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Original Article

Factors associated with different levels of postpartum hemorrhage in patients experiencing blood transfusion during cesarean section

Yiying Huang, Yirong Bao, Xiaoxian Qu, Ling Yuan, Hao Ying

Department of Obstetrics, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Shanghai 201204, China

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Abstract: Objective: This study aimed to examine risk factors correlated with different levels of blood loss during cesarean section (CS), with an emphasis on massive obstetric hemorrhage. Methods: A retrospective study was conducted involving 271 women who experienced postpartum hemorrhage (PPH) during CS from January 2006 to December 2013: Based on the volume of blood loss during CS, these women were divided into 3 groups: low (<1500 ml), moderate (≥1500 ml and <3000 ml) and massive (≥3000 ml). All cases received packed red blood cell (PRBC) transfusions. Risk factors were compared between the low and moderate, low and massive, and moderate and massive PPH groups. Results: Women with placenta previa (PP) were more likely to have moderate bleeding (adjusted odds ratio [aOR], 2.947; 95% confidence interval [CI], 1.336-6.498) but less likely to have massive bleeding (aOR, 2.322; 95% CI, 0.854-6.310). Placenta accreta may increase the risk of moderate (aOR, 2.358; 95% CI, 1.130-5.397) or massive PPH (aOR, 3.242; 95% CI, 1.209-8.692). Pernicious placenta previa (PPP) significantly increased the risk of massive bleeding (aOR, 20.234; 95% CI, 3.617-113.250). Conclusions: Various risk factors are associated with the severity of PPH. In particular, PPP was a significant indicator of massive PPH.

Keywords: Cesarean section, placenta accreta, placenta previa, postpartum hemorrhage, transfusion

Introduction

Postpartum hemorrhage (PPH) is a common emergency and remains the leading cause of maternal death worldwide even though various guidelines and conservative therapies have been developed and implemented. It has been reported that 10-35% of maternal death scan be attributed to PPH worldwide [1]. In China, one-third of maternal deaths are linked to obstetric hemorrhage, especially severe PPH [2].

The severity of maternal complications varies with different amounts of blood loss. Massive PPH may lead to hypovolemic shock, disseminated intravascular coagulation (DIC), peripartum hysterectomy, and even maternal death. Many cases that proceed to massive PPH occur due an underestimation of a patient's risk factors and insufficient preoperative evaluation [3]. Therefore, sufficient risk assessment and adequate preparations must be conducted to decrease maternal morbidity. The well-known risk factors for PPH in CS include uterine atony, abnormal placenta implantation, previous uterine surgery, preeclampsia, prolonged labor, obesity, and advanced maternal age [4]. However, little is known about the respective risk factors for blood loss at different levels, in particular, those for extensive blood loss that requires blood transfusion.

The purpose of our study was to evaluate the respective risk factors for blood loss at different levels in patients who experience blood transfusion during CS.

Materials and methods

Patients and grouping

The Institution Review Board of our hospital approved the study. A retrospective study of women who experienced PPH in CS was conducted. The database of the obstetric depart-

Table 1. Clinical and demographic characteristics of the 3 study groups

	Low group (n=118)	Medium group (n=97)	Massive group (n=56)	F	*P*
Age, y	30.39±4.36	31.89±4.51	30.82±4.49	3.091	0.047
BMI, kg/m^2	22.57±3.37	24.06±3.41	24.17±3.86	5.145	0.007
Birth weight, g	3209.30±934.05	3168.14±937.36	3029.55±944.93	0.579	0.561
Gestational week, wk	35.97±5.42	36.52±4.13	36.03±3.53	0.417	0.659
Blood loss, ml	1035.2±255.5	1985.0±415.59	4418.9±1718.36	303.716	0.000
PRBCs, u	4.26±1.53	7.04±2.94	16.02±5.84	130.457	0.000

Notes: BMI, Body mass index; PRBC, Packed red blood cell. Values are given as the mean ± SD or number (n) unless otherwise indicated.

ment of our hospital was searched. A time limit of Jan 2006 to Dec 2013 and the key words "PPH, CS, Transfusion" were applied. All patients with PPH during CS who required blood transfusion were included. Patients with preexisting medical conditions such as heart disease, chronic hepatic or renal insufficiency, or primary coagulation defects were excluded. A total of 271 cases met the criteria and were included. All cases were reviewed by a resident.

The 271 PPH cases were divided into 3 groups based on blood loss. In the low group, 118 women had blood loss of <1500 ml; in the moderate group, 97 women were noted (≥1500 ml and <3000 ml); the remaining 56 women were in the massive group (≥3000 ml). The following data were collected for each woman: age at delivery, gravidity, parity, gestational week at delivery, and body mass index (BMI). The following risk factors were examined: method of conception, presence of a scarred uterus, placenta previa, pernicious placenta previa, placenta accreta, and uterine contraction atony. The primary outcomes were estimated blood loss and units of packed red blood cells (PRBCs). One unit of PRBC was considered equal to 200 ml of whole blood.

Pernicious placenta previa (PPP) defines placenta previa covers previous uterine scar [5]. Women with placenta previa (PP) or PPP were confirmed by ultrasound examination. Placenta accreta was diagnosed primarily by a clinical diagnosis or histopathology report. The clinical diagnosis was based on an operative report of the difficulty of manually removing the placenta during CS with excessive bleeding from the placental site. The area of accreta was categorized as partial or total.

Statistical analysis

SPSS 19.0 software (SPSS, Inc., Chicago, IL) was used for the statistical analysis. For continuous variables, one-way analysis of variance (ANOVA) tests were used for comparisons among groups, and medians were expressed as the means ± standard deviation. Multiple ordinal logistic regression analyses were used to quantify the different levels of blood loss. All tests were two-tailed with the risk set at the 5% level, and statistical significance was defined as $P<0.05$. For multiple comparisons among groups, multivariable logistic regression analyses were used to calculate odds ratios (ORs) and their 95% confidence intervals (95% CI). We applied the Bonferroni correction and the *P*-value was adjusted to 0.017 (0.05/3).

Results

A total of 271 women who met the inclusion criteria were identified. The clinical and demographic characteristics of the patients are shown in **Table 1**. Statistically significant differences in maternal age ($P=0.047$), BMI ($P=0.007$), blood loss and transfusion volume ($P<0.001$) were observed among the 3 study groups. Differences in birth weight and gestational weeks among the 3 groups did not reach statistical significance.

As shown in **Table 2**, PPP ($P=0.019$), placenta accrete ($P=0.048$) and uterine atony ($P=0.046$) showed significant differences among the 3 groups. These factors were correlated with the severity of PPH. Associations between PPH and the other risk factors were not significant among the 3 study groups.

Factors associated with the severity of PPH were further analyzed between the low and

Table 2. Adjusted odds ratios for PPH for low vs. moderate, low vs. massive, and moderate vs. massive groups

	Low group % (n=118)	Moderate group % (n=97)	Massive group % (n=56)	*P*	Low vs. Moderate		Low vs. Massive		Moderate vs. Massive	
					AOR	95% CI	AOR	95% CI	AOR	95% CI
Gravidity (≥3)	29.7 (35)	41.2 (40)	44.6 (25)	0.363	1.009	0.422-2.414	1.281	0.439-3.743	0.603	0.179-2.038
Parity (≥1)	16.9 (25)	26.8 (26)	28.6 (16)	0.800	1.218	0.429-3.552	0.436	0.094-2.031	0.761	0.191-3.027
Assisted conception	20 (22/115)[a]	18.8 (18/96)	9.3 (5/54)	0.224	0.715	0.316-1.616	0.276	0.080-0.956	0.386	0.114-1.312
PP	16.1 (19)	37.1 (36)	28.6 (16)	0.061	2.947	1.336-6.498	2.322	0.854-6.310	0.788	0.315-1.970
PPP	2.5 (3)	6.2 (6)	17.9 (10)	0.019	3.570	0.676-18.860	20.234	3.617-113.250	5.669	1.316-24.414
Placenta accreta	16.9 (20)	28.9 (28)	26.8 (15)	0.048	2.358	1.030-5.397	3.242	1.209-8.692	1.375	0.558-3.388
Uterine atony	33.9 (40)	39.2 (38)	41.1 (23)	0.046	1.975	0.980-3.981	3.653	1.538-8.680	1.850	0.788-4.344

Notes: BMI, Body mass index; PP, Placenta previa; PPP, Pernicious placenta previa. Values are given as the percentage (number) unless otherwise indicated. [a]: (n/n) 22 women experienced bleeding in the low group among 115 assisted conception patients, and 3 were lost to follow-up. AOR, Adjusted for maternal age and BMI.

moderate PPH, low and massive PPH, and moderate and massive PPH groups, as shown in **Table 2**. Assisted conception was not correlated with PPH (low vs. moderate aOR, 0.715; 95% CI, 0.316-1.616; low vs. massive aOR, 0.276; 95% CI, 0.080-0.956). PP was associated with an increased risk of moderate PPH (aOR, 2.947; 95% CI, 1.336-6.498). Interestingly, this association did not exist between PP and massive PPH (aOR, 2.322; 95% CI, 0.854-6.310). PPP is a strong indicator of massive PPH (aOR, 20.234; 95% CI, 3.617-113.250), although the difference between the low and moderate PPH groups was not significant (aOR, 3.570; 95% CI, 0.676-18.860). Uterine atony (aOR, 3.653; 95% CI, 1.538-8.680) was a factor associated with massive PPH. Placenta accreta increased the risk of PPH (low vs. moderate aOR, 2.358; 95% CI, 1.030-5.397; low vs. massive aOR, 3.242; 95% CI, 1.209-8.692).

Discussion

Obstetric hemorrhage remains a leading cause of maternal morbidity and mortality. Serious complications such as peripartum hysterectomy are common among women who experience massive blood loss and require blood transfusion. Many previous studies focused primarily on the risk factors of PPH in general [6, 7]. Little is known about risk factors specific to blood loss at different levels, particularly the moderate to massive level. A review of the literature suggested that the key to a favorable outcome following maternal hemorrhage lies in sufficient risk assessment and a multi-disciplinary schedule. In 2010, the California Maternal Quality Care Collaborative Risk Stratification established guidelines for assessing peripartum hemorrhage using clinical and laboratory indicators [8]. The establishment of risk stratification is of critical importance to decreasing maternal morbidity and mortality. Our study aimed to evaluate risk factors correlated with different levels of blood loss in patients who experienced transfusion.

PP is an important risk factor that leads to postpartum hemorrhage [9]. Prior to the wide application of surgical measures, uterotonics were an insufficient means of controlling this type of bleeding from the placental bed. PP is usually the reason for massive hemorrhage. Since the publication of an initial report in 1997 by B-Lynch, many local uterine suture compressions have been reported to control intractable bleeding from the lower segment of the uterus among women with PP [10]. Our study found that women with PP were more likely to bleed moderately (<3000 ml) than massively (≥3000 ml). In 2011, the study reported that among 131,731 women who had an elective CS for a singleton, 4,332 (3.3%) had placenta previa [11]. Placenta previa increased the risk of PPH, blood transfusion and hysterectomy. However, the risk of blood transfusion and caesarean hysterectomy may be lower than before. The results of our study are consistent with this finding. This decreased risk is possibly due to improvements in clinical practice such as the wide application of uterine compression sutures and earlier intervention. How and when to intervene are of a vital influence on the prognosis [12].

PPP is a special type of PP. Chattopadhyay proposed the concept of PPP in 1993 [5]. Women with PPP have been shown to have a high risk of PPH. In our study, women with PPP were more likely to bleed massively (≥3000 ml) than moderately (<3000 ml). Blood loss in patients with PPP was more severe than in those with PP. It has been reported that the average bleeding volume of PPP is 3000-5000 ml [8]. Traditional conservative treatments such as medical and surgical methods usually fail to control the bleeding of PPP. The lack of smooth muscle in the lower uterine segment makes it unresponsive to uterotonic agents. Uterine balloon compression is also unable to effectively arrest such bleeding. Another important reason for massive PPH is that PPP is usually accompanied by placenta accreta or increta, even percreta into the bladder. Endometrial defects and abnormal decidualization and vascularization at the scar area are associated with abnormal deep trophoblastic infiltration. In a large prospective observational study that considered the number of prior cesarean deliveries and the presence or absence of placenta previa, with the presence of PP, the risk of placenta accreta was 3% at the first cesarean delivery. The likelihood of placenta accreta increases dramatically to 40% or more at the third cesarean delivery [13]. Separation of the placenta from its underlying vascular myometrial bed may lead to strong bleeding. Surgical sutures sometimes fail to arrest bleeding from

the large utero-placental sinuses, particularly in cases of placenta increta and percreta. When all conservative measures fail, hysterectomy is performed. Almost 40-50% of peripartum hysterectomies are due to abnormal placentation [14, 15]. Our study indicated that PPP can be a strong risk factor for massive bleeding, especially bleeding of more than 3000 ml. Preoperative diagnosis of abnormal adherent placenta by ultrasound or magnetic resonance imaging (MRI) is imperative. In our medical center, we lack equipment for arterial embolization and prophylactic artery balloon catheterization, and therefore, surgical sutures remain the major method for controlling PPP bleeding. Could interventional treatment reduce the rate of massive PPH or hysterectomy in patients with PPP. Some studies have found a role for prophylactic uterine artery balloon catheters in the management of women with suspected placenta accreta or increta, although few have reported their use in women with PPP [16]. Further research is needed.

Placenta accreta is considered a severe pregnancy complication that may be associated with PPH. In recent years, abnormal placentation has become a predominant indication for peripartum hysterectomy, especially in women with PP or PPP [17, 18]. In 2011, Wright et al. reported that among women with placenta accreta, 77.9% bleed less than 5000 ml [19]. Similar findings were discovered in our study. Placenta accreta increased the risk of moderate to massive bleeding. The amount of blood loss was related to the area and the degree of trophoblastic invasion. Women with focal or less severe abnormal placenta implantation are less likely to have massive bleeding [20]. In our report, we selected 1500 and 3000 ml as the cut-off points for moderate and massive PPH. Sixty-three patients experienced PPH due to placenta accreta. Among them, 48 patients (76.2%) had blood loss less than 3000 ml. In most cases, placenta accrete was focal and mild, and local uterine suture compressions were able to control the bleeding quickly and effectively, as the bleeding was more likely moderate. Previous uterine surgery or curettage may increase the risk of placenta accreta. If placenta accrete is combined with placenta previa or previous uterine scarring, as mentioned previously for PPP, the degree of placenta accrete may be severe because of decidua defects at the uterine scar. Thus, the possibility of massive bleeding could increase dramatically. The severity of bleeding was determined by the area and degree of placenta accreta.

It was previously reported that obesity during pregnancy increases the risk of PPH. A statistically significant difference in BMI was observed among the 3 groups in our study. Morbid obesity is a risk factor associated with significant peripartum hemorrhage. Increased BMI is associated with uterine atony and a higher rate of CS [8, 21]. The association between assisted conception and PPH may be attributed to increases in multiple pregnancy and abnormal placentation [22]. However, our data did not identify any relationship between these two factors. Women with assisted conception may have an increased risk of PPH, although any association with blood loss more than 1500 ml remains equivocal.

Our hospital is a tertiary medical center in Shanghai. Our large patient body includes women at high risk for PPH who have been drawn from lower-tier health care institutions. Thus, we were able to study associations between risk factors and different levels of PPH.

Most previous studies have focused on risk factors of overall PPH. The classification of blood loss levels and the evaluation of the correlated risk factors are the major strengths of our study. In contrast with past studies, we sought to evaluate the severity of various risk factors for PPH preoperatively. We aim to prevent massive PPH on the basis of adequate preoperative evaluation.

This study was conducted retrospectively. In our hospital, the primary management for PPH includes medical uterotonics, uterine compression sutures, artery ligation, and Bakri balloon compression. We lack equipment for arterial embolization and artery balloon catheterization. The management of bleeding may not be standardized because each obstetrician has his or her own familiar hemostasis method to control bleeding.

The definitive diagnosis of placenta accreta relies on histopathology. However, histopathology is not always possible because the majority of cases are managed conservatively, with hysterectomy serving as a last resort to preserve

life. Thus, the diagnosis of placenta accrete is often a matter of subjectivity.

Another limitation of our study is that our target patient population was focused only on women delivering by CS. Further research is needed to obtain a better understanding of the same subject among women undergoing vaginal delivery.

In conclusions, different risk factors are associated with PPH of different severity. Our study showed that PPP was a risk factor for extremely severe PPH. Therefore, reducing the rate of primary cesarean deliveries is important. Careful antepartum surveillance for women with previous uterine surgery is essential, and ultrasound monitoring of abnormal placentation is necessary. Proactive preparation prior to the operation with a multi-disciplinary approach is also critical. Timely delivery may help minimize the occurrence of maternal complications associated with massive PPH. Given adequate risk assessment and constant monitoring, the rate of massive PPH will decrease.

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Disclosure of conflict of interest

None.

Address correspondence to: Hao Ying, Department of Obstetrics, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, No. 2699 Gaokexi Road, Pudong, Shanghai 201204, China. Tel: +862120261222; Fax: +862150730190; E-mail: yinghaoshdoc@163.com

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