The risk factor of postpartum hemorrhage after cesarean section for placenta previa: A retrospective study

Hiroki Ishibashi
National Defence Medical College

Morikazu Miyamoto (morikazu1118@hotmail.co.jp)
National Defence Medical College
https://orcid.org/0000-0003-4763-0926

Hiroaki Soyama
National Defence Medical College

Hideki Iwahashi
National Defence Medical College

Haruka Kawauchi
National Defence Medical College

Kazuki Takasaki
National Defence Medical College

Hiroko Matuura
National Defence Medical College

Masaya Nakatsuka
National Defence Medical College

Taira Hada
National Defence Medical College

Masashi Takano
National Defence Medical College

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Abstract

Background Placenta previa could induce postpartum hemorrhage (PPH). Even cases with less intraoperative hemorrhage during cesarean section had the potential risk to develop PPH. But, there were less report about the predictive factor of PPH associated with placenta previa. The aim of this study was to identify the predictive factor for PPH for women with placenta previa after cesarean section. Methods Women with placenta previa who underwent cesarean section at our institution between January 2003 and February 2015 were identified. Women that received any hemostatic procedure such as intrauterine balloon tamponade and gauze infiltration during cesarean section were excluded. All women were classified into two groups: Group A or with PPH, defined as over 500 ml of hemorrhage after cesarean section, and Group B or without PPH. A retrospective analysis to identify the predictive factor of PPH was conducted. Results Out of 128 women, 10 (7.8%) women were included in Group A and 118 (92.2%) women in Group B. There was no statistical significance in maternal history between both groups. The number of women suspected to have placental adhesion was higher in Group A than Group B (p=0.006). Furthermore, the amount of intraoperative hemorrhage in Group A was higher than that in Group B (p=0.025). As treatment for PPH, more women in Group A received allogenic blood transfusion (p=0.003), and uterine artery embolization (p = 0.010). In univariate analysis, placental adhesion suspected by surgeon during cesarean section was the predictive factor for PPH with placenta previa (p=0.046). Conclusion When placental adhesion is suspected by surgeons during cesarean section, additional hemostatic procedure should be performed for possible PPH.

Background

Until now, placenta previa has caused maternal and neonatal mortality and morbidity by massive hemorrhage [1,2]. As a result, a more precise and appropriate strategies of prediction and preparation should be developed with the purpose of avoiding these adverse obstetrical outcomes [3,4]. The timing of massive hemorrhage for placenta previa was either in the operative or in the postoperative period [5]. Consequently, prediction and strategies for intraoperative hemorrhage or postpartum hemorrhage (PPH) are needed.

In previous reports, several factors had been used to predict massive hemorrhage in placenta previa, such as high maternal age, cesarean section history, placental adhesion, antenatal bleeding, and heavier birth weight. [6-9]. Also, imaging findings were useful to predict intraoperative hemorrhage. The ultrasonographic (US) findings including sponge like consistency, complete placenta previa, anterior placentation, and shortening of a third-trimester cervical length [6,7,9-15] and magnetic resonance imaging (MRI) findings such as uterine bulging, heterogeneous placenta, adjacent organ invasion, and cervical varicosities could predict placenta accrete [16-18]. Furthermore, effective strategies to decrease intraoperative hemorrhage in placenta previa were intrauterine balloon tamponade and perioperative temporary balloon occlusion of internal iliac artery [19,20].
Placenta previa is well known to be one of the diseases which induced massive PPH [21]. Even cases with less intraoperative hemorrhage during cesarean section had the potential risk to develop massive PPH [22]. Without rapid and appropriate treatment, massive PPH might induce adverse obstetrical outcomes including maternal death [22]. As a strategy for massive PPH associated with placenta previa, previous studies demonstrated that intrauterine balloon tamponade was useful to decrease massive PPH [23-25]. In these reports, the timing of insertion of balloon was after massive PPH [23,24]. Once massive PPH developed, the mother frequently received several treatments including blood transfusion [21]. Therefore, if predictive factors of massive PPH related with placenta previa are identified, hazardous situations can be avoided before massive PPH develop. Therefore, the purpose of this study was to identify predictive factors of massive PPH after cesarean section in cases with placenta previa.

Methods

All singleton pregnancy cases who underwent cesarean section due to placenta previa at our institution, between January 2003 and February 2015, were identified. The inclusion and exclusion criteria were decided according to surgical procedures. The details were indicated as follows. The basic surgical procedure for placenta previa was performed as previously described by Soyama et al [25]. Briefly, after abdominal wall incision, a transverse incision into the lower segment of the uterus was done. In cases with a placenta in the anterior uterine wall, surgeons avoided the placenta and, incision was guided by ultrasound [25]. After delivery and until 24 h after cesarean section, oxytocin 5 IU was started intravenously in a 500-mL saline drip. Methods to remove the placenta and to treat postoperative hemorrhage were as follows: surgeon did not remove the placenta by hand and waited until the placenta separated from uterine wall spontaneously; after, placenta was gently removed by hand when part of placenta was exfoliated and another part was retained in the uterine wall. If intraoperative hemorrhage developed, gauze packing or brace sutures, such as placental bed sutures or compression sutures, alone or combined, were performed at the surgeon’s discretion. Cases that did not receive any hemostatic procedures, as mentioned above, were included in our study. Hence, when no sign of placenta separation was completely developed, placenta was not removed and surgeons closed uterine wall and skin incision, performing instead prophylactic uterine artery embolization (UAE) before the development of massive PPH. All these cases were excluded from this study.

Maternal history and intraoperative information were obtained from medical charts and operative records. In all cases, US and MRI examinations for the diagnosis of placenta previa were performed by experienced obstetricians and radiologists after 30 weeks of gestation. At our institution, elective cesarean section was performed before 38 weeks of gestation according to the Guidelines for Obstetrical Practice in Japan [26]. However, if persistent antenatal bleeding over 100 ml or uncontrollable uterine contractions occurred before prearranged date of cesarean section, an emergency cesarean section was performed. Antenatal bleeding was defined as painless genital bleeding from the placenta. The amount of intraoperative hemorrhage was measured from the time of the skin incision to the time of scar closure, based on suction count and towel weight. PPH was defined as the amount of bleeding from the end of the cesarean section procedure until 24 h after surgery and, PPH as a blood loss over 500 ml within 24
hours after birth [27]. All included cases were categorized into two groups: Group with PPH (Group A) and Group without PPH (Group B). Cases that underwent allogenic blood transfusion included patients who received blood transfusion at pre-parturition, intraoperation, and postpartum time. Placental adhesion was defined by the surgeon's clinical judgement when attempting to remove the placenta, after appearance of the placenta peeling sign, but the placenta did not separate smoothly.

We classified placenta previa into two categories according to Calì et al [28]. If the placenta edge covered internal os, it was diagnosed as major type. If, instead, the placenta edge did not cover cervical internal os and was located in the lower uterine segment, it was classified as minor type.

Antenatal diagnosis of adherent placenta was assessed by MRI findings such as uterine bulging, heterogeneous placenta, adjacent organ invasion, and cervical varicosities [16-18].

Statistical analysis was performed using JMP Pro 14 software (SAS Institute Inc., Cary, NS, USA). Chi-squared test, Fisher’s exact test, and Mann-Whitney U test were used to evaluate the clinical significance of clinical factors. Statistical significance was defined as a p-value < 0.05.

This retrospective study was approved by the Institutional Review Board of the National Defense Medical College, Tokorozawa, Japan.

Results
During the period of this study, 243 cases with placenta previa were identified. Among them, 115 cases were excluded. One case had twin pregnancy and 114 cases received hemostatic procedures during cesarean section. Finally, the total number of 128 cases were included in our study. The rate of cesarean section was 100% and incidence of postpartum hemorrhage was 7.8%.

The clinical characteristics of both groups are presented in Table 1. All cases underwent cesarean section. There was no statistically significant difference in maternal history. According to operative information, there were more patients with suspected placental adhesion in Group A than in Group B (p=0.006). Furthermore, the amount of intraoperative hemorrhage was higher in Group A (p=0.025). The number of cases with antenatal diagnosis of placenta accrete spectrum was 3 in Group A and 7 in Group B. Also, final pathological findings revealed 3 cases in Group A and 2 cases in Group B was complicated with placenta accrete spectrum.

Table 2 showed the procedure after hemorrhage. More cases in Group A received uterine artery embolization (p=0.010) and allogenic blood transfusion (p=0.003) as additional treatment for PPH.

Univariate analysis for massive PPH with placenta previa revealed that placental adherence was the predictive factor (Table 3).

Discussion
In our study, multivariate analysis revealed that only placental adhesion suspected by surgeon during cesarean section was a predictive factor for PPH in placenta previa.

In this study, patients who received any hemostatic procedure, such as intrauterine balloon tamponade, during cesarean section were excluded. The reasoning was that intrauterine balloon tamponade was the effective management of PPH associated with placenta previa. In fact, some reports demonstrated that intrauterine balloon tamponade was effective to decrease both intraoperative and postoperative hemorrhage [19,23,24]. In our institution since March 2015, rapid insertion of intrauterine balloon tamponade to reduce hemorrhage have been performed after spontaneous separation of the placenta and it succeeded in reducing PPH [25]. To make the predictive model for PPH, we considered that the exclusion criteria was valid.

Also, placental adhesion was defined by surgeon’s intraoperative judgement in this study. The definition of placental adhesion by surgeon might be different from that of true placental adhesion using pathological examination [29]. The reason for diagnosing placental adhesion clinically rather than pathologically in our study was because PPH of placenta previa occurred suddenly, particularly within one day after termination [27], and we could not afford to wait for a pathological diagnosis. Therefore, from this point of view, we considered the design of our study to be an appropriate clinical model to predict PPH.

Our results might suggest, that if surgeons suspect placental adhesion, any hemostatic procedures should be performed even though intraoperative massive hemorrhage do not develop. Although our study did not examine the appropriate strategy for PPH, the development of PPH was the urgent problem. According to Soyama et al., intrauterine balloon tamponade could decrease PPH [25]. Also, some studies reported the efficacy of routine prophylactic use of uterotonic drug, such as oxytocin and tranexamic acid [30,31]. Further studies need to examine the effective methods, including these, for patients with a risk factor of PPH.

This study has some limitations which have to be point out. The retrospective design, single institutional study and the small sample size did not allow us to develop an appropriate strategy for this problem. Our study has a strong selection bias because of our exclusion criteria. Further prospective studies are necessary to reveal the correlation between PPH with placenta previa and risk factors and, to develop appropriate strategies.

**Conclusions**

Placental adhesion was the predictive factor for PPH associated with placenta previa. The prevention for PPH might be necessary for women with placental adhesion.

**Abbreviations**

PPH: Postpartum hemorrhage
Declarations

Disclosure of potential conflicts of interest

None.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. For this type of study, formal consent is not required. For the retrospective analysis, informed consent was not obtained. This study was approved by the Clinical Research Ethics Committee of the National Defense Medical College.

Consent to publication

All data was anonymised so individual consent for publication was not applicable.

Availability of data and materials

All data analysed in this study are available from the corresponding author upon reasonable request.

Competing interests

All authors declare that they have no competing interests.

Fundings

None.

Author Contributions

Protocol/project development: H I, M M, and M T.

Data collection or management: H I, H S, H I, H K, K T, H M, and M N.

Data analysis: H I and M M.
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Table 1: Characteristics of patients with placenta previa.
| Clinical factors                              | Group A† | Group B‡ | p-value  |
|----------------------------------------------|----------|----------|----------|
|                                              | n=10     | n=118    |          |
| **Maternal history**                         |          |          |          |
| Maternal age (y), mean ±SD§                  | 33.9±3.6 | 33.5±4.9 | 0.814    |
| Gestational age (w), mean ±SD                | 36.4±1.5 | 36.4±1.5 | 0.859    |
| Primipara, number (%)                        | 3 (30.0) | 61 (51.69)| 0.324    |
| ART¶ pregnancy, number (%)                  | 2 (20.0) | 8 (6.78) | 0.176    |
| Repeat cesarean section, number (%)          | 2 (20.0) | 15 (12.7)| 0.621    |
| Tocolytic agent use, number (%)              | 3 (30.0) | 44 (37.3)| 0.745    |
| Complication of myoma, number (%)            | 0 (0.0)  | 12 (10.2)| 0.597    |
| Placental classification                     |          |          | 0.192    |
| Major placenta, number (%)                  | 7 (70.0) | 54 (45.8)|          |
| Minor placenta, number (%)                  | 3 (30.0) | 64 (54.2)|          |
| Placenta on anterior wall, number (%)        | 2 (20.0) | 17 (14.41)| 0.643   |
| Antenatal bleeding, number (%)               | 5 (50.0) | 36 (30.51)| 0.289   |
| **Operative information**                    |          |          |          |
| Emergency delivery, number (%)              | 3 (30.0) | 30 (25.4)| 0.717    |
| Transverse uterine incision, number (%)      | 2 (20.0) | 5 (4.2)  | 0.094    |
| Baby weight (g), mean ±SD                    | 2660.0±387.6 | 2549.6±421.2 | 0.667   |
| Placental adhesion, number (%)               | 3 (30.0) | 3 (2.5)  | 0.006    |
| Operation time (min), mean ±SD               | 80.9±61.0| 55.3±24.3| 0.267    |
| Intraoperative hemorrhage (ml), mean ±SD     | 1713.1±898.6 | 1120.1±531.5 | 0.025   |
| Postpartum hemorrhage (ml), mean ±SD         | 1438.8±920.2 | 113.4±89.4 | <0.001   |

† Group A; patients with massive postpartum hemorrhage.

‡ Group B; patients without massive postpartum hemorrhage.

§ SD; standard deviation

¶ ART; assisted reproductive technologies

Table 2: Comparison of additional treatment for postpartum hemorrhage.
Additional treatment for postpartum hemorrhage

|                          | Group A† | Group B‡ | p-value |
|--------------------------|----------|----------|---------|
|                          | n=10     | n=118    |         |
| Uterotonic drugs§, number (%) | 10 (100.0) | 118 (100.0) | 0.999   |
| Intrauterine balloon tamponade, number (%) | 1 (10.0) | 1 (0.9) | 0.151   |
| Uterine artery embolization, number (%) | 3 (30.0) | 4 (3.39) | 0.010   |
| Allogenic blood transfusion, number (%) | 5 (50.0) | 11 (9.3) | 0.003   |
| Total abdominal hysterectomy, number (%) | 1 (10.0) | 1 (0.9) | 0.151   |

†Group A; patients with massive postpartum hemorrhage.

‡Group B; patients without massive postpartum hemorrhage.

§Uterotonic drugs; several drugs including oxytocin, methylergometrine, and dinoprostone.

Table 3: Univariate analysis for postpartum hemorrhage in placenta previa’s cases.

| Clinical factors                   | Odds Ratio | (95% CI†)   | p-value |
|-----------------------------------|------------|-------------|---------|
| Age                               | 0.818      | (0.219-3.049) | 0.764   |
| Repeat cesarean section           | 1.717      | (0.333-8.862) | 0.519   |
| Placental classification           | 2.765      | (0.682-11.216) | 0.155   |
| Placental location                | 1.485      | (0.290-7.599) | 0.635   |
| Antenatal bleeding                | 2.278      | (0.621-8.358) | 0.215   |
| Adherent placenta                 | 16.429     | (2.790-96.729) | 0.002   |
| Intraoperative hemorrhage         | 2.933      | (0.794-10.839) | 0.107   |

†CI; confidence interval