume, mL	288.0±164.2	499.9±344.7	-10.926	<0.001
Preoperative HGB, g/L	138.5±13.9	136.1±13.6	2.822	0.005
Age, <i>n</i> (%)			-3.488	<0.001
<14yrs	109(11.2)	66(19.4)		
14≤age<65yrs	676(69.5)	224(65.7)		
≥65yrs	187(19.2)	51(15.0)		
Preoperative anemia, <i>n</i> (%)			-1.396	0.163
No	896(92.2)	306(89.7)		
Yes	76(7.8)	35(10.3)		
Blood loss/EBV, <i>n</i> (%)			-17.646	<0.001
<20%	873(89.8)	150(44.0)		
20%-49%	98(10.1)	178(52.2)		
≥50%	1(0.1)	13(3.8)		

§: Plus-minus values are means±standard deviation.

Table 3. Logistic regression analysis of risk factors for irrational allogeneic RBC transfusion in group B ($n=1313$)

Variables	β	SE	Wald	<i>P</i>	OR	95% CI
Salvaged blood volume	0.002	0.000	21.079	<0.001	1.002	1.001-1.003
Body weight	-0.011	0.005	3.921	0.048	0.989	0.979-1.000
Preoperative HGB	0.680	0.243	7.818	0.005	1.975	1.226-3.182
Blood loss/EBV	1.685	0.210	64.277	<0.001	5.392	3.571-8.139
Age	-0.046	0.148	0.096	0.757	0.955	0.714-1.277

Note: The salvaged blood volume, body weight and preoperative HGB were calculated in continuous variables, while the ratio of blood loss to EBV and age were calculated in categorical variables, setting the ratio of blood loss to EBV <20% and age <14 years old as the reference values.

1487), which was comparable to 38.3% and 39.4% as reported in the literatures.^{2,13} It was reported that in some regions of China, the rate of intraoperative irrational allogeneic blood transfusion was approximately 58.7%,¹⁴ and the rate of irrational allogeneic RBC transfusion ranged from 33.6% to 49.2%.^{15,16} In USA and Australia, the reported rate of surgical related irrational allogeneic RBC transfusion reached up to 63.3%, and in 70% of these patients, the HGB values were between 80 g/L and 99 g/L.¹⁷ The irrational allogeneic RBC transfusion may also exist in patients of ICS. Dr. Wong *et al* reported that the autologous transfusion

at the mean (standard deviation) hemoglobin level of 92.6 (8.7) g/L and above was irrational transfusion. They also assessed the adherence of doctors to blood transfusion guideline and found that 20.3% of patients whose HGB between 71g/L and 100 g/L received RBC transfusion just because of their anemic symptoms; nevertheless, only 2.2%(4/180) patients whose HGB levels was greater than 100 g/L received allogeneic RBC transfusion.¹⁸ When doctors strictly followed the blood transfusion protocol, the relative risk of allogeneic RBC transfusion in ICS patients was reduced by 48%.¹³

In the institution where this study was conducted, the point-of-care HGB test is not routinely done before and after blood transfusion, and the transfusion decisions are usually made based on the experience of anesthesiologists or surgeons. Therefore, this study evaluated the irrationality of allogeneic RBC transfusion by calculating the theoretical HGB level instead of actual HGB value. Another reason is that the actual HGB level is of little value in evaluating the rationality of allogeneic RBC transfusion when both autologous and allogeneic RBC was transfused. Our results showed that the patients whose theoretical HGB was >100 g/L accounted for 88.3% (1313/1487) of all cases in this study. Among them, 341 patients received transfusion, yielding an irrational RBC transfusion rate of 26.0%, though according to the Technical Specifications of Clinical Blood Transfusion of China, these patients should not have received blood transfusion.

Furthermore, we found that the preoperative HGB and ratio of blood loss to EBV were independent risk factors for irrational allogeneic RBC transfusion in ICS patients, particularly, the ratio of blood loss to EBV greater than 50% could approximately quintuple the risk for irrational RBC transfusion in patients with ratio of blood loss to EBV under 20%. Although logistic regression analysis also found the body weight and the salvaged blood volume were statistically risk factors, the ORs of both factors approximated 1, indicating clinically they may have small influence on the irrational RBC transfusion in ICS patients.

Patients' preoperative HGB level was highly related to the rate of allogeneic RBC transfusion in this study. It has been reported that in patients with preoperative HGB > 160 g/L, 141~160 g/L, 121~140 g/L, 101~120 g/L and 81~100 g/L, the rates of allogeneic RBC transfusion were 8.3%, 7.8%, 28.2%, 60.2% and 85.7% respectively ($P<0.0001$).¹⁸ The incidence of preoperative anemia in patients receiving non-cardiac surgeries (except for colorectal surgery) was 34%, and preoperative anemia significantly correlated to the increased requirements of perioperative allogeneic blood, increased risks of postoperative infections, mortality, complications and prolonged hospitalization.¹⁹ However, in this study, regardless of transfusion or not, the mean pre-operative HGB level of group B did not meet the diagnostic criteria of anemia, and the pre-operative anemia rate in non-transfusion patients was comparable to that of transfusion patients ($P=0.163$). These data suggested that physicians were apt to take

a liberal transfusion strategy in practice for patients with low preoperative HGB level, disregarding whether the preoperative HGB level had reached the suggested trigger level for transfusion, or whether the degree of anemia would really affect the outcomes of patients.

Some studies have also concluded that massive blood loss was an independent risk factor in perioperative allogeneic RBC transfusion in ICS patients.^{6,20} However, it is interesting that salvaged blood volume was not a major factor influencing the decision of allogeneic RBC transfusion in our study. Additionally, by calculation, we observed that the theoretical HGB level remained above 100 g/L after re-infusing washed salvaged cell in most cases. So most of the ICS patients might not need allogeneic RBC. Thus, we presumed that the surgeons or anesthesiologists did not consider ICS to be able to reduce the intraoperative demand of allogeneic RBC, and still chose allogeneic blood transfusion if patients experienced heavy blood loss.

The main limitation of our study is that the actual HGB values were not examined before and after blood transfusion in clinical practice of our hospital, so we had to use theoretical HGB level instead. Besides, this study was conducted in a single medical center, and multi-centric study is needed for further investigation.

To conclude, irrationality of allogeneic RBC transfusion in ICS patients may be associated with the patient body weight, salvaged blood volume, preoperative HGB and ratio of blood loss to EBV, especially the latter two. Determining the HGB levels should be done before transfusion to avoid unnecessary blood administration. Doctors' knowledge in blood management should be updated, and the awareness of rational transfusion need to be improved for better patients' care.

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