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Original Article

Effect of intraoperative cell salvage on coagulation function outcomes in patients with massive post-Cesarean section hemorrhage

Huabei Zeng[1,2*], Chunhua Xia[2*], Zhiyong Cheng[2], Yidong Shan[2], Yu Zhang[2], Zhongjun Zhang[1]

[1]Wuxi Medical College, Jiangnan University, Wuxi 214122, Jiangsu, China; [2]Department of Anesthesiology, Suqian Maternity and Children's Hospital, Suqian 223800, Jiangsu, China. [*]Equal contributors.

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Abstract: Objective: To examine the impact of using intraoperative cell salvage (ICS) for the restoration of coagulation function in cases of massive Post-Cesarean Section Hemorrhage (PCSH). Methods: A retrospective analysis was conducted on 60 cases of massive PCSH meeting inclusion criteria at Suqian Maternity and Children's Hospital from January 2020 to July 2022. Patients were divided into two groups: allogeneic blood transfusion group (Group A, n = 30) and ICS group (Group B, n = 30), based on transfusion methods. Blood parameters, coagulation function, and adverse reactions were assessed before (T0) and after (T1) transfusion. Patients were categorized into good prognosis (GP) and poor prognosis (PP) groups based on adverse reaction occurrence. Clinical profiles were compared between groups, and multivariate binary logistic regression analysis was employed to evaluate the factors that may affect the prognosis in women with PCSH. Results: No significant differences in routine blood parameters were observed between groups at T0 and T1 (P>0.05). At T0, no significant differences in PT, APTT, TT, or FIB were found between groups (P>0.05). Both groups showed a reduction in PT, APTT, and TT values at T1 compared to T0, with Group B experiencing a more significant decrease than Group A (P<0.05). FIB increased in both groups at T1 compared to T0, with Group B demonstrating a higher increase than Group A (P<0.05). Both groups showed increased blood pressure at T1 compared to T0, with Group B showing a more pronounced elevation than Group A (P<0.05). The occurrence of adverse reactions was significantly lower in Group B (1/30, 3.33%) compared to Group A (7/30, 23.33%) (P<0.05). Logistic regression analysis identified FIB<1.52 g/L and HR<45.35 times/min as factors associated with increased risk of unfavorable outcome in women with PCSH. Conclusion: In patients experiencing significant PCSH, ICS may lead to better postoperative recovery of blood parameters, faster restoration of coagulation function, and reduced risk of adverse events compared to ABT. Moreover, early detection of coagulation function and blood gas indexes is crucial for clinicians to implement timely prevention and treatment measures.

Keywords: Intraoperative cell salvage, cesarean section, postpartum hemorrhage, coagulation function, clinical outcome

Introduction

With the adjustment of China's fertility policy, the number of women facing high-risk cesarean sections is increasing year by year, including those with scarred uterus, placenta previa, and placenta accreta. These patients often experience significant bleeding during delivery, putting them at high risk for postpartum hemorrhage. Postpartum hemorrhage, characterized by rapid and substantial blood loss, can lead to a sudden decrease in blood volume, resulting in acidosis and deterioration of maternal coagulation function, and possibly leading to hemorrhagic shock [1]. Moreover, cesarean section procedures themselves can induce changes in hemorheology and increase coagulation factors and platelet activity, predisposing pregnant women to thrombosis after delivery and posing serious risks to maternal safety [2]. Therefore, prompt intervention is crucial to restore coagulation function. Blood transfusion remains the primary treatment method, rapidly replenishing lost blood volume. In cases of severe bleeding and critical conditions, massive blood transfusion can be life-saving. However, reliance on allogeneic blood transfusion (ABT) from blood banks presents challenges, particularly con-

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cerning the shortage of allogeneic blood resources, especially for patients with rare blood types. This difficulty in matching suitable blood resources may delay maternal blood transfusion after massive hemorrhage, prolonging rescue time and hindering postpartum recovery [3]. Furthermore, ABT poses significant safety concerns, including the risk of infection, allergy, immunosuppression, and lung injury resulting from transfusion reactions [4, 5]. These safety issues can undermine the therapeutic efficacy of blood transfusion for cesarean section patients.

Intraoperative cell salvage (ICS) is a technique that uses a blood transfusion device to collect, anticoagulate, filter, and wash intraoperative blood loss from the patient, then reinfuses it back into the patient. It serves as an effective first-aid measure for patients experiencing massive bleeding during surgery [6, 7]. Studies have shown that compared to ABT, the use of ICS during surgery not only reduces the need for integrated blood products but also buys critical time for effective patient rescue, thereby improving the success rate of resuscitation [8, 9]. Moreover, autologous blood transfusion from ICS is relatively fresh, exhibiting superior coagulation function and oxygen-carrying capacity compared to stored allogeneic blood. Additionally, repeated blood draws stimulate the patient's bone marrow hematopoietic cell viability, promoting accelerated post-surgical hematopoiesis and facilitating patient recovery [10]. Based on the above background, this study focused on patients with Post-Cesarean Section Hemorrhage (PCSH) admitted to our hospital, evaluating the application of recycled autologous blood transfusion technology in such cases.

Materials and methods

General information

This study was approved by the Ethics Committee of Suqian Maternity and Children's Hospital. It involved 60 women who underwent cesarean section and experienced postpartum hemorrhage at Suqian Maternity and Children's Hospital between January 2020 and July 2022.

Inclusion criteria: (1) women of childbearing age who underwent elective cesarean section at Suqian Maternity and Children's Hospital of Jiangsu Province, with expected postpartum hemorrhage exceeding 1000 mL or blood loss exceeding 20% of systemic blood volume, accompanied by symptoms or signs of reduced blood volume [11]; (2) aged 26~41 years old. Exclusion criteria: (1) emergency cesarean section; (2) patients who were unconscious or unable to cooperate effectively; (3) patients with severe medical or surgical conditions; (4) anemia or abnormal coagulation function; (5) participation in other intervention studies; (6) allergic to blood products; (7) mental disorders; (8) patients who were transferred to cesarean section after failed vaginal trial of labor; (9) intraoperative assessment determining no need for blood transfusion.

Criteria for blood transfusion

(1) The criteria are not strictly regulated. Instead, the decision to transfuse red blood cells is based on the clinical condition of parturients, considering factors beyond just hemoglobin levels. The recommended goal for blood transfusion in treating postpartum hemorrhage, as per the RCOG guidelines, is a hemoglobin level above 8 g/dl and platelet count above 50×10^3/L [11]. (2) For pregnant women, if the hemoglobin content of their total blood volume was 40%, red blood cells should generally be administered immediately. When hemoglobin levels were between 70 and 100 g/L, and blood loss constituted 30% to 40% of the total blood volume, doctors would evaluate maternal cardiopulmonary compensatory ability, metabolic rate, active bleeding, and other factors to decide whether red blood cell transfusion is necessary. It is recommended to maintain a hemoglobin concentration between 70 and 80 g/L [12]. (3) In cases where postpartum hemorrhage causes coagulation dysfunction, especially disseminated intravascular coagulation, prompt supplementation of coagulation factors such as fresh frozen plasma, platelets, cryoprecipitate, and fibrinogen would be essential. The aim was to maintain prothrombin time and activated partial thromboplastin time below 1.5 times the normal upper limit, platelet levels above 50×10^9/L, and fibrinogen levels above 1 g/L. At present, there is no standardized obstetric massive blood transfusion protocol. However, it is recommended to transfuse red blood cells, plasma, and platelets at a ratio of 1:1:1 (such as 10 U

red blood cell suspension + 1000 ml fresh frozen plasma + 1 U apheresis platelets) based on commonly used protocols [13]. (4) For pregnant women at risk of significant blood loss (exceeding 20% of their blood volume or ≥1000 ml), rare blood type, those with multiple antibodies, or rejection of allogeneic blood transfusion, hospitals with appropriate resources may consider autologous blood transfusion [14].

Patients who met the inclusion criteria were divided into two groups based on the method of blood transfusion: the ABT group (Group A, n = 30) and the ICS group (Group B, n = 30). In Group B, patients underwent blood collection using an autologous blood recovery machine at the beginning of cesarean section. When maternal blood loss exceeded 1000 ml and blood gas analysis indicated a hemoglobin level of <70 g/L, the collected autologous blood underwent washing, centrifugation, and transfusion. Conversely, in Group A, patients experienced significant blood loss during cesarean section, with blood gas analysis revealing a hemoglobin level of <70 g/L, meeting the criteria for ABT, and thus received this treatment.

Intraoperative management and blood transfusion methods

Upon admission, patients underwent routine monitoring and a comprehensive examination, including blood group identification, cross-matching tests, and assessment of coagulation function and other biochemical indicators to ensure smooth surgical procedures. In the operating room, patients received routine electrocardiogram (ECG) monitoring and intravenous infusion of sodium lactated Ringer's solution (manufacturer: China Dazhong Pharmaceutical Co., Ltd.; batch number: H20059628) at a dose of 10 ml/kg. Combined spinal-epidural anesthesia was administered via L2~3 puncture following routine preoperative preparations. In Group A, patients received ABT in the event of postpartum hemorrhage, based on assessment of hemodynamic changes and actual bleeding during the operation. When a patient's hemoglobin dropped below 70 g/L, they were infused with 2-3 units of allogeneic packed red blood cells.

In Group B, intraoperative bleeding was collected using an autologous blood recovery machine (manufacturer: Shanghai Weimei Management Co., Ltd.; model: SB-2000C) through a suction tube at the beginning of cesarean section. The automatic autologous blood recovery system processed the collected blood, incorporating anticoagulants into the suction tubes. Typically, the anticoagulant concentration comprised a mixture of 13,000 units of heparin (manufacturer: Changzhou Qianhong Biochemical Pharmaceutical Co., Ltd.; drug specifications: 2 ml:12,500 U; batch number: Guoyao Zhunzi H32022088) and 500 mL of 0.9% sodium chloride solution (Shandong Qidu Pharmaceutical Co., Ltd., Guoyao Zhunzi H20113297, specification: 500 mL:45 g). The collected blood underwent filtration, separation, and double washing to yield concentrated red blood cells, which were then reinfused into the patient through a pipeline equipped with a white blood cell filter.

Observation indicators

Blood samples were obtained from peripheral veins prior to surgery (T0) and 12 hours post-surgery (T1). The BC-5000 Mindray automatic blood cell analyzer (Shenzhen Mindray Biomedical Electronics Co., Ltd., Yuejizhun 201722-20313) was used to determine blood routine indices such as red blood cell count (RBC), hemoglobin (Hb), and hematocrit (HCT) in both groups. The acl-top-300 cts coagulation analyzer (American Wofen Medical Devices Co., Ltd.) was employed to assess coagulation function indices including prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), and fibrinogen (FIB). (2) Hemodynamic parameters, including systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) at T0 and T1, were monitored using an ECG monitor (Shanghai Jumu Medical Device Co., Ltd., XD2000A). The measurements were conducted in strict accordance with relevant instructions. (3) The occurrence of infection, allergy and fever in both groups was observed and recorded, and the total incidence rate was calculated. (4) Participants were categorized into those with good prognosis (GP) and those with poor prognosis (PP) based on the presence of adverse reactions. A comparison of clinical profiles between the groups was conducted. Additionally, a multivariate binary logistic regression analysis was employed to evaluate possible factors affecting the outcomes of women with PCSH.

Table 1. General information of patients

Group	Age ($\bar{x}$±s, year)	Gestational age ($\bar{x}$±s, week)	Blood loss ($\bar{x}$±s, mL)	Blood transfusion ($\bar{x}$±s, mL)	BMI ($\bar{x}$±s, Kg/m^2)	Type of maternity [n (%)]		
						Scarred uterus and placenta implantation	Complete placenta previa	Hemorrhage in placental abruption
Group A (n = 30)	27.66±5.79	38.26±1.47	1090.30±130.10	772.52±51.20	24.61±2.93	10 (33.33)	13 (43.33)	7 (23.34)
Group B (n = 30)	26.92±5.35	38.53±1.39	1128.20±112.40	760.66±53.10	23.87±2.88	9 (30.00)	15 (50.00)	6 (10.00)
t/χ^2	0.533	-0.722	-1.259	0.918	0.992		0.272	
P	0.596	0.473	0.213	0.362	0.326		0.873	

Table 2. Comparison of blood indexes in the two groups of patients

Group	Time	Hb (g/L)	HCT (%)	RBC (10^{12}/L)
Group A (n = 30)	T0	122.81±16.23	0.39±0.04	3.39±0.44
	T1	116.32±16.45	0.34±0.06	3.22±0.45
t		1.468	1.892	1.700
P		0.153	0.068	0.100
Group B (n = 30)	T0	120.61±16.43	0.40±0.05	3.42±0.45
	T1	119.51±16.32	0.37±0.07	3.33±0.52
t		0.256	1.771	0.689
P		0.800	0.087	0.496

Note: Hb: hemoglobin; HCT: hematocrit; RBC: red blood cell count.

Statistical methods

Data analysis was performed using SPSS version 20.0. Numerical data were expressed as mean ± standard deviation, and group comparisons were conducted using the t-test. Categorical data were presented as [n (%)], and group comparisons were analyzed using the χ^2 test. Logistic regression analysis was employed to explore potential factors influencing postpartum hemorrhage in women undergoing cesarean section. Differences were significant when P<0.05.

Results

Comparison of general information

A total of 60 cases were included in the study. The general information analysis showed that there were no significant differences in the basic data, such as weight, age, and gestational age (P>0.05), indicating that the two groups were comparable, as shown in **Table 1**.

Comparison of blood parameters

No significant differences in routine blood parameters were observed between the two groups at both T0 and T1 (P>0.05). See **Table 2**.

Comparison of coagulation function

At T0, there were no significant differences observed in the PT, APTT, TT, or FIB between the groups (P>0.05). However, upon comparison with T0, both groups experienced a reduction in the PT, APTT, and TT values at T1, with Group B experiencing a more striking decrease than Group A (P<0.05). Additionally, FIB levels at T1 increased in both groups compared to T0, with Group B demonstrating a higher increase compared to Group A (P<0.05). See **Figure 1**.

Comparison of hemodynamic indexes

At T0, the blood pressure and heart rate measurements between both groups were comparable, with no notable differences (P>0.05). At T1, however, there was a noticeable increase in blood pressure in both groups compared to T0, with Group B showing a more pronounced elevation than Group A (P<0.05). See **Table 3**.

Incidence of adverse reactions

The occurrence of adverse reactions was significantly lower in Group B (1/30, 3.33%), compared to Group A (7/30, 23.33%) (P<0.05). See **Table 4**.

Investigation of factors contributing to adverse outcome

According to the occurrence of adverse reactions, the subjects were redivided into GP and PP groups, comprising 52 cases with prognosis outcomes and 8 cases with poor outcomes. Cut-off values for PT, APTT, TT, FIB, SBP, DBP, and HR after blood transfusion (T1) were deter-

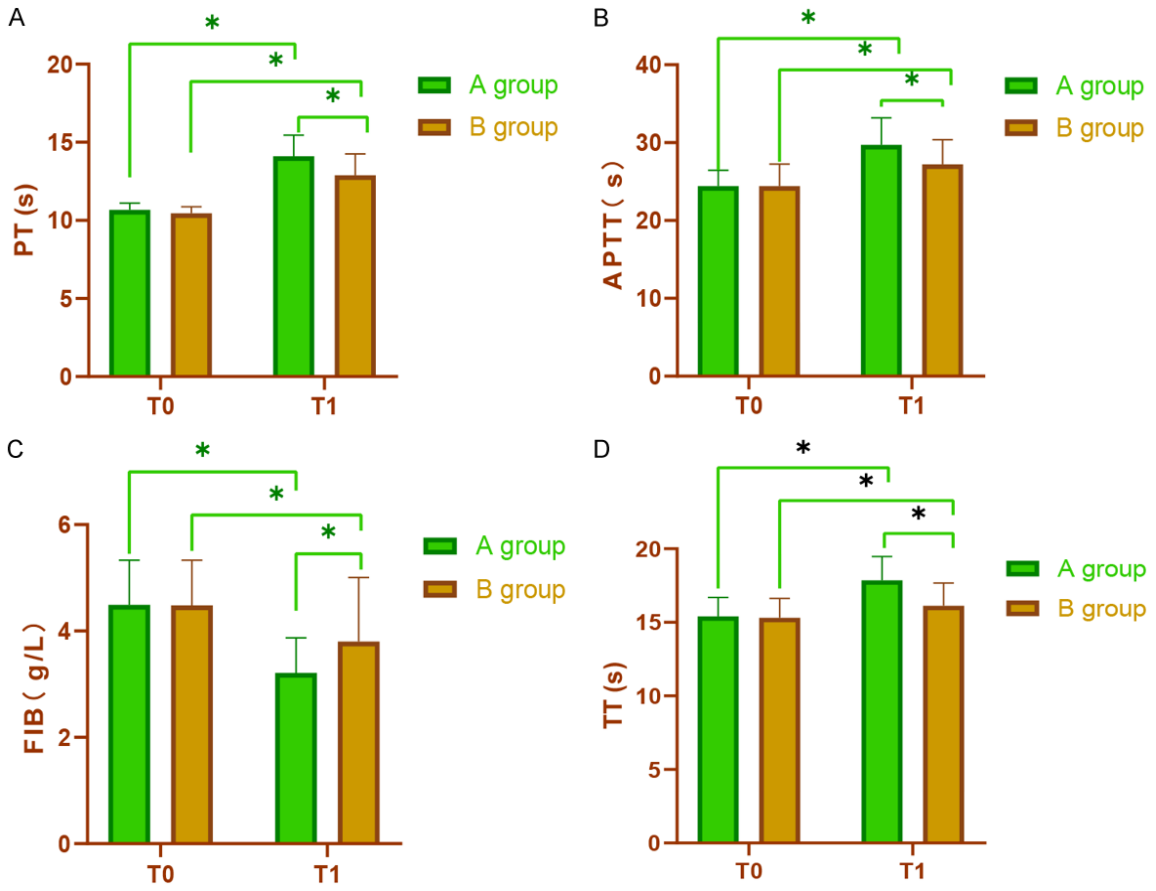

Figure 1. Comparison of coagulation function between the two groups. Note: *P<0.05; A: PT; B: APTT; C: FIB; D: TT; PT: prothrombin time; APTT: activated partial thromboplastin time; TT: thrombin time; FIB: fibrinogen.

Table 3. Comparison of hemodynamic indexes between the two groups

Group	Time	SBP (mmHg)	DBP (mmHg)	HR (times/min)
Group A (n = 30)	T0	87.42±7.32	45.07±8.04	106.39±10.14
	T1	102.03±8.29	61.27±9.43	72.52±8.47
t		-7.692	-6.482	13.763
P		<0.001	<0.001	<0.001
Group B (n = 30)	T0	90.31±7.46	44.41±8.65	107.62±9.24
	T1	115.55±10.15*	70.34±8.36*	78.62±8.82*
t		-13.488	-12.396	11.559
P		<0.001	<0.001	<0.001

Note: Compared toGroup A at T1: *P<0.05; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate.

Table 4. Comparison of the incidence of adverse reactions between the two groups [n (%)]

Group	Fever	Pulmonary edema	Rash	Hemolysis	Total
Group A (n = 30)	1 (3.33)	2 (6.67)	4 (13.33)	0 (0.00)	7 (23.33)
Group B (n = 30)	0 (0.00)	0 (0.00)	1 (3.33)	0 (0.00)	1 (3.33)
χ^2					5.192
P					0.023

Table 5. Univariant analysis of factors affecting the prognosis [n (%)]

Items		GP (n = 52)	PP (n = 8)	χ^2	P
Blood transfusion method	ICS	29 (55.77)	1 (12.50)	5.192	0.023
	ABT	23 (44.23)	7 (87.50)		
PT (s)	<14.33	39 (75.00)	7 (87.50)	0.606	0.436
	≥14.33	13 (25.00)	1 (12.50)		
APTT (s)	<28.41	23 (44.23)	5 (62.50)	0.930	0.335
	≥28.41	29 (55.77)	3 (37.50)		
TT (s)	<19.58	48 (92.31)	0 (0.00)	0.659	0.417
	≥19.58	4 (7.69)	8 (100.00)		
FIB (g/L)	<1.52	10 (19.23)	5 (62.50)	6.923	0.009
	≥1.52	42 (80.77)	3 (37.50)		
SBP (mmHg)	<95.08	19 (36.54)	2 (25.00)	4.220	0.040
	≥95.08	33 (63.46)	6 (75.00)		
DBP (mmHg)	<67.72	4 (7.69)	2 (25.00)	2.308	0.129
	≥67.72	48 (92.31)	6 (75.00)		
HR (times/min)	<69.83	9 (17.31)	5 (62.50)	7.916	0.005
	≥69.83	43 (82.69)	3 (37.50)		

Note: GP: good prognosis; PP: poor prognosis; PT: prothrombin time; APTT: activated partial thromboplastin time; TT: thrombin time; FIB: fibrinogen; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate.

Table 6. Assignment table

Prognosis	Good prognosis (GP) group = 0, poor prognosis (PP) group = 1
Blood transfusion method	ICS = 0, ABT = 1
FIB (g/L)	<1.52 = 1, ≥1.52 = 0
SBP (mmHg)	<95.08 = 1, ≥95.08 = 0
HR (times/min)	<45.35 = 1, ≥45.35 = 0

Note: FIB: fibrinogen; SBP: systolic blood pressure; HR: heart rate.

mined as follows: 14.33 s, 28.41 s, 19.58 s, 1.52 g/L, 95.08 mmHg, 67.72 mmHg, and 69.83 times/min, respectively. Based on these thresholds, subjects were categorized accordingly. Univariate analysis showed the significance of FIB, SBP, and HR at T1. Subsequently, these factors were included in multivariate logistic regression analysis (binary assignment detailed in **Table 6**). It was found that FIB<1.52 g/L and HR<69.83 times/min were associated with an increased risk of poor outcomes in women experiencing PCSH. See **Table 5** and **Figure 2**.

Discussion

Postpartum hemorrhage stands as the most prevalent complication following cesarean section deliveries. Once postpartum bleeding exceeds 500 ml, it can disrupt the patient's systemic blood supply, resulting in abnormal fluctuations in vital signs like blood pressure and heart rate. With escalating bleeding volumes, maternal life becomes increasingly endangered [15, 16]. Statistics reveal that about 100,000 individuals worldwide die from postpartum hemorrhage annually, constituting 27.1% of total maternal deaths [17]. Treatment modalities for postpartum hemorrhage primarily encompass intraoperative hemostasis, pharmaceutical interventions, fluid resuscitation, and blood transfusion. Among these, blood transfusion plays a pivotal role, encompassing both ABT and ICS. While ABT offers clinical convenience, it carries a risk of transmitting various viruses and may elicit adverse reactions due to allogeneic immune responses [18]. Extensive research demonstrates the relative safety of ICS, effectively conserving blood resources and mitigating the occurrence of adverse reactions such as blood-borne infection and allergic responses associated with

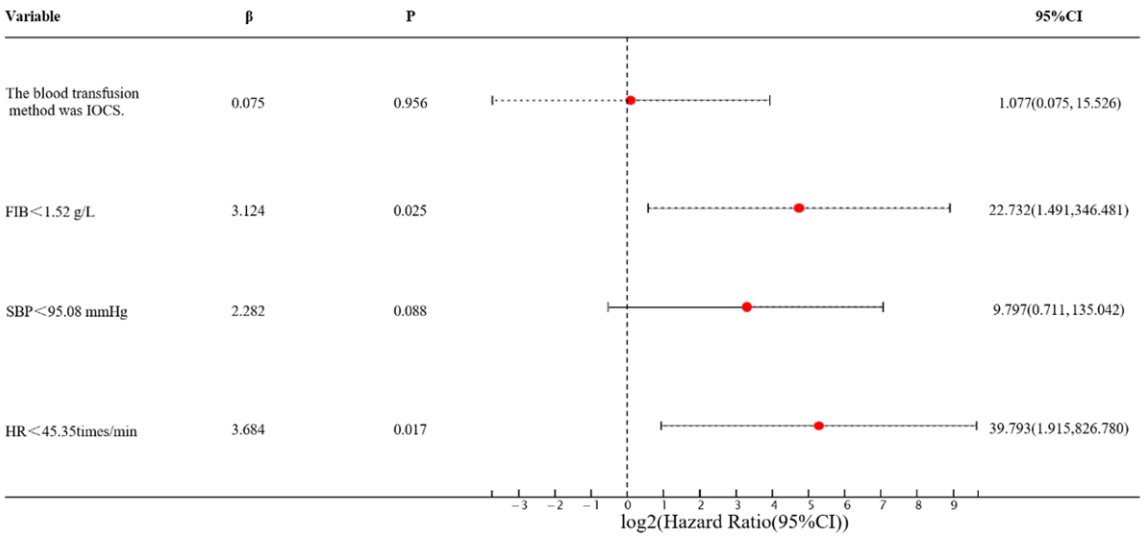

Figure 2. Multivariate logistic regression analysis of factors contributing to poor prognosis in patients with postpartum hemorrhage after cesarean section. Note: FIB: fibrinogen; SBP: systolic blood pressure; HR: heart rate.

ABT. Therefore, it is widely used in cardiac surgery, orthopedics and other surgical procedures characterized by substantial intraoperative blood loss [19, 20].

With advancements in medical technology, the application of ICS in the management of postpartum hemorrhage following cesarean section has demonstrated promising outcomes. Clark et al. [21] found that while amniotic fluid components can be detected in maternal blood, the concentration of these components in autologous blood recovered during operation, after being processed by recycling machines, is lower than that of maternal blood itself. This suggests that the presence of amniotic fluid components in autologous blood transfusion during cesarean section is insufficient to induce adverse effects in parturients. Additionally, studies have highlighted the efficacy of white blood cell filters, in conjunction with blood recycling machines, for effectively removing amniotic fluid and fetal squamous cells. This not only mitigates the risks associated with ABT but also conserves blood volume, enhances immune function, and facilitates maternal postoperative recovery [22]. In this study, 60 parturients experiencing PCSH were treated with either ICS or ABT were compared. The results indicated no significant differences in HCT, RBC, and Hb levels at T1 ($P>0.05$), suggesting that ICS did not markedly alter the patients' blood profiles. Moreover, the incidence of adverse reactions in the ICS B was significantly lower at 3.33% (1/30) compared to 23.33% in Group A, consistent with findings by Li et al. [23]. This suggests that the application of ICS in parturients with PCSH does not interfere with the treatment process and can reduce the incidence of adverse reactions after blood transfusion. This improvement is attributed to ICS reducing the risk of infection and rejection of allogeneic blood transfusion, because of its safety profile of preserving the stability of the internal environment of the parturient, resulting in relatively fewer adverse reactions [24].

A large amount of autologous blood recovery can indeed disrupt the body's electrolyte balance and coagulation function, posing challenges to treatment [25]. In this study, the effects of two blood transfusion methods on maternal coagulation function were compared and analyzed. The findings revealed that both groups experienced prolonged APTT and PT after blood transfusion, indicating a certain degree of impact on the parturients' coagulation function. However, these changes remained within the normal range and may be attributed to postpartum hemorrhage. Interestingly, the prolongation of APTT and PT in the ICS group was less significant than that in the ABT group. This difference could be attributed to the use of the parturient's own blood in ICS, which reduces the immune response to foreign blood and minimizes interference with

the coagulation system compared to ABT. Furthermore, the post-transfusion FIB level was higher in the ICS group compared to the ABT group ($P<0.05$). This observation may be attributed to the normal range of coagulation factors, typically between 20% and 30%, crucial for maintaining proper clotting mechanisms in the body. During the blood recovery process, factors such as filtration, centrifugation, and anticoagulant addition can lead to a loss of coagulation factors and a reduction in platelet numbers. Excessive blood recovery can result in abnormal coagulation function. Therefore, recovered autologous blood transfusion necessitates washing and filtration by a blood recovery machine before reinfusion. Real-time supplementation of the patient's blood volume through circulating reinfusion ensures compatibility with the patient's own blood and helps maintain coagulation factors within the normal range [26].

Furthermore, this study also compared and analyzed the hemodynamic parameters of the two groups. The findings revealed a significant increase in blood pressure following blood transfusion in both groups compared to pre-transfusion levels. Notably, the ICS group exhibited a more substantial increase in blood pressure and heart rate compared to the ABT group. Tsuggests that the application of autologous blood transfusion technology can enhance patient his hemodynamics and mitigate the drop in blood pressure and increase in heart rate induced by postpartum hemorrhage. The rationale behind this analysis lies in the use of the mother's own blood in recycled autologous blood transfusion, which reduces interference from immune responses and foreign blood coagulation systems, thereby promoting hemodynamic stability. Additionally, autologous blood transfusion recovery helps mitigate the risk of transfusion reaction and infectious diseases associated with ABT, minimizing the negative impact on the pregnant woman. Moreover, univariate and multivariate logistic regression analyses were employed to identify factors influencing the poor prognosis of patients with PCSH. It was determined that FIB<1.52 g/L and HR<69.83 times/min were associated with an increased risk of unfavorable outcome in such patients. Consequently, timely assessment of coagulation function and vigilant monitoring of vital sign changes, including FIB levels and heart rate, are crucial for the prevention and treatment of complications in patients experiencing massive PCSH.

Conclusions

ICS emerged as a superior alternative to ABT for restoring blood parameters among parturients, while also significantly reducing the incidence of postoperative adverse reactions. This method is particularly suitable for patients experiencing PCSH. However, this study has certain limitations. The small sample size may not entirely capture the comprehensive application effectiveness of ICS in patients with PCSH. Future research should aim to address this limitation by expanding the sample size, thus further validating the clinical value of this blood transfusion approach.

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Disclosure of conflict of interest

None.

Address correspondence to: Zhongjun Zhang, Wuxi Medical College, Jiangnan University, No. 1800, Lihu Avenue, Binhu District, Wuxi 214122, Jiangsu, China. Tel: +86-0527-82086316; E-mail: zhongjunzhang2023@163.com

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