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Perioperative and transfusion outcomes in women undergoing cesarean hysterectomy for abnormal placentation

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Abstract

Background—Women with placenta increta (PI) and placenta percreta (PP) are at high risk of obstetric hemorrhage, however the severity of hemorrhage and perioperative morbidity may differ according to the degree of placental invasion. We sought to compare blood component usage and perioperative morbidity between women with PI vs. PP undergoing CH (Cesarean hysterectomy).

Study Design and Methods—We identified 77 women who underwent CH for PI or PP from the NICHD MFMU Network Cesarean registry, which sourced data from 19 centers from 1999–2002. We examined demographic, obstetric and surgical data, and rates of transfusion and perioperative morbidity. We performed statistical tests for between-group analyses; $P < 0.05$ as statistically significant.

Results—Rates of intraoperative or postoperative red blood cell (RBC) transfusion were similar between groups (PI=84% vs. PP=88%; $P=0.7$). We observed no between-group differences in rates of fresh frozen plasma (FFP) transfusion (intraoperative FFP: PI=30% vs. PP=41%; $P=0.3$; postoperative FFP: PI=28% vs. PP=18%; $P=0.4$) or platelet (PLT) transfusion (intraoperative PLTs: PI=14% vs. PP=29%; $P=0.2$; postoperative PLTs: PI=9% vs. PP=9%; $P=1.0$). Among the morbidities, a higher proportion of PP women underwent cystotomy (PI=14% vs. PP=38%, $P=0.02$) and postoperative mechanical ventilation (PI=14% vs. PP=35%; $P=0.03$).

Conclusion—Rates of intraoperative RBC, FFP and PLT transfusion are similar for PI and PP women, and perioperative outcomes are worse for PP women. We suggest the same mobilization transfusion medicine support for both groups, including blood-ordering (type and crossmatch for CH), and availability of emergency blood protocols including fibrinogen-containing preparations.

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Keywords

increta; percreta; transfusion; morbidity

Introduction

Women with abnormal placentation are at increased risk of major maternal and perinatal morbidity, including cesarean hysterectomy (CH),^{1,2} major hemorrhage and blood transfusion.³⁻⁶ The incidence of abnormal placentation is speculated to have increased from 0.8 per 1000 deliveries in the 1980s to 3 per 1000 deliveries in the last 10 years.⁷ The rising incidence of abnormal placentation has important clinical and public health implications, especially as abnormal placentation has become the leading indication for emergency postpartum hysterectomy for uncontrolled postpartum hemorrhage.¹ Furthermore, the peripartum management of women with abnormal placentation is particularly challenging as the blood loss at the time of delivery can be extremely high with median values ranging from 2000 ml to 7800 ml.^{3,6,8} As a consequence, CH is commonly performed in order to limit the rate and magnitude of intraoperative and postpartum bleeding.⁷

The three main subtypes of abnormal placentation are (i) placenta accreta which describes the attachment of the chorionic villi to the myometrium without an intervening layer of decidua, (ii) placenta increta (PI) which describes invasion of the chorionic villi into the myometrium, and (iii) placenta percreta (PP) which describes invasion of the chorionic villi through the myometrium.⁹ Based on pathologic differences between placenta accreta, PI and PP, it is presumed that the risk of major bleeding increases with more invasive placentation. Studies of postpartum hysterectomy specimens have demonstrated that both the increased depth of trophoblast invasion and incomplete remodeling of the uteroplacental arteries in placental development contribute to PI and PP.^{10,11} Larger blood vessels within the placental bed are also located closer to the placental-myometrial interface in PI specimens compared to normal placental specimens, which may explain why placental separation in PI cases results in massive bleeding at the time of delivery.¹²

Despite the known differences in placental invasiveness between subtypes, it is unclear whether differences exist in rates of blood component use and hemorrhage-related perioperative morbidity during CH among women with the most invasive subtypes: PI and PP. Few studies have evaluated rates of blood component utilization and perioperative morbidity among women with PI and PP.^{3,5} Using data sourced from a registry of >57,000 women who underwent Cesarean delivery, the primary aim of this retrospective study was to investigate whether differences exist in rates of transfusion between women with PI vs. PP undergoing CH. The secondary aims were to compare perioperative morbidities between the study groups, and to identify patient and perioperative factors associated with RBC perioperative and postpartum transfusion.

Materials and Methods

After obtaining IRB approval, we identified women who underwent CH for abnormal placentation from a National Institute of Child Health and Human Development Maternal

Fetal Medicine Units (NICHD MFMU) Network registry (hereafter referred to as the Cesarean registry).¹³ As part of a multicenter observational study involving 19 centers between 1999 and 2002, the Cesarean registry was established to collect data on maternal complications in women undergoing Cesarean delivery or vaginal birth after Cesarean delivery. All women delivered at a gestational age of 20 weeks or greater or delivered an infant weighing ≥ 500 g. Between 1999 and 2000, women who underwent successful vaginal birth after Cesarean delivery or primary or repeat Cesarean delivery were enrolled. Between 2001 and 2002, women with repeat Cesarean delivery and successful vaginal birth after Cesarean delivery were enrolled. Women who underwent either Cesarean delivery or vaginal birth after Cesarean delivery were identified from the labor and delivery log book or a computer database at each participating center. At delivery, information was collected through chart review, and information regarding perioperative morbidity was collected from discharge summaries.

A flow diagram for patient selection in this study is presented in Figure 1. A total of 57,182 women underwent primary or repeat Cesarean delivery. For women with abnormal placentation, the diagnosis was based upon either medical documentation of adherence of the placenta to the uterine wall without easy separation and/or by post-CH pathologic examination of the uterus. We identified 131 women who underwent CH for abnormal placentation of which 77 had PI or PP. Fifty-four women who underwent CH for abnormal placentation were excluded as the subtype of abnormal placentation was not described.

We collected demographic data (maternal age, pre-pregnancy body mass index (BMI), race/ethnicity), obstetric data (gestational age at delivery, parity, number of prior Cesarean deliveries, presence of labor or attempted induction of labor) and mode of anesthesia data. We evaluated peripartum hematologic indices: preoperative hemoglobin (Hb); platelet (PLT) count; lowest postpartum Hb and PLT count. The administration of intraoperative and postoperative transfusion of red blood cells (RBC), fresh frozen plasma (FFP) and PLTs were recorded as dichotomous variables. In the Cesarean registry, continuous data for the number of units transfused was available only for RBC. The number of RBC units transfused was categorized into 4 groups: 0 units, 1–4 units, 5–8 units, >8 units. Maternal morbidity outcomes included: intraoperative cystotomy or ureteral injury, wound complication, intensive care unit (ICU) admission, postoperative mechanical ventilation, adult respiratory distress syndrome (ARDS), pulmonary edema, and coagulopathy.

Data are presented as n (%), mean (SD), and median [IQR]. For continuous data, the student's t-test and Mann-Whitney U test were used to compare groups. For categorical data, χ^2 test or Fishers-exact test were used to compare groups. As the Cesarean registry did not contain data on estimated blood loss after Cesarean delivery, we constructed a surrogate measure for blood loss by calculating the percentage change in Hb using preoperative and nadir Hb values. Univariate linear regression analyses were performed to assess whether relevant candidate variables (presence or absence of labor, mode of anesthesia, gestational age, maternal age, subtype of abnormal placentation) predicted the number of units of intraoperative or postoperative RBC transfused (as separate dependent variables). As data for the number of RBC units transfused intraoperatively and postoperatively were non-parametric, we logarithmically transformed these data for the regression analyses (hereafter

referred to as log RBC units). Independent variables that were associated with the outcome of interest ($P = 0.1$) on univariate analysis were considered as covariates in a multiple linear regression model. All analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC) and SPSS version 21.0 (IBM SPSS, Armonk, NY). A P value <0.05 was considered statistically significant.

Results

Demographic, obstetric, and anesthetic data are presented in Table 1. We found no significant differences between groups for maternal age, pre-pregnancy BMI, gestational age at delivery, race/ethnicity, parity, and the presence of labor or attempted induction of labor. A higher proportion of women with PP had undergone ≥ 3 prior cesarean deliveries compared to women with PI (53% vs. 25%). Additionally, a higher proportion of women in the PP group underwent general anesthesia compared to the PI group (79% vs. 58%; $P=0.05$), although this difference was not significant.

Transfusion data and hematologic indices for PI and PP women are presented in Table 2. Preoperative and nadir Hb and PLT counts were similar in each group, and there were no between group differences for the percentage change in Hb values. There were no between group differences in rates of RBC transfusion during the intraoperative and postpartum periods (Table 2). During the intraoperative period, the rate of RBC transfusion in each group was high ($>70\%$), with moderately lower rates of RBC transfusion observed in the postpartum period in both groups. There were no significant differences in the proportion of women with PI or PP who received massive RBC transfusion (>8 units RBC) (14% vs. 29% respectively; $P=0.16$). During the intraoperative and postoperative periods, similar rates of FFP and PLT transfusion were also observed in both groups, with higher utilization rates occurring in the intraoperative period.

Based on univariate linear regression analyses, we did not observe statistically significant associations between log RBC units transfused intraoperatively with subtype of abnormal placentation ($P=0.31$), maternal age ($P=0.11$), gestational age ($P=0.12$), presence of labor or attempted induction of labor ($P=0.6$), and mode of anesthesia (general vs. neuraxial) ($P=0.49$). We did not observe a significant association between log RBC units transfused postoperatively with subtype of abnormal placentation ($P=0.46$), maternal age ($P=0.85$), gestational age ($P=0.84$), presence of labor or attempted induction of labor ($P=0.14$), and mode of anesthesia (general vs. neuraxial) ($P=0.07$). Due to the lack of significant associations between log RBC units (intraoperative or postoperative) with individual predictors of interest, we were unable to perform multivariate linear regression analyses.

Medical and surgical morbidity data for PI and PP women are presented in Table 3. Compared to PI women, PP women had significantly higher rates of cystotomy ($P=0.02$) and postoperative mechanical ventilation ($P=0.03$). No significant between-group differences were observed for other perioperative or surgical morbidities and postoperative length of stay.

Discussion

Transfusion therapy is an essential component of hemorrhage management in women with abnormal placentation. The goals of transfusion therapy are to ensure rapid resuscitation and maintain circulating volume, maintain tissue oxygenation using red blood cells, and reverse or prevent coagulopathy.¹⁴ Although the risk of major bleeding is presumed to increase with the degree of invasiveness of the placenta, blood component utilization and obstetric morbidities related to major perioperative hemorrhage have not been evaluated in detail in a large patient cohort with PI and PP. In our study, we observed no significant differences between women with PI and PP in blood component utilization (RBC, FFP, PLTs) during or after CH.

In our study, we observed high rates of intraoperative RBC transfusion (>73%) in both study groups, and relatively high incidences of massive transfusion (>8 units RBC) for women with PI and PP (14% vs. 29% respectively). In support of our findings, Stotler et al⁵ found no difference in the incidence of massive transfusion (>10 RBC units) between women with placenta accreta, PI, or PP (36%, 50%, 46%, respectively). Wright et al³ also reported no difference in the incidence of massive transfusion in women with PI or PP compared to placenta accreta (40% vs. 28.9%, respectively). In contrast, Tan et al¹⁵ investigated maternal morbidity among women with abnormal placentation over a 10 year period at a single institution. In this study, the authors reported that a higher proportion of women with PP required major transfusion support (>10 RBC units) compared to women with PI or placenta accreta (29% vs. 8% respectively; $P=0.1$). However, this study had small numbers of women with PP ($n=14$) and PI or placenta accreta ($n=13$).

In our study, the intraoperative transfusion rates for RBC, FFP and PLTs were high in women with PI and PP. Based on these data, we recommend that pre-delivery blood ordering practices should be identical when either PI or PP is suspected. The high rates of blood product utilization in both groups support the need for a system-wide process to facilitate the early delivery of adequate volumes and types of blood products for women with PI and PP who experience major intraoperative hemorrhage. Although it is uncertain whether variation exists in blood product ordering practices for women with abnormal placentation prior to CH, there is growing appreciation of the value in implementing a massive transfusion protocol (MTP) for obstetrics that allows for the early and ongoing delivery of adequate volumes and types of blood products.^{5,16} The availability of an MTP ensures that anesthesiologists and obstetricians who manage major obstetric hemorrhage are able to obtain blood products early as well as an ongoing supply of blood products until hemorrhage control has been achieved.¹⁷ This system-wide resource is vital in instituting early transfusion therapy in the event of major or catastrophic obstetric hemorrhage, especially if the blood loss is unanticipated. Based on data from the UK Obstetric Surveillance System, Fitzpatrick et al. reported that only 50% of patients with placenta accreta, PI or PP were suspected prior to delivery.¹⁸ In addition, the authors of this study also observed that the total estimated blood loss at the time of delivery was higher in unsuspected cases of PI or PP compared to suspected cases (6100 ml vs. 2750 ml), and the transfusion incidence was also substantially higher in the unsuspected vs. the suspected cases (94% vs. 59%).¹⁸ These data support the need for an MTP which entails a formal

process for the early release and rapid transit of blood products to patients experiencing major obstetric hemorrhage. At Stanford Medical Center, our MTP protocol for emergency release blood products has been previously described and comprises: six units RBC units, 4 units plasma, and 1 apheresis PLT unit.¹⁹ The initial request may be issued as either O negative RBC, AB plasma or as type-specific RBC and plasma, depending on the ability to achieve a 5 minute turnaround time from receipt of order to issuance to courier. Despite the difficulty in predicting perioperative transfusion requirements for patients with PI and PP undergoing CH, we have demonstrated that the use of blood products from an MTP may compensate for the acute and massive loss of whole blood and any resultant dilutional and consumptive coagulopathy that occurs during major obstetric hemorrhage.¹⁷ This important resource should be made accessible to obstetricians and anesthesiologists who manage any patient with major antenatal, peripartum and postpartum hemorrhage, including patients undergoing CH for suspected or unsuspected PI or PP.¹⁹

The early availability of fibrinogen-containing preparations is also important as there is increasing awareness that coagulopathy, notably hypofibrinogenemia, develops early after the onset of major obstetric hemorrhage.²⁰ In our study, the proportion of patients in the PI and PP groups receiving intraoperative FFP was relatively high (30% and 41% respectively), however cryoprecipitate data was unavailable in the Cesarean registry. Results from studies investigating treatment approaches for traumatic hemorrhage in non-obstetric patients suggest that early treatment of hypofibrinogenemia is associated with a reduced risk of death.²¹ Although there is currently no data to support this approach for obstetric hemorrhage, case studies of women who received fibrinogen concentrate for hypofibrinogenemia secondary to obstetric hemorrhage suggest that this approach may prove beneficial.²⁰

We did not identify any demographic or obstetric variables that were significantly associated with either the total number of units of intraoperative or postoperative RBC transfused. Similar findings were observed by Stotler et al.⁵ who did not identify clinical or laboratory variables associated with blood component use. As these were secondary outcomes, we speculate that both these studies were underpowered to observe statistically significant associations between relevant candidate variables and blood component usage. Large population-wide studies are needed to investigate predictors for blood component use for women undergoing CH for abnormal placentation.

We observed high rates of perioperative morbidity among women with PI and PP, including cystotomy, mechanical ventilation, and ICU admission. Although the incidence of bladder involvement in women with PP is uncertain, previous case reports highlight the surgical and medical morbidity associated with placental invasion of the bladder, such as: major bleeding, disseminated intravascular coagulation, partial cystectomy and postoperative mechanical ventilation.^{22,23} In keeping with these observations, we found significantly higher rates of cystotomy and need for mechanical ventilation for PP compared to PI. Tan et al.⁸ also found significantly higher rates of renal tract injury (93% vs. 38%) and ICU admissions (64% vs. 8%) among women with PP vs. PI and placenta accreta. These results suggest that the obstetricians and anesthesiologists should anticipate a greater degree of

surgical morbidity in women with PP compared to less invasive subtypes, and ensure postoperative ICU care is made available for PP women who undergo CH.

In our study, we observed high rates of general anesthesia for PI and PP women (58% and 79% respectively). Currently, there is debate in the anesthetic literature about the preferred mode of anesthesia for women who require CH for abnormal placentation.²⁴ The use of a neuraxial anesthetic technique offers potential advantages over general anesthesia for CH including: a lower risk of complications associated with general anesthesia (such as failed or difficult intubation), high-quality peri- and post-operative pain control,²⁵ a reduced incidence of uterine atony,²⁶ and reduced blood loss.^{27,28} However, using a general anesthetic approach as the primary anesthetic technique ensures airway access is established and can optimize maternal oxygen delivery during periods of hypoperfusion secondary to major blood loss, which may also explain why general anesthesia was more common for women with PP in our study.

We acknowledge that there are some limitations to our study. Due to the relatively low numbers of patients with PI and PP who underwent CH, our study may have been underpowered to detect statistical differences in blood product utilization between study groups. We could not determine if patients with abnormal placentation had been identified by ultrasound or magnetic resonance imaging prior to delivery. We appreciate that variability may exist in the clinical management of patients with PI or PP depending on whether or not patients are suspected of abnormal placentation prior to delivery. Obstetric decision-making for delivery (such as planned CH and planned attempts to deliver the placenta), total blood loss values and transfusion requirements may be influenced by pre-delivery suspicion of abnormal placentation.¹⁸ The Cesarean registry lacked nuanced hospital-level data on interventions (such as placental management) and anesthetic pharmacologic data for patients undergoing CH. The Cesarean registry also lacked hemorrhage and transfusion-related data, including: total estimated blood loss; the number of units of FFP, PLTs, and cryoprecipitate transfused; MTP availability; and peripartum coagulation indices (such as prothrombin time, partial thromboplastin time, and fibrinogen). Lastly, data in the Cesarean registry is over 10 years old and does not account for more recent pharmacologic and interventional practices for the management of obstetric hemorrhage related to abnormal placentation, such as prothrombotic drugs and interventional radiologic techniques (including uterine artery balloon catheterization and uterine artery embolization). Despite these limitations, the Cesarean registry sourced clinical data from a population-wide study of more than 57,000 women who underwent cesarean delivery at 19 different US obstetric centers. As a result, this allowed us to review clinically rich perioperative data from a cohort of women identified with PI and PP who underwent CH.

The lack of transfusion and hematologic data make it difficult to provide concrete recommendations for blood product ordering for patients undergoing CH. Based on our prior experience in the development of an MTP protocol for major obstetric hemorrhage at our institution,¹⁷ we have implemented a process for formalized blood product ordering for patients with abnormal placentation scheduled for CH. Prior to surgery, six units RBCs, four units FFP and 1 platelets are typically type and crossed and are available in the operating

room. During the perioperative period, if additional blood products are required for managing major perioperative hemorrhage, obstetricians and anesthesiologists can repeat the MTP order and request further MTP packets until adequate surgical and hemostatic control have been achieved.¹⁹

We conclude that the perioperative and postoperative rates of blood component utilization are similar for women with PP and PI undergoing CH. Institutions that deliver patients with PI and PP should consider adopting similar preoperative blood ordering practices for both groups. In anticipation for large volume blood product replacement in women with suspected and unsuspected PI and PP, protocols to allow access to adequate volumes of emergency-release blood products (such as an MTP) are advised. Further research is needed to optimize pre- and peri-operative blood ordering practices for women with abnormal placentation and to study surgical and anesthetic approaches for further reducing rates of hemorrhage-related morbidity.

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Figure 1.
Flow Diagram for Patient Selection
CH = Cesarean Hysterectomy

Table 1

Demographic, Obstetric and Anesthetic Data

	Placenta Increta N = 43	Placenta Percreta N = 34	P value
Maternal Age (y)			0.05
< 16 y	0	0	
16 – 19 y	0	0	
20–33 y	17 (39.5%)	21 (61.8%)	
34 y	26 (60.5%)	13 (38.2%)	
Prepregnancy BMI (kg/m ²)	26 [22, 31]	25 [22, 31]	0.9
Gestational age at delivery (wks)	35 [33, 37]	35 [33, 35]	1.0
Race/Ethnicity			
African-American	12 (28%)	4 (12%)	0.1
Caucasian	18 (42%)	17 (50%)	
Hispanic	11 (26%)	7 (21%)	
Other	2 (5%)	6 (18%)	
Parity			
0–2	22 (51%)	13 (38%)	0.5
3–4	16 (37%)	17 (50%)	
>4	5 (12%)	4 (12%)	
Number of previous CDs			
0–2	32 (75%)	16 (47%)	0.02
3–4	7 (16%)	16 (47%)	
>4	4 (9%)	2 (6%)	
Labor or Attempted Induction of Labor			
Yes	8 (19%)	7 (21%)	1.0
No	35 (81%)	27 (79%)	
Primary Mode of Anesthesia			
General	25 (58%)	27 (79%)	0.05
Neuraxial	18 (42%)	7 (21%)	

Data presented as n (%); mean (SD); median [interquartile range]

BMI = Body Mass Index; CD = Cesarean Delivery

Table 2

Transfusion Data and Hematologic Indices for Women with Placenta Increta and Placenta Percreta undergoing Cesarean Hysterectomy.

	Placenta Increta N = 43	Placenta Percreta N = 34	P value
Preoperative Hb (g/dL)	11.3 (1.5)	10.9 (1.6)	0.4
Preoperative platelets (X 10 ⁹ /L)	223 (67)	199 (45)	0.09
Lowest Hb (g/dL)	7.7 (1.7)	8.1 (1.6)	0.2
Percentage change in Hb (%) [*]	-31.1 (17.7)	-23.5 (19.2)	0.09
Lowest platelets (X 10 ⁹ /L)	129 (51)	128 (70)	0.9
Intraoperative or postoperative use of RBCs			
Yes	36 (84%)	30 (88%)	0.7
No	7 (16%)	4 (12%)	
Intraoperative use of RBCs			
Yes	32 (74%)	27 (79%)	0.8
No	11 (26%)	7 (21%)	
Number of units of RBCs transfused intraoperatively			
0	11 (26%)	7 (21%)	0.2
1-4	15 (35%)	13 (38%)	
5-8	11 (26%)	4 (12%)	
> 8	6 (14%)	10 (29%)	
Use of RBCs in the Postpartum Period			
Yes	18 (42%)	19 (56%)	0.3
No	25 (58%)	15 (44%)	
Number of units of RBCs transfused postoperatively			
0	25 (58%)	15 (44%)	0.5
1-4	12 (28%)	15 (44%)	
5-8	4 (9%)	3 (9%)	
> 8	2 (5%)	1 (3%)	
Intraoperative use of FFP			
Yes	13 (30%)	14 (41%)	0.3
No	30 (70%)	20 (59%)	
Use of FFP in the Postpartum Period			
Yes	12 (28%)	6 (18%)	0.4
No	31 (72%)	28 (82%)	
Intraoperative Use of Platelet Transfusion			
Yes	6 (14%)	10 (29%)	0.2
No	37 (86%)	24 (71%)	
Platelet Transfusion in the Postpartum Period			
Yes	4 (9%)	3 (9%)	1.0
No	39 (91%)	31 (91%)	

Data presented as n (%), mean (SD)

RBC = Red blood cells, FFP = Fresh frozen plasma, Hb = Hemoglobin

* Percentage change in hemoglobin = ((Lowest hemoglobin – Preoperative hemoglobin) / Preoperative hemoglobin)*100

Table 3

Rates of Medical and Surgical Morbidity among Women with Placenta Increta and Placenta Percreta undergoing Cesarean Hysterectomy.

	Placenta Increta N=43	Placenta Percreta N=34	P value
Cystotomy during procedure	6 (14%)	13 (38%)	0.02
Ureteral injury during procedure	1 (2%)	3 (9%)	0.3
Wound complication	4 (9%)	1 (3%)	0.4
ICU admission	14 (33%)	18 (53%)	0.1
Postoperative mechanical ventilation	6 (14%)	12 (35%)	0.03
Postoperative ARDS	1 (2%)	1 (3%)	1.0
Postoperative coagulopathy	5 (12%)	8 (24%)	0.2
Postoperative pulmonary edema	0 (0%)	3 (9%)	0.08
Hospital readmission	1 (2%)	3 (9%)	0.3
Postpartum length of stay (days)	10 [4, 24]	9.5 [4.75, 23.25]	0.8

Data presented as n (%); median [interquartile range]

ICU = Intensive care unit; ARDS = Adult respiratory distress syndrome