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Original Research

Retained products of conception in placenta previa without placenta accreta spectrum: who requires transarterial embolization and/or hysterectomy?

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Abstract

Background: To characterize patients with retained products of conception (RPOC) in placenta previa (PP), and to determine who requires transarterial embolization (TAE) and/or hysterectomy after cesarean section (CS). We focused on RPOC in PP without placenta accreta spectrum. **Methods**: The retrospective cohort study was performed in patients with RPOC in PP between April 2006 and June 2019 in our institute. **Results**: Of 498 patients with PP, RPOC were observed in 25. The median RPOC length was 4.4 cm (interquartile range: 2.8–5.7). RPOC hypervascularity was observed in 10 (10/18, 56%) patients. Of the 25 patients, an additional hemostatic intervention (TAE and/or hysterectomy) was required in 12 (48%). The duration between CS and TAE and/or hysterectomy ranged from 0–66 days. Of those, eight (8/12: 67%) patients needed the interventions on the day of surgery (day 0). Univariate analyses showed that patients having received TAE and/or hysterectomy bled more at CS ($p = 0.011$) and more frequently required blood transfusions at CS ($p = 0.011$), and were more likely to have hypervascular RPOC ($p = 0.036$). **Conclusion**: Hypervascular RPOC and bleeding episodes at CS may predict the requirement of TAE and/or hysterectomy after CS in patients with PP.

Keywords: Hysterectomy; Intrauterine balloon; Placenta previa; Postpartum hemorrhage; Uterine compression suture

1. Introduction

Retained products of conception (RPOC) cause obstetric hemorrhage. In placenta previa (PP), RPOC may become more problematic than non-PP. In PP, the placenta is mainly located in the lower uterine segment, the part with less contractility, which is one of the reasons for massive bleeding at cesarean section (CS) in PP. In PP, RPOC usually occurs in the lower uterine segment, the placental attachment site. Whether less contractility and/or anatomical characteristics of this segment also cause more RPOC-related bleeding in PP is not known. However, PP frequently causes massive bleeding and then RPOC may cause further bleeding, making the situation worse. Therefore, special attention should be paid to RPOC in PP.

Three hemostatic procedures, uterine compression sutures (UCS) [1–4], intrauterine hemostatic balloon (IUB) [5,6], and Matsubara-Takahashi (MT) cervix-holding technique (MT-holding) [7] proved to be effective in achieving hemostasis of obstetric hemorrhage, which we have described previously. In PP, RPOC becomes evident either intra-surgically or postpartum, and we have been employing one or a combination of these three procedures to achieve hemostasis either intra-surgically or postpartum. When hemostasis is not achieved with these three procedures, we must resort to hysterectomy that leads to loss of fertility and/or transarterial embolization (TAE) that preserves fertility. However, in this setting, TAE is usually performed as an emergency procedure. If we can predict who requires TAE and/or hysterectomy for RPOC in PP, we can prepare for them, which will promote patient safety.

In the present study, we characterized patients with RPOC in PP. We excluded patients with placenta accreta spectrum (PAS), which requires special attention in clinical practice. We focused our present attention on patients with PP (without PAS) in whom RPOC were determined either intra-surgically or postpartum. We placed special emphasis on those requiring TAE and/or hysterectomy.

2. Materials and methods

This retrospective observational study was approved by the Institutional Review Board of our center (approval number: A19-099). Because of the retrospective observational design, the ethics committee did not demand informed consent from individual patients. Information on how to opt out if desired was shown on our institute's freely-accessible website. No patients asked to opt out. We focused our attention on patients with PP who delivered between April 2006 and June 2019 after the second trimester. While some patients were reported previously [4,6–12], the purpose of the present study was different from that of our previous ones.

The diagnosis of PP was confirmed within 7 days before delivery using transvaginal ultrasound. The delivery mode was CS with the lower uterine segment transverse hysterotomy. Regarding placental delivery, it was induced by pulling the umbilical cord. If the placenta was not delivered, manual removal was performed. Uterotonic agents (oxytocin, methylergometrine, and prostaglandin F2-alpha, or their combination) were administered intravenously or intramuscularly after placental removal according to the guidelines [13,14]. If no significant bleeding occurred after placental removal, no hemostatic procedures (UCS, IUB, and/or MT-holding) were employed. If significant bleeding occurred after placental removal, we employed UCS, IUB, and/or MT-holding as described below. The decision of whether and which procedure should be employed depended on the judgement of the attending obstetrician (HT, YB, HS, RU, AO, or SM). In several cases of anterior-dominant PP, the hysterotomy portion was elevated to avoid the placental incision. For suturing, we used Matsubara-Yano (MY) UCS [13,14]. A 70-mm round needle with a No. 1 thread was used to transfix the uterine caudal part (lower uterine body) from anterior to posterior and then transfix the uterine fundus from posterior to anterior (longitudinal suture). Then, transverse sutures were deployed laterally to the longitudinal sutures [4,9]. Regarding IUB, we basically use the Bakri balloon [5]. The inflation volume was 100–300 mL, depending on the situation. In MT-holding, both the anterior and posterior cervical lips are held with forceps, thereby closing the uterine cervix, which has been employed in our department from approximately 2000 [7,8]. Hemostasis was achieved as follows: an intrauterine balloon tamponade was inserted into the uterine luminal surface because handling the cervix can cause uterine muscle contraction, and cervical clamping reduces the blood flow from the cervix to the uterus. IUB and MT-holding were discontinued approximately 12–24 hours following CS. When significant bleeding occurred after CS, TAE and/or hysterectomy were employed, and their use was decided on the basis of the attending obstetrician's judgement. We performed a hysterectomy instead of TAE if (1) vital signs were unstable, (2) the patient did not desire to preserve their uterus; or (3) TAE was not available.

We excluded patients with apparent PAS. However, sometimes it was difficult to make a PAS diagnosis and therefore we excluded patients if one of the following two conditions were met. First, PAS was diagnosed presurgery; this required that the patient have a history of a prior CS, a placenta that was covering the previous CS incision, and an ultrasound that showed signs indicative of PAS (loss of a clear zone, multiple placental lacunae, and uterovesical hypervascularity) [15]. In this presurgery diagnosed PAS case, we fundamentally performed a cesarean hysterectomy without placental removal [16]. When we considered the cesarean hysterectomy without placental removal, several obstetricians discussed the strategy. Second, placental removal was impossible because of tight placental adhesion to the uterus and thus, hysterectomy was required. Sixteen patients with apparent PAS were excluded from this study during the observation period. They all showed PAS histologically.

RPOC were detected (1) during CS (placental remnants in the uterine cavity were confirmed by surgeons); (2) at the time or follow-up of postpartum hemorrhage (PPH); and (3) during routine postpartum check-up. The routine postpartum check-up was performed approximately at one week and one month after delivery. The presence of RPOC is difficult to judge in cases with PPH. Regarding the timing of the diagnosis in patients with PPH, RPOC were also examined in the follow-up ultrasound. The RPOC image findings have been described previously [17,18]. Briefly, there was an intrauterine high-echoic lesion adjacent to the myometrium using B-mode. In addition, a hypervascular lesion in the uterine cavity in color-Doppler mode was also suggestive of RPOC. Hypervascularity, defined as a color Doppler-positive (pulse repetition frequency 15–25 cm/s) lesion, was detected in the high echoic lesion. Regarding RPOC length, we employed the longest axis in the sagittal view. Thus, we quote the longer axis of the two dimensions in the sagittal view. Enhanced computed tomography (CT) or magnetic resonance imaging (MRI) was used when sonographic confirmation of RPOC was difficult [19,20]. CT showed an intense enhancing mass in the uterine cavity during the arterial phase in RPOC with vascularity. MRI showed a polypoid mass with heterogenous signals in T1- and T2-weighted images. The junctional zone in contact with the mass was broken. A variable enhancement can be seen on postcontrast images caused by the vascularity of the RPOC.

The following information was retrieved from the medical records: maternal age, parity, mode of conception including the presence or absence of assisted reproductive technology (ART), history of abortion, history of CS, mode of abortion or delivery, weeks at delivery, birth weight, fetal sex, Apgar score, umbilical artery pH, neonatal intensive care unit admission, cause of PPH, employment of three procedures (MY UCS, IUB, and MT-holding), blood loss, lowest level of hemoglobin, lowest level of fibrinogen, autologous transfusion, and intensive care unit admission. Information on RPOC was also retrieved, including the maximum length in the ultrasound and the flow in RPOC and/or myometrium. Patient background, characteristics, and outcomes were compared between those requiring vs. those not requiring TAE and/or hysterectomy for RPOC.

Blood was transfused in principle with Hb $<$6.0 g/dL, systolic blood pressure $<$70 mmHg, or estimated blood loss $>$2500 mL. Autologous blood was first transfused when available, and when it was insufficient, allogeneic blood was transfused. Data were retrieved on the amounts of allogeneic blood transfusion (containing red cell concentrate [RCC], fresh frozen plasma [FFP], and platelet concentrate

Table 1. Patient backgrounds.

Characteristic	n = 25
Age (years), median (IQR)	35 (31–38)
<30, *n* (%)	5 (20)
30–34, *n* (%)	6 (24)
35–39, *n* (%)	10 (40)
≥40, *n* (%)	4 (16)
Primipara, *n* (%)	16 (64)
History of CS, *n* (%)	7 (28)
History of D&E, *n* (%)	2 (8)
Pregnancy by ART, *n* (%)	6 (24)
Multiple pregnancy, *n* (%)	2 (8)
Placental position, *n* (%)	
Anterior	9 (36)
Posterior	16 (64)
Degree of PP	
Marginalis	12 (48)
Total	13 (52)
Gestational age at delivery, *n* (%)	
<30 weeks, *n*	3 (12)
30^{+0}–33^{+6} weeks, *n*	3 (12)
34^{+0}–36^{+6} weeks, *n*	8 (32)
≥37 weeks, *n*	11 (44)
Blood loss at delivery (mL), median	2020
IQR	1340–2875
Range	230–12,010
Concomitant hemostatic procedure*, *n* (%)	17 (68)
Transfusion at delivery†, *n* (%)	16 (64)

*Intrauterine balloon use, uterine compression suture, or holding the uterine cervix. These three methods were concomitantly or individually employed. †Including autotransfusion. ART, assisted reproductive technology; CS, cesarean section; D&E, dilatation and evacuation including curettage; IQR, interquartile range; PP, placenta previa.

Table 2. Characteristics of RPOC.

	n = 25
Trigger of detection, *n* (%)	
intraoperative findings	22 (88)
PPH after CS	2 (8)
incidental detection on routine ultrasound	1 (4)
Additional imaging study employed for RPOC, *n* (%)	
CT	7 (28)
MRI	2 (8)
RPOC length* (cm), median (IQR)	4.4 (2.8–5.7)
RPOC hypervascularity**, *n* (%)	10 (56: 10/18)
Disappearance of RPOC† (days), median (IQR)	70 (30–118)

*Maximum length. Of the 25 patients, RPOC could be measured in 18 cases because additional procedures (e.g., hysterectomy) were needed just following CS. **Using color Doppler in ultrasound. The vascularity was measured in 18 cases. †Maximum length <5 mm was defined as disappearance in ultrasound. CS, cesarean section; CT, computed tomography; IQR, interquartile range; MRI, magnetic resonance imaging; PPH, postpartum hemorrhage; RPOC, retained products of conception.

Table 3. Intervention for RPOC.

Characteristic	n = 25
Additional hemostatic intervention required, *n* (%)	12 (48: 12/25)
Trigger event, *n* (%)	
significant bleeding	12 (100: 12/12)
Duration between CS and intervention, range (days)	0–66
day 0	8 (67: 8/12)
1–7	1 (8: 1/12)
8–30	2 (17: 2/12)
31-	1 (8: 1/12)
Regimen of intervention, *n* (%)	
TAH	4 (33: 4/12)
TAE*	8 (67: 8/12)

*In one patient, TAH was necessary because of continuous bleeding following TAE. CS, cesarean section; MTX, methotrexate; RPOC, retained products of conception; TAE, transarterial embolization; TAH: transabdominal hysterectomy.

[PC]) transfused from the beginning of CS to 24 hours after.

The Mann–Whitney U test and Fisher's exact test (two-tailed) were used to compare RPOC characteristics, maternal backgrounds, and outcomes between additional hemostatic interventions (+) vs. none (–) associated with RPOC. Parameters significant ($p < 0.15$) on univariate analysis were subjected to multivariate logistic regression analysis. All analyses were performed using JMP software version 10 (SAS Institute, Tokyo, Japan), with $p < 0.05$ considered statistically significant.

3. Results

Table 1 shows patient backgrounds. Of 498 patients with PP, RPOC were observed in 25. The median age was 35 (interquartile range (IQR): 31–38) years. Six women became pregnant after ART. Regarding the placental position, 16 (64%) patients had a posterior placenta. Eleven (44%) patients were delivered at term. The median blood loss at delivery was 2020 mL (IQR: 1340–2875). UCS, IUB, and/or MT-holding were required in 17 (68%) patients. Transfusion at delivery was performed in 16 (64%) patients.

Table 2 shows the clinical characteristics of RPOC. RPOC were diagnosed during CS (e.g., difficult placental removal) in 22 (88%) patients, at examination for PPH after CS in two (8%), and at routine ultrasound observation in one (4%). The diagnosis of RPOC was supported by CT and MRI in seven and two patients, respectively. The median

Table 4. Univariate analysis among patients with RPOC in the presence or absence of an intervention.

	Intervention (+) (n = 12)	Intervention (–) (n = 13)	OR (95% CI) ***	*p*-value
Age (years), median (IQR)	33 (29–37)	35 (33–38)		0.368
Primipara, *n* (%)	8 (67)	8 (62)	1.3 (0.15–4.12)	0.790
Pregnancy by ART, *n* (%)	4 (33)	2 (15)	2.8 (0.40–18.9)	0.378
History of CS	3 (25)	4 (31)	0.8 (0.13–4.36)	1.000
History of D&E	1 (8)	1 (8)	1.1 (0.06–19.6)	1.000
Anterior placenta, *n* (%)	6 (50)	3 (23)	0.3 (0.05–1.67)	0.226
Total previa, *n* (%)	8 (67)	5 (38)	3.2 (0.06–1.61)	0.238
Gestational age at delivery (weeks), median (IQR)	36.5 (34.3–37.0)	36.0 (30.5–37.0)		0.573
Blood loss at delivery (mL), median (IQR)	2690 (1788–5518)	1560 (1155–2125)		0.011
Transfusion, *n* (%)	11 (92)	5 (38)	17.6 (1.71–181)	0.011
Concomitant hemostatic procedure, *n* (%)	10 (83)	7 (54)	4.3 (0.66–17.8)	0.202
RPOC length* (cm), median (IQR)	5.0 (3.1–7.0)	3.0 (2.0–5.1)		0.133
RPOC hypervascularity**, *n* (%)	5 (100: 5/5)	5 (38: 5/13)		0.036

*RPOC size in five cases was missing. **RPOC vascularity in seven cases was missing. ART, assisted reproductive technology; CS, cesarean section; D&E, dilatation and evacuation including curettage; IQR, interquartile range; RPOC, retained products of conception. ***We performed multivariate logistic regression analysis using transfusion, RPOC length, and RPOC hypervascularity. The RPOC vascularity showed the significance ($p = 0.014$). However, due to a small sample size, appropriate model could not be constructed, and, thus, we did not show the result in this table.

RPOC length was 4.4 cm (IQR: 2.8–5.7). RPOC hypervascularity was observed in 10 (10/18: 56%) patients.

Table 3 shows the interventions for RPOC. Of 25 patients, an additional hemostatic intervention was required in 12 (48%). TAE and hysterectomy were required in eight and four patients, respectively, because of bleeding. Of the four patients requiring TAH, two were diagnosed with partial placenta accreta histologically. The duration between CS and TAE or hysterectomy ranged from 0–66 days. Of those, eight (67%) patients needed the interventions on the day of surgery (day 0).

Table 4 shows the comparison between patients with and without TAE and/or hysterectomy. Univariate analyses showed that patients having received TAE and/or hysterectomy bled more at CS ($p = 0.011$) and more frequently required blood transfusion at CS ($p = 0.011$), and they were more likely to have hypervascular RPOC ($p = 0.036$). Patients with larger RPOC also more frequently required TAE and/or hysterectomy, but this was not statistically significant ($p = 0.133$).

4. Discussion

In patients with RPOC after PP delivery, almost half (48%: 12/25) required TAE and/or hysterectomy. These two procedures were required in patients with massive bleeding at CS and hypervascular RPOC; thus, these conditions should be considered as a high risk for TAE/hysterectomy-requiring RPOC.

Few reports are available on the outcomes of RPOC after PP delivery. A recent study showed that emergent hysterectomy was required in 31% (11/36) of such patients [21]. When it comes to RPOC without PP, TAE and/or hysterectomy was less often required. Of non-PP patients who had RPOC after 2nd trimester abortions/deliveries or 3rd trimester deliveries, 19% of them required TAE and/or hysterectomy [22]. Other studies showed that surgical interventions were required in approximately 25% of patients with non-PP RPOC [23,24]. TAE and/or hysterectomy was more frequently required in PP in the present study (in almost 50%). This may be because of the increased incidence of "hidden" PAS in PP. We excluded clinically evident PAS; however, theoretically, there were some "hidden" (clinically unrecognizable) cases of PAS. Such "hidden" PAS is more likely to be involved in PP than in non-PP [25,26]. In such cases, RPOC may have a richer blood flow. This may cause marked bleeding, which may account for the more frequent requirement of TAE and/or hysterectomy.

TAE and/or hysterectomy was required in patients with massive bleeding at CS and hypervascular RPOC. First, massive bleeding at delivery is a risk factor for TAE and/or hysterectomy. This may be because of "hidden" PAS, as described. Of note, a recent study showed positive associations of the degree of PAS and blood loss in cases of RPOC in PP [24]. Second, RPOC vascularity may account for the requirement of TAE and/or hysterectomy. Several studies suggest a positive association between RPOC vascularity and surgical interventions in patients without PP [22,23]. RPOC vascularity may also be a risk factor for TAE and/or hysterectomy in patients with PP. Our previous study on the normal placental position also showed that

RPOC length ≥4 cm significantly necessitated TAE and/or hysterectomy [22]. A recent study also showed an association between the RPOC longer axis and additional interventions [27]. All these studies suggest that a "larger" placenta remaining in utero, larger RPOC, may account for the massive bleeding, which is consistent with the present findings.

Regarding the timing of TAE and/or hysterectomy, these procedures were required on the day of the surgery (day 0) in more than 67% of cases (8/12), whereas they were required 22 days (median) after delivery in patients without PP in our previous study [22]. We do not know the reason why bleeding, and thus the requirement of TAE and/or hysterectomy, occurred more rapidly after delivery in PP. Putting this aside, it may be obstetricians' common sense that the day of the surgery is the day when we must pay attention to bleeding. This is true also for bleeding caused by RPOC in PP patients.

5. Conclusions

Almost half the patients with RPOC after PP delivery required TAE and/or hysterectomy. Additionally, in patients with hypervascular RPOC that was associated with massive bleeding, TAE and/or hysterectomy was required. We should prepare for TAE and/or hysterectomy in patients with these conditions. This was a retrospective study and thus, treatment was decided depending on the discretion of the attending obstetrician. Further studies are necessary.

Abbreviations

ART, assisted reproductive technology; CS, cesarean section; CT, computed tomography; FFP, fresh frozen plasma; IUB, intrauterine balloon; MRI, magnetic resonance imaging; MT-holding, Matsubara-Takahashi cervix holding technique; MY, Matsubara-Yano; PAS, placenta accreta spectrum; PC, platelet concentrate; PP, placenta previa; PPH, postpartum hemorrhage; RCC, red cell concentrate; RPOC, retained products of conception; TAE, transarterial embolization; UCS, uterine compression suture.

Author contributions

MOh, HT contributed to the conception and design of the study, data collection, data analysis, and writing the manuscript. YB, HS, and KH contributed to data collection and revising the manuscript. SN, MOg contributed to data analysis, and writing the manuscript. AO supervised the study. SM contributed to writing the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This retrospective observational study was approved by the Institutional Review Board in our center (approval number: A19-099). Because of the retrospective observational design, the ethics committee did not demand informed consent from individual patients.

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Conflict of interest

The authors declare no conflict of interest.

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