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Prophylactic uterine artery embolization in second-trimester pregnancy termination with complete placenta previa

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Abstract

Objective: This study was performed to assess whether prophylactic uterine artery embolization (UAE) is beneficial for second-trimester abortion with complete placenta previa (CPP).

Methods: Patients with CPP who underwent second-trimester pregnancy termination by labor induction with or without UAE from January 2010 to January 2018 were retrospectively reviewed. In total, 25 patients were eligible for analysis. The primary outcomes were the abortion success rate and bleeding volume, and the secondary outcomes were the induction-to-abortion time, length of hospital stay, and complications.

Results: CPP occurred in all 25 patients. Fifteen patients underwent prophylactic UAE (UAE group) and 10 did not (control group). Abortion was successful in 13 of 15 (86.7%) women in the UAE group and in 9 of 10 (90.0%) women in the control group. There was no significant difference in the bleeding volume or induction-to-abortion time between the two groups. The hospital stay was longer and pyrexia was more common in the UAE than control group.

Conclusion: Prophylactic UAE did not markedly improve the outcomes of second-trimester abortion in patients with CPP. Conversely, it may increase the risk of complications and prolong the hospital stay.

Keywords

Uterine artery embolization, second trimester, placenta previa, termination of pregnancy, sepsis, postpartum hemorrhage

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Introduction

Complete placenta previa (CPP), defined as coverage of the internal cervical os by the placenta, is a high-risk factor for obstetric hemorrhage. The overall prevalence of placenta previa is 5.2 per 1000 pregnancies.[1] With the improvement of prenatal screening programs, patients with CPP now more commonly undergo termination of pregnancy (TOP) because of fetal demise or major structural malformations, especially during the second trimester.[2] This is a dilemma for both patients and obstetricians. Vaginal delivery by labor induction may cause intractable hemorrhage, whereas delivery by cesarean section increases the risk of maternal morbidities that affect future pregnancies, such as repeat cesarean section, uterine rupture, placenta accreta, and scar formation.[3–5]

Uterine artery embolization (UAE) was first introduced to control postpartum bleeding in 1979.[6] UAE blocks the main blood supply of the placenta, thereby reducing bleeding during labor, and has been recommended as an effective method for TOP with CPP in recent years.[7,8] However, whether UAE is necessary for second-trimester TOP with CPP without accreta remains controversial. The incidence of placenta previa is overestimated because of the performance of routine, second-trimester ultrasonic scanning.[9] In one study, only about 4.6% of patients in whom placenta previa was detected in the second trimester had persistent placenta previa at the time of delivery.[10] Placentation is a dynamic process, and the placenta migrates cephalad due to uterine segment stretching, which can also be observed during the progression of labor.[11] Some studies have suggested that the risk of hemorrhage is not particularly high during second-trimester TOP in patients with placenta previa that is not complicated by placenta accreta.[12]

In this retrospective cohort study, we evaluated the effects of UAE in second-trimester TOP for CPP without accreta. The study was performed to provide information to clinicians in an effort to avoid overuse of UAE.

Patients and Methods

Patients

We retrospectively reviewed our database of women who underwent TOP at 14 to 27 weeks of gestation from January 2010 to January 2018. The inclusion criteria were diagnosis of CPP using ultrasonography (Figure 1(a)), magnetic resonance imaging (Figure 1(b)), or both within 1 week before TOP; singleton pregnancy; TOP due to fetal death or malformation; and TOP from 14 to 27 weeks of gestation. The exclusion criteria were multiple pregnancies; placenta accreta; partial placenta previa, marginal placenta previa, and low-lying placenta; and TOP due to maternal diseases such as severe cardiopulmonary dysfunction.

Procedure

Whether UAE was performed was based on the patients' will after being counselled regarding the potential risks and benefits of this intervention. All patients underwent ultrasound-guided amniocentesis with intra-amniotic injection of 100 mg of ethacridine lactate followed by oral administration of 50 mg of mifepristone at 0, 12, and 24 hours. UAE was performed 2 hours after amniocentesis using the Seldinger technique (Figure 2). This procedure was performed under local anesthesia by two experienced interventional radiologists. The uterine artery was selectively catheterized with a 5-Fr Yashiro catheter (Terumo Corporation, Tokyo, Japan) through a right femoral artery puncture. The procedure was monitored by X-ray

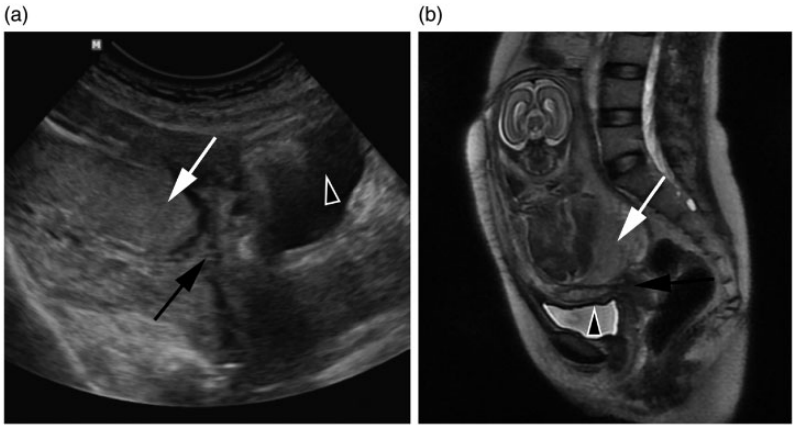

Figure 1. Ultrasound and magnetic resonance imaging findings. (a) Transabdominal ultrasonographic image and (b) T2-weighted magnetic resonance image showing the placenta (white arrow) completely covering the cervical os (black arrow) without signs of placenta accreta. Arrowhead: bladder

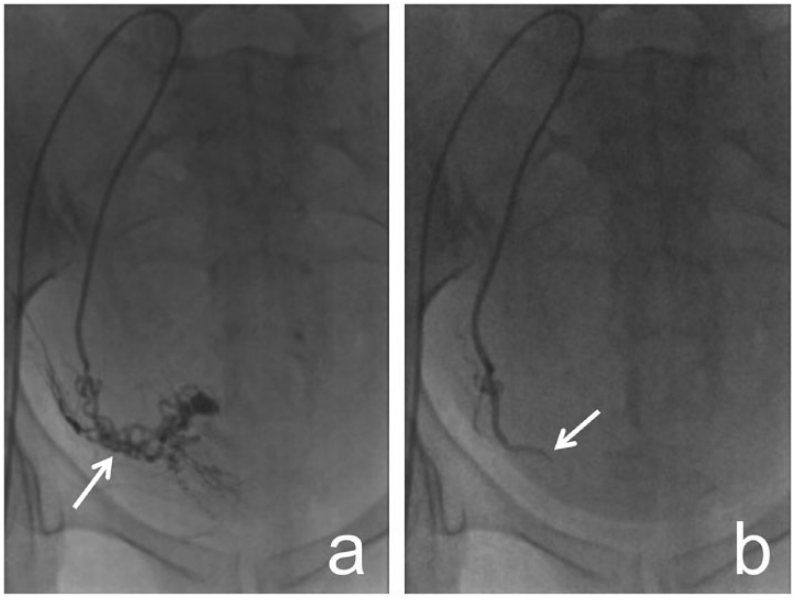

Figure 2. Angiography findings. Angiograms of the right uterine artery revealed (a) diffuse contrast staining before embolization and (b) devascularized placenta after embolization (white arrow: initial point of uterine artery)

screening in real time. Bilateral UAE was performed with an absorbable gelatin sponge (Gelfoam; Pfizer, New York, NY, USA) of 1400 to 2000 μm and 90 to 150 mg. Uterine arteriography was performed before and after embolization to ensure successful embolization. We evaluated and compared the differences in the abortion

success rate, bleeding volume, induction-to-abortion time, hospital stay, and complications between the two groups.

Statistical analysis

The data were analyzed using PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA). All the data are expressed as mean ± standard deviation or number (percentage). Statistical significance of continuous variables was analyzed using Student's t-test (if the database exhibited homogeneity and normality) or the Mann–Whitney U test (if the database was heterogeneous and lacked normality). Statistical significance of categorical variables was analyzed using Fisher's exact test. A P value of <0.05 was considered statistically significant.

Ethics

The present study was approved by the local ethics committee. Written informed consent was obtained from all the participants included in this study.

Results

Of all 1440 women identified in the database, 25 (1.74%) were eligible for the study. Fifteen patients underwent prophylactic UAE (UAE group), and 10 patients did not undergo UAE (control group). The characteristics of the women in each of these two groups are shown in Table 1. There were no significant differences in age, gestational age, history of abortion, history of cesarean section, reason for TOP, placental attachment sites, or fetal positions between the two groups.

The abortion success rate was 86.7% in the UAE group and 90.0% in the control group, with no significant difference. In the UAE group, 13 of the 15 patients underwent successful vaginal delivery. Two patients developed sepsis after UAE, and TOP was performed by cesarean section. In the control group, 9 of the 10 patients underwent successful vaginal delivery. One patient in the control group underwent cesarean section without hysterectomy because of massive vaginal bleeding.

The total blood loss volume in the UAE group was 392 ± 136 mL, and that in the

Table 1. Clinical features of patients in the UAE group and control group.

	UAE group (n = 15)	Control group (n = 10)	P
Reason for labor induction			
Malformation	2 (13.3)	2 (20.0)	0.656
Stillbirth	13 (86.7)	8 (80.0)	
Age, y	29.27 ± 1.412	28.50 ± 1.258	0.707
Gestational weeks	22.67 ± 1.059	22.40 ± 1.335	0.876
History of abortion	8 (53.3)	4 (40.0)	0.404
History of cesarean section	4 (26.7)	0 (0.0)	0.108
Site of placental attachment			
Anterior wall	10 (66.7)	5 (50.0)	0.337
Posterior wall	5 (33.3)	5 (50.0)	
Fetal position			
Vertical	12 (80.0)	8 (80.0)	0.687
Transverse	3 (20.0)	2 (20.0)	

Data are expressed as mean ± standard deviation or n (%) of patients.
UAE, uterine artery embolization.

control group was 327 ± 127 mL; the difference between the two groups was not statistically significant. The greatest blood loss volume was 1820 mL in the UAE group and 1400 mL in the control group. One patient in each group required a blood transfusion. Prophylactic UAE did not prolong the induction-to-abortion time, but it significantly prolonged the length of hospital stay (9.8 ± 0.6 vs. 7.0 ± 0.7 days, P = 0.002).

Pyrexia was a common complication in UAE-assisted TOP. The incidence of fever was significantly higher in the UAE than control group (53.3% vs. 10.0%, respectively; P = 0.04) (Table 2).

Discussion

The blood supply to the placenta is an important factor in intrapartum hemorrhage.[2,13] Some research groups have recently suggested that a decrease in the uteroplacental blood flow, such as that caused by preinduction feticide or UAE, may reduce the risk of maternal hemorrhage.[8,14] UAE is widely used in patients with various gynecologic and obstetric conditions, such as postpartum hemorrhage and cesarean scar pregnancies.[15–17] UAE is an important life-saving technique used to treat intractable postpartum hemorrhage while preserving fertility. TOP assisted by UAE is recommend as an effective and safe method for addressing placenta previa.[8] Peng and Zhang[7] reported that compared with cesarean section, UAE-assisted induction of labor reduced the risk for hemorrhage without increasing the duration of labor. However, no reports have stated whether UAE is beneficial for second-trimester TOP. The present study suggests that prophylactic UAE does not increase the abortion success rate, reduce total hemorrhage, shorten the induction-to-abortion time, or reduce the risk of blood transfusion. In contrast, it increased the risk of complications and prolonged the hospital stay in the present study.

Importantly, the fact that UAE did not reduce the blood loss volume during the induction process may be related to the method used to induce labor. Ethacridine lactate in combination with mifepristone is a commonly used method for termination of unwanted pregnancies in China.[18] Ethacridine lactate is a weak base that belongs to the acridine dye group. Intra-amniotic injection of ethacridine lactate can cause uterine contraction by the activation of uterine mast cells, leading to the release of mediators such as prostaglandin F2α, prostaglandin E2, prostacyclin, and thromboxane A2.[19] The reported success rate using ethacridine lactate is about 96%, and complications are rare.[20] Mifepristone is an active anti-progesterone agent that can induce uterine contraction, ripen the uterine cervix, and increase

Table 2. Univariate analysis of the outcomes in the UAE group and control group.

	UAE group (n = 15)	Control group (n = 10)	P
Abortion success rate	13 (86.7)	9 (90.0)	0.654
Total blood loss, mL	392 ± 136	327 ± 127	0.802
Pyrexia	8 (53.3)	1 (10.0)	0.04*
Induction-to-delivery interval, h	47.73 ± 9.266	45.44 ± 5.210	0.621
Hospital stay, days	9.80 ± 0.595	7.00 ± 0.683	0.002*

Data are expressed as mean ± standard deviation or n (%) of patients.
UAE, uterine artery embolization.
*P < 0.05.

myometrial sensitivity to prostaglandins.[21] In our clinical work, we have found that fetal death is induced about 24 hours after intra-amniotic injection of ethacridine lactate. Delivery usually occurs in about 48 to 72 hours. We speculate that fetal death causes a decline in placental circulation; however, this hypothesis was not tested in the present study. The decline in placental circulation after injection of ethacridine lactate into the amniotic cavity should be confirmed in further studies. Cephalad migration of the placenta is another reason for vaginal delivery. That is, the placenta, which is attached to the lower segment of the uterus, may migrate upward during the process of labor.[22] In the present study, placenta migration occurred in 13 of 15 patients in the UAE group and 9 of 10 patients in the control group. Although it is an invasive method, induction of labor by injection of ethacridine lactate into the amniotic cavity makes vaginal delivery possible.

Adverse effects of UAE are rare, although some reports have described acute ovary insufficiency, uterine infarction,[23] and uterine necrosis.[24] No such complications occurred in our cohort. Sepsis is a rare but serious complication during normal pregnancy and is one of the leading factors resulting in maternal mortality.[25,26] Two patients developed intra-amniotic infection in our UAE group. Both patients had three common elements: each had a history of vaginal bleeding during pregnancy, which may have been associated with subclinical chorioamnionitis; no evidence of infection was present, while sepsis symptoms were observed shortly after UAE; and broad-spectrum antibiotics administered before cesarean section were ineffective to eliminate the tissue infection. Although the underlying mechanism is unclear, we speculate that the main cause of sepsis is the reduced blood supply after UAE, which hampers the ability of antibiotics to reach the uterus, causing acceleration of bacterial growth in the ischemic uterus.[27,28]

Post-embolization syndrome is not a rare condition after UAE and is characterized by a low-grade fever, pelvic pain, leukocytosis, nausea, and other symptoms.[29] Although the etiology of post-embolization syndrome is unknown, the inflammatory process secondary to uterine tissue ischemia may be the main cause.[30] Similar to previous reports in the literature,[29,31] pyrexia was the most common non-serious complication in the present study. When the fever was $<38^{\circ}C$ and lasted <24 hours, the patients were not given antipyretic drugs and were encouraged to drink more water. Antibiotics were given to patients when their temperature reached $>38^{\circ}C$ with elevated serum inflammatory marker levels or when their infection was confirmed by microbial culture. The patients were discharged 24 to 48 hours after a normal temperature was achieved. Pyrexia was the main reason for a prolonged hospital stay in the UAE group.

This study has several potential limitations. The retrospective design did not allow us to draw definitive conclusions. Additionally, the sample size may have been small to detect statistical significance. Further research with higher statistical power is required to assess the value of UAE for second-trimester TOP in patients with CPP to avoid overuse of this procedure.

In conclusion, it seems that prophylactic UAE possesses few advantages for second-trimester TOP in patients with with CPP. In contrast, it increased the risk of complications and prolonged the hospital stay in the present study. Patients are at risk of sepsis after UAE, especially those with a history of vaginal bleeding. Chorioamnionitis should be comprehensively considered before UAE.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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