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Uterine Artery Embolization following Cesarean Delivery but prior to Hysterectomy in the Management of Patients with Invasive Placenta

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Abstract

Purpose: To evaluate outcomes of patients with placenta accreta spectrum (PAS) disorders who underwent uterine artery embolization (UAE) following cesarean delivery but before hysterectomy.

Materials and Methods: A retrospective review of patients with PAS treated with cesarean-hysterectomy (C-hyst) was performed. Patients in the UAE group underwent UAE after cesarean delivery but before hysterectomy; patients in the control group underwent C-hyst alone. Estimated blood loss (EBL), transfusion requirements, length of intensive care unit (ICU) stay, and adverse events were evaluated.

Results: The study included 31 patients, 7 in the UAE group and 24 in the control group. Median EBL, transfusion requirements, and length of ICU stay in the UAE group compared with control group were 1,500 mL (range, 500–2,000 mL) vs 2,000 mL (range, 1,000–4,500 mL) ($P = .04$), 150 mL (range, 0–650 mL) vs 550 mL (range, 0–3,125 mL) ($P = .10$), and 0 d (range, 0–1 d) vs 0.5 d (range, 0–2 d) ($P = .07$). All patients in the UAE group had placenta increta; patients in the control group had placenta accreta (29%), increta (54%), and percreta (17%) ($P = .10$). Subgroup analysis of patients with placenta increta demonstrated that the UAE group had a significant decrease in

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median EBL (P = .004), transfusion requirements (P =.009), and length of ICU stay (P = .04). No adverse events following UAE were noted.

Conclusions: UAE following cesarean delivery but before hysterectomy in patients with placenta increta appears to be safe and effective in decreasing EBL, transfusion requirements, and length of ICU stay compared with C-hyst alone.

Placenta accreta spectrum (PAS) refers to the abnormal invasion of placental tissue into the uterine wall (1,2). Although PAS is considered rare, its incidence has increased over the last decade, likely owing to the increased rate of cesarean deliveries and uterine surgeries, and the pathology is currently estimated to affect 1 in 500–700 pregnancies (2). PAS is the most common indication for peripartum hysterectomy, which is associated with perioperative hemorrhage, intraoperative injury to surrounding organs, postoperative multiorgan failure, and maternal death (3). Average blood loss at delivery is 3,000–5,000 mL, and the maternal mortality rate is reported to be 7% (4).

The recommended management for PAS is scheduled delivery via cesarean-hysterectomy (C-hyst) (2,5,6). Several multidisciplinary approaches to reduce intraoperative blood loss have been described, including internal iliac artery ligation, internal iliac artery and aortic balloon occlusion catheter placement, and intrauterine balloon placement (7–11). However, the available data are conflicting. Whereas some observational studies showed reduced blood loss with internal iliac artery balloon catheter placement (8,12), one small randomized trial comprising 27 women showed no benefit (10). These prior studies in the literature are difficult to interpret owing to inclusion of women who attempted delivery of the placenta without planned hysterectomy, different techniques in catheter placement and balloon inflation, and grouping of different perioperative procedures in the same analysis. In addition, many studies use the term “placenta accreta” as a general term to describe all cases of PAS and do not stratify cases based on level of invasion (13,14), which may act as a significant confounding factor, as increasing depth of invasion is known to correlate with increasing risk for blood loss (15,16).

Uterine artery embolization (UAE) to reduce bleeding during cesarean sections has shown promising results, but available data on efficacy are scarce (17–20). Prior studies typically evaluated UAE in the setting of catheterization before delivery and embolization after delivery, resulting in fetal radiation and limited fluoroscopic evaluation during catheterization (18–20). The purpose of this study is to evaluate outcomes, including mean estimated blood loss (EBL), transfusion requirements, length of intensive care unit (ICU) stay, and adverse events, of patients with PAS who underwent UAE following cesarean delivery but before hysterectomy compared with C-hyst alone.

MATERIALS AND METHODS

Patient Selection

This study was approved by the institutional review board, and informed consent waiver was obtained. Patient demographics, obstetric history, operative reports, and clinical notes were obtained and reviewed through the electronic medical report. UAE procedural images and reports were obtained and reviewed through the picture archiving and communication

system. A retrospective record review of the pathology database at a single institution from May 2014 to April 2018 identified 31 women (median age 34 y; range, 26–40 y) with a diagnosis of PAS who underwent C-hyst. Patients who underwent UAE following cesarean delivery but before hysterectomy comprised the UAE group. Patients who underwent C-hyst without adjunctive UAE comprised the control group. The decision to perform UAE was made on a case-by-case basis by the multidisciplinary team caring for the patient. Patients who did not have histopathologically proven PAS, underwent emergent delivery, or did not undergo hysterectomy were excluded.

Of the 31 patients included, 7 were in the UAE group and 24 were in the control group. Patient demographics are provided in Table 1. There was no significant difference between the 2 groups with regard to patient age, gestational age, gravidity, parity, type of pregnancy, prenatal imaging diagnosis of PAS, and number of previous uterine surgeries and cesarean deliveries ($P > .5$). Although the preoperative imaging diagnosis of placenta accreta, increta, and percreta based on prenatal ultrasound (US) or magnetic resonance imaging was similar between the 2 groups, postoperative histologic diagnosis was notably different, although not reaching statistical significance ($P = .10$). In the treatment group, all 7 patients (100%) had placenta increta. In the control group, 7 patients (29%) had placenta accreta, 13 patients (54%) had placenta increta, and 4 patients (17%) had placenta percreta. Among patients with placenta increta, no significant differences were seen in patient age, gestational age, gravidity, parity, type of pregnancy, and number of previous uterine surgeries and cesarean deliveries ($P > .5$).

UAE Procedure

Three interventional radiologists, 9 obstetricians, and 5 gynecologic oncologic surgeons were involved in this study. A general overview of the technique follows, allowing for some variability owing to operator preference or available equipment. Following cesarean delivery, the hysterotomy was closed with looped polydioxanone sutures. The anterior abdominal wall was then closed in a temporary fashion using penetrating towel clamps, and the patient was transferred to the interventional radiology suite. All patients were placed under general anesthesia for the UAE procedure. Vascular access was obtained with 5-F vascular sheaths. A right transfemoral approach was used to select the left and then the right uterine arteries with a 5-F catheter (C2 Cobra; Cook, Inc, Bloomington, Indiana) under fluoroscopic guidance. Embolization was performed with absorbable gelatin sponge slurry (Gelfoam; Pfizer Inc, New York, New York) until Gelfoam was noted in the distal branches of the uterine artery and complete stasis in the main uterine artery was achieved. Following UAE, an aortogram was performed using a 5-F pigtail catheter to confirm absence of blood flow to the uterus. Next, hemostasis of the femoral access site was achieved using manual compression, and the patient was transferred back to the operating room for hysterectomy. Following hysterectomy, the uterus and placenta in situ were sent for histopathologic analysis. Degree of placental invasion was classified as placenta accreta (attachment of the placenta to myometrium without intervening decidua basalis), placenta increta (invasion of the trophoblast into the myometrium), or placenta percreta (invasion through the myometrium and serosa into surrounding structures) (2).

Study Outcomes and Statistical Analysis

Study outcomes evaluated were EBL; transfusion requirements, including packed red blood cells and cell salvage; length of ICU stay, and adverse events. Adverse events were defined as any untoward medical occurrence associated with the intervention. Serious adverse events were defined as causing hospitalization or prolongation of existing hospitalization, substantial disruption of the ability to conduct normal life functions, or death. Statistical analysis was performed on Prism 8 software (GraphPad Software, San Diego, California). Unpaired *t* test was used for continuous variables with normal distribution, Mann-Whitney test was used for continuous variables with non-normal distribution, and Fisher exact test was used for nominal variables. $P < .05$ indicated statistical significance.

RESULTS

Bilateral UAE was performed to stasis in all 7 cases. Median EBL during hysterectomy was significantly lower in the UAE group (1,500 mL, interquartile range [IQR] 950–1,500 mL) compared with the control group (2,000 mL, IQR 1,275–3,125 mL) ($P = .04$). Median transfusion requirements trended lower in the UAE group (150 mL, IQR 75–450 mL) compared with the control group (550 mL, IQR 138–2,230 mL) ($P = .10$). Mean length of ICU stay trended lower in the UAE group (0 d, IQR 0–0 d) compared with the control group (0.5 d, IQR 0–1 d) ($P = .07$). No adverse events attributed to UAE were noted. Surgical complications, including peritonitis, ureteral injury, and ongoing intra-abdominal bleeding, were not seen in the UAE group but occurred in 17% (4 patients) of the control group ($P = .55$). No serious adverse events, defined as causing hospitalization or escalation of treatment prolonging existing hospitalization, substantial disruption of the ability to conduct normal life functions, or death, were noted in either group. Mean fluoroscopy time was 32.7 minutes ± 17.5. Study outcomes are presented in Table 2.

There were no pathology-proven cases of placenta accreta or percreta in the UAE group, precluding further subgroup analyses. Subgroup analysis for patients with placenta increta was performed and is presented in Table 3. Among patients with placenta increta, the UAE group compared with the control group had significantly lower median EBL (1,500 mL, IQR 950–1500 mL vs 2,500 mL, IQR 2000–3000 mL; $P = .004$), transfusion requirements (150 mL, IQR 75–450 mL vs 700 mL, IQR 380–1,750 mL; $P = .009$), and length of ICU stay (0 d, IQR 0–0 d vs. 1 d, IQR 0–1 d; $P = .04$). No adverse events attributed to UAE were noted. Surgical complications were seen in 0% (0 patients) of the UAE group and 15% (2 patients) of the control group ($P = .52$).

DISCUSSION

The incidence of PAS has dramatically increased in the last decade, and C-hyst is considered the current standard for management of patients with PAS (1). However, this procedure may result in extensive blood loss, morbidity, and maternal death (3–5). In the present study, UAE after cesarean delivery but before hysterectomy significantly decreased EBL compared with C-hyst alone and demonstrated a trend in decreasing transfusion requirements and length of ICU stay. Among patients with placenta increta, UAE after cesarean delivery but before hysterectomy was associated with significantly decreased EBL, transfusion

requirements, and length of ICU stay. Prior reports hypothesized that a potential advantage of embolization over proximal uterine artery ligation is the occlusion of the distal arterial bed and reduction of collateral flow (21). In this study for each case of UAE, embolization was performed to occlude the distal uterine arterial branches with complete occlusion of blood flow in the main uterine artery, precluding bleeding from collateral vasculature beds. Incidentally, none of the patients in the UAE group experienced intraoperative injury to surrounding organs, which may be attributed to a “dry” surgical bed, facilitating surgical dissection.

Several case series and retrospective studies reported the use of UAE to be safe and effective in reducing perioperative hemorrhage in the setting of PAS (17–20,22–24). Niola et al (17) showed efficacy of UAE before delivery in reducing bleeding during cesarean section. Izbizky et al (18) demonstrated feasibility of catheterization before delivery and UAE after delivery in 83 patients with no maternal deaths and 14% of patients receiving large-volume blood transfusion. However, PAS was confirmed by histology in only 83% of patients included in the study. Including patients without confirmed PAS may confound results. Pan et al (19) reported that mean EBL in the study group patients, who received catheterization before delivery and UAE after delivery, was lower compared with the control group, but this result did not reach statistical significance. In addition, reported cases differ in the timing of UAE with respect to the cesarean delivery in the management paradigm of patients with PAS. In the literature, UAE has been described as a prophylactic measure before delivery, a prophylactic measure with uterine artery catheterization before delivery and UAE after delivery, or a technique used to manage primary postpartum hemorrhage (11,17–20). An approach using UAE or catheterization before delivery exposes the fetus to radiation and potential oxygen deprivation and may cause obstetricians to rush to perform delivery to minimize embolization-to-delivery time. Of the 4 studies (17–20) that used these techniques, 2 studies (17,19), 1 using UAE before delivery and 1 using catheterization before delivery, measured and reported mean uterine radiation exposure and mean maternal radiation exposure as 15.61 mGy to 30.6 mGy (range, 5.9–104.0 mGy) and 70.37 mGy to 117.5 mGy (range, 18.5–248.0 mGy), respectively. The other studies did not measure or report fetal and maternal radiation exposure for all patients. The present study evaluated UAE after delivery, resulting in no fetal radiation exposure or potential oxygen deprivation.

Other studies have grouped UAE with the use of concomitant procedures (22,23). Tan et al (23) reported that in patients who underwent internal iliac artery occlusion balloon placement, mean EBL, transfusion requirements, and duration of surgery all were significantly lower than the control group. UAE was performed only in patients who attempted delivery of the placenta and in whom the placenta was retained. Mei et al (22) reported on the use of prophylactic internal iliac artery balloon occlusion, but UAE was added only if necessary following cesarean delivery. Therefore, treatment effect of UAE is difficult to determine from these studies.

Postoperative histologic diagnosis of placenta accreta, increta, or percreta was noted to differ between the treatment and control groups, although the difference did not reach statistical significance. Several factors could explain this finding, including selection bias, nonstandardized usage of the term “placenta accreta,” and varying levels of invasion within

a single patient. Sample selection bias may occur, as physicians may be more likely to consider prophylactic perioperative procedures in patients considered to be high risk owing to medical or surgical history. In high-risk patients, physicians may also be more likely to proceed with C-hyst without attempt at placental delivery owing to risk of hemorrhage, which may explain the high incidence of placenta increta and percreta in our study. In addition, the term “placenta accreta” has historically been used both as a general term meaning all PAS disorders and as a specific term meaning placental attachment to the myometrium. Imprecise screening can also contribute to inexact usage of terminology. US is the most commonly used method of prenatal screening but may not differentiate clearly between levels of invasion. Reported sensitivity of 53.5%–88% and specificity of 88%–97% for US diagnosis (25,26) are for the presence of PAS pathology, not the specific level of invasion. Different degrees of invasion can be present within a single patient, which can result in histologic results discordant with imaging or intraoperative findings (27). As increasing depth of placental invasion is known to correlate with higher intraoperative risk for hemorrhage and morbidity, it is important to directly compare similar pathologies across patients. Of note, although many patients included in this study were upstaged on histologic diagnosis, 10 patients with prenatal imaging diagnosis of placenta accreta were found to have normal histology and excluded from analysis.

This study is limited by its small sample size, owing partially to the rarity of the disease process. The exclusion criteria used in this study, although limiting, were designed to address confounding factors found in the literature. Not all prior studies in the literature differentiated between women who underwent planned C-hyst or women who attempted placental delivery, which may confound results, as attempted placental delivery is associated with higher hemorrhagic morbidity (1). Similarly, emergent C-hyst results in greater blood loss and complication rate versus planned C-hyst (28). As a result, this study included only patients who underwent nonemergent, planned C-hyst without attempted placental delivery. Another limitation is the single-center, retrospective design. Moreover, intraoperative blood loss was estimated, and the transfusion requirements were based on the judgment of the surgeon and anesthesiologist. Surgical approach may have varied among different surgeons, and the decision to pursue UAE after delivery may have been affected by findings on prenatal imaging. Prospective randomized data are necessary to determine the ideal treatment algorithm for patients with PAS, but obtaining such data may be challenging owing to the rarity of the disease process and the complex nature of the multidisciplinary team necessary to care for such patients.

In conclusion, UAE following cesarean delivery but before hysterectomy may be a feasible and potentially advantageous option in the multidisciplinary treatment of patients with PAS, resulting in reduced EBL, transfusion requirements, and length of ICU stay for patients with placenta increta. Performing UAE after cesarean delivery avoids fetal radiation exposure and facilitates surgical dissection, which may prevent intraoperative injury to surrounding structures. A potential challenge of this approach is the transportation of the patient from the operating room to the interventional radiology suite, which can be avoided in the setting of a hybrid operating room.

ABBREVIATIONS

C-hyst	cesarean-hysterectomy
EBL	estimated blood loss
ICU	intensive care unit
IQR	interquartile range
PAS	placenta accreta spectrum
UAE	uterine artery embolization

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Table 1.

Patient Demographics

	UAE (n = 7)	Control (n = 24)	*P*
Age, y, median (range)	34.3 (28–39)	34.0 (26–40)	.88
Gestational age, weeks, mean (SD)	34.7 (1.9)	34.0 (2.2)	.36
Gravidity, median (range)	5 (4–11)	5 (2–12)	.20
Parity, median (range)	3 (1–8)	3 (1–10)	.24
Type of pregnancy, n (%)			1.00
Singleton	7 (100)	24 (100)	
Twin	0 (0)	0 (0)	
Prior cesarean deliveries, median (%)			.52
≤ 1	2 (29)	10 (42)	
> 1	5 (71)	14 (58)	
Prior uterine operations, median (%)			1.00
0	7 (100)	23 (96)	
≥ 1	0 (0)	1 (4)	
Prenatal imaging diagnosis, n (%)			.99
Accreta	6 (86)	17 (71)	
Increta	1 (14)	5 (21)	
Percreta	0 (0)	2 (8)	
Histologic diagnosis, n (%)			.10
Accreta	0 (0)	7 (29)	
Increta	7 (100)	13 (54)	
Percreta	0 (0)	4 (17)	
Concomitant placenta previa	6 (86)	23 (96)	0.41

UAE = uterine artery embolization.

Table 2.

Study Outcomes for All Patients

	UAE (n = 7)		Control (n = 24)		*P* (Mean)	*P* (Median)
	Mean ± SD	**Median (IQR)**	**Mean ± SD**	**Median (IQR)**		
Mean EBL, mL	1,271 ± 562	1,500 (950–1,500)	2,288 ± 1,167	2,000 (1,275–3,125)	.03	.04
Mean transfusion requirement, mL	264 ± 278	150 (75–450)	1,050 ± 1,119	550 (138–2,230)	.08	.10
Mean length of ICU stay, days	0.14 (0.38)	0 (0–0)	0.67 (0.76)	0.5 (0–1)	.09	.07
Adverse events	0 (0%)		4 (17%)		.55	

EBL = estimated blood loss, ICU = intensive care unit; IQR = interquartile range; UAE = uterine artery embolization.

Table 3.

Study Outcomes for Patients with Placenta Increta

	UAE (n = 7)		Control (n = 13)		*P* (Mean)	*P* (Median)
	Mean ± SD	**Median (IQR)**	**Mean ± SD**	**Median (IQR)**		
Mean EBL, mL	1,271 ± 562	1,500 (950–1,500)	2,608 (1,001)	2,500 (2,000–3,000)	.007	.004
Mean transfusion requirement, mL	264 (278)	150 (75–450)	1,125 (996)	700 (380–1,750)	.04	.009
Mean length of ICU stay, days	0.14 (0.38)	0 (0–0)	0.85 (0.80)	1 (0–1)	.04	.04
Adverse events	0 (0%)		2 (15%)		.52	

EBL = estimated blood loss, ICU = intensive care unit; IQR = interquartile range; UAE = uterine artery embolization.

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