Conventional MRI features for predicting the clinical outcome of patients with invasive placenta

Ting Chen
Xiao-Quan Xu
Hai-Bin Shi
Zheng-Qiang Yang
Xin Zhou
Yi Pan

PURPOSE
We aimed to evaluate whether morphologic magnetic resonance imaging (MRI) features could help to predict the maternal outcome after uterine artery embolization (UAE)-assisted cesarean section (CS) in patients with invasive placenta previa.

METHODS
We retrospectively reviewed the MRI data of 40 pregnant women who have undergone UAE-assisted cesarean section due to suspected high risk of massive hemorrhage caused by invasive placenta previa. Patients were divided into two groups based on the maternal outcome (good-outcome group: minor hemorrhage and uterus preserved; poor-outcome group: significant hemorrhage or emergency hysterectomy). Morphologic MRI features were compared between the two groups. Multivariate logistic regression analysis was used to identify the most valuable variables, and predictive value of the identified risk factor was determined.

RESULTS
Low signal intensity bands on T2-weighted imaging ($P < 0.001$), placenta percreta ($P = 0.011$), and placental cervical protrusion sign ($P = 0.002$) were more frequently observed in patients with poor outcome. Low signal intensity bands on T2-weighted imaging was the only significant predictor of poor maternal outcome in multivariate analysis ($P = 0.020$; odds ratio, 14.79), with 81.3% sensitivity and 84.3% specificity.

CONCLUSION
Low signal intensity bands on T2-weighted imaging might be a predictor of poor maternal outcome after UAE-assisted cesarean section in patients with invasive placenta previa.

Placenta previa is often associated with abnormal placentation (placenta accreta, increta, or percreta) when overlapping the previous cesarean section (CS) scar, leading to severe intrapartum hemorrhage during placenta removal and further increasing the rates of hysterectomy and maternal mortality (1, 2). To overcome this problem, many doctors have tried to use the uterine artery embolization (UAE) procedure to control intractable intrapartum bleeding during scheduled CS (3, 4). However, the volume of blood loss and the rate of hysterectomy have been variable at different clinical centers, and the treatment efficacy has not been uniform (3–6). A common and simple method that can help to predict the maternal clinical outcome after UAE-assisted CS is urgently needed, particularly for presurgical preparation and doctor-patient communication.

Previously, ultrasonography was the most commonly used imaging method in presurgical evaluation of abnormal placentation in patients with placenta previa (7). There are several reports on sonographic evaluation to predict the risk of massive bleeding in patients with placenta previa and previous CS (8–12). However, ultrasonography is an extremely subjective evaluation modality and mainly depends on the experience of the operator. In recent years, with the advance of improved soft tissue resolution, larger fields of interest, and ultra-fast scanning sequences, MRI has been increasingly used in the evaluation of placental invasiveness and to classify the degree of placenta invasion, particularly in cases of diagnostic doubt by ultrasonography, maternal obesity, and posterior placentation (13, 14). MRI can provide topographic and morphologic information regarding the placenta, and clarify the degree of invasion for optimal diagnosis and planning of surgical management. Abnormal uterine bulging sign, heterogeneous placental signal intensity, dark intraplacental bands
on T2-weighted images, focal disruption of placental-myometrial interface, and placental protrusion sign were listed as distinctive findings of placental invasion on MRI (15–18). However, to the best of our knowledge, there has been no study correlating MRI features with maternal clinical outcome after UAE-assisted CS delivery until now.

Therefore, our study aimed to evaluate whether morphologic features on conventional MRI could be used to predict the maternal clinical outcome after UAE-assisted CS in patients with invasive placenta previa.

**Methods**

**Patients**

The protocol of this study was approved by the ethics committee of our hospital, and written informed consent was waived due to the retrospective nature of the study.

From February 2012 and March 2015, a total of 53 consecutive pregnant women underwent abdominal MRI in our department due to placenta previa overlying the previous CS scar. All of these patients were suspected to experience significant hemorrhage due to placenta accreta, increta, or percreta on the surface of a previous CS scar. The inclusion criteria included: 1) an exact history of CS; 2) diagnosis of placenta previa overlying the previous CS scar based on both ultrasonography and MRI; and 3) invasive placenta confirmed during the CS delivery and pathologic exam result. The final diagnostic criteria used in this study included the following: 1) clinical diagnosis during the CS based on a difficult manual piecemeal removal of the placenta if there is no separation after 20 min despite active management of the third stage of labor; 2) heavy continuous bleeding from the implantation site of a well-contracted uterus and a vaginal or percreta sign were more frequently observed in patients with poor outcome.

**Imaging analysis**

Conventional morphologic MRI features were analyzed as follows: 1) Placenta previa subtype classified as complete or partial depending on whether the placenta completely or partially overlapped the internal cervical ostium (B); 2) Attachment site of the placenta to the uterine wall classified in situ; 3) Signs of placental invasion. The MRI features indicating invasive placentation were low signal intensity bands on T2-weighted imaging.
imaging that appear as areas with nodular or linear disposition, extending from the uterine-myometrial surface to placenta (Fig. 1a); a focally disrupted interface between myometrium and placenta at the site of placenta accreta, increta, or percreta (Fig. 1b); heterogeneous intraplacental signal intensity owing to repeated hemorrhage or lacunae (Fig. 1c); bulging of the lower segment of the uterus owing to the mass effect of placenta in the lower segment of uterus (Fig. 1d) (15); the placental cervical protrusion sign, which indicates placenta tissue protrusion into the cervical canal (Fig. 1e) (16); the tenting of the bladder and/or infiltration of the pelvic organ (Fig. 1f) (17).

The images were independently and retrospectively reviewed by two radiologists (reader 1 and reader 2 with 10 and 7 years of experience in gynecology and obstetrics imaging, respectively), who were blinded to clinical and pathologic outcome. The imaging assessment results of the two radiologists were used to calculate interobserver agreement. In case of disagreement, a third senior radiologist with 20 years of experience in gynecology and obstetrics MRI was consulted. Reader 1 reviewed the images twice in one month for intraobserver agreement calculation.

Statistical analysis

Numeric data was averaged over all patients, reported as mean ± standard deviation (SD), and the Kolmogorov-Smirnov’s test was used to determine whether the quantitative parameters were normally distributed. Demographic data, including age, average gestational age, gravidity and parity, were compared between good outcome and poor outcome groups using unpaired t-test. The frequency distribution of qualitative MRI features between two groups was compared with chi-square test. Fisher exact test was performed if the sample size in the subgroup was too small. Multivariate logistic regression analysis was performed to determine the most significant risk factor that was predictive for poor outcome during UAE-assisted CS. Receiver operating characteristic curve analysis was used to determine the predictive value of the identified risk factor.

Interobserver agreement for the assessment of placental MRI between two readers was assessed using Kappa analysis. Intraobserver agreement of reader 1 was assessed using Kappa analysis. The Kappa value ranged between 0 and 1.00, and values closer to 1.00 meant better reproducibility. They were interpreted as follows: (slight, 0.00–0.20; fair, 0.21–0.40; moderate, 0.41–0.60; substantial, 0.61–0.80; perfect, 0.81–1.00). Statistical analysis was performed using SPSS software (SPSS version 19.0, IBM Inc.). A two-sided P value less than 0.05 was considered statistically significant.

Results

Forty parturient women (average gestation age, 34 weeks) underwent prophylac-
tic UAE-assisted CS, and no fetal or maternal mortality occurred. The average blood loss during CS was 1832 mL (range, 200–6500 mL). The poor outcome group contained 16 patients who had a significant hemorrhage of more than 1000 mL. Among these 16 patients, seven patients suffered an emergency hysterectomy due to refractory hemorrhage, including four patients who were diagnosed with placenta percreta preoperatively (Table 1). Meanwhile the good outcome group included 24 patients who had minor bleeding of less than 1000 mL, and the uterus was preserved in all 24 patients. The average blood loss of poor outcome group was significantly more than that of the good outcome group (3543 mL vs. 691 mL, P < 0.001). The maternal age, prior CS, dilation and curettage, prothrombin time, activated partial thromboplastin time, and international normalized ratio did not differ significantly between the two groups (P > 0.05). Detailed comparison of general obstetrical characteristics between the two groups is shown in Table 2.

Perfect interobserver agreement was achieved during the evaluation of complete placenta previa and anterior placental signal intensity bands on T2-weighted imaging, heterogeneous intraplacental signal intensity, placental cervical protrusion sign, placenta percreta (k = 0.624–0.767). Moderate agreement was achieved in the evaluation of low signal intensity bands on T2-weighted imaging, heterogeneous intraplacental signal intensity, placental cervical protrusion sign, placenta percreta and cervical involvement (k = 0.578 and k = 0.532, respectively). Detailed kappa values for interobserver agreement of MRI findings are shown in Table 3. The intraobserver agreement was perfect with a k value of 0.816 for reader 1.

Low signal intensity bands on T2-weighted imaging (P < 0.001), the placental cervical protrusion sign (P = 0.002), the placenta percreta (P = 0.011) were more frequently observed in patients with poor outcome compared with those with good outcome (Table 3), while no significant difference was observed between the two groups on the following factors: complete placenta previa, placenta located on the anterior wall, presence of a focally interrupted myometrial border, heterogeneous intraplacental signal intensity, and bulging of the lower uterine segment (P > 0.05). Representative cases are shown in Figs. 2 and 3.

Multivariate logistic regression analysis indicated that low signal intensity bands on T2-weighted imaging was the only risk factor for a poor outcome after UAE-assisted CS (OR 14.79, P = 0.02), while placental cervical protrusion sign and placenta percreta were not significant risk factors (Table 4). Low signal intensity bands on T2-weighted imaging showed 81.3% sensitivity and 84.3% specificity in predicting a poor outcome.

### Discussion

Patients with invasive placenta previa are at high risk of massive hemorrhage during CS delivery (8–10). Previously, ultrasonography was the most frequently used imaging modality to identify abnormal placenta-
ported anterior placenta position as a risk factors for massive bleeding during CS in cases of placenta previa. Baba et al. (9) reported anterior placenta position as a risk factor of massive hemorrhage during CS for placenta previa. Choi et al. (10) reported complete placenta previa as one of the risk factors for massive hemorrhage and peripartum hysterectomy. Recently, MRI has gained popularity in the evaluation of abnormal placenta. In the last two decades, UAE has become the first-line alternative treatment in controlling intractable peripartum hemorrhage, with a success rate of >90% (4–6, 20). This study focused on the preoperative evaluation of placental MRI features that can potentially predict high risk for significant hemorrhage associated with UAE-assisted CS in patients with invasive placenta previa. Our study demonstrated that the low signal intensity bands on T2-weighted imaging might be a high-risk factor that potentially correlates with poor maternal outcome after UAE-assisted CS in patients with invasive placenta previa. Low signal intensity bands on T2-weighted imaging is a promising predictor of greater blood loss or hysterectomy after UAE-assisted CS. The cervical protrusion sign and placenta percreta were potential risk factors for poor maternal outcome in univariate analysis; however, their significance was lost in the multivariate analysis. To the best of our knowledge, our study was the first to use the MRI features to predict the maternal outcome after UAE-assisted CS in patients with invasive placenta previa.

In the present study, we found the low signal intensity bands on T2-weighted imaging to be a high risk factor of significant intraoperative bleeding or hysterectomy during the UAE-assisted CS. Low signal intensity bands on T2-weighted imaging appear as areas with nodular or linear disposition, extending from the uterine-myometrial surface to placenta (16, 17). They represent abnormally thickened fibrous tissue or areas of fibrin deposition because of repetitive intraplacental hemorrhage. Alamo et al. (18) found that the presence of low signal intensity bands on T2-weighted imaging was the best single MRI feature indicating invasive placentalation. These investigators also demonstrated higher sensitivity, specificity, and interobserver agreement compared with other MRI manifestations of placental invasion. In a review of MRI features of the gravid uterus, Azour et al. (21) indicated that the intraplacental thick T2 dark bands have been shown to be a significant feature of morbidly adherent placenta, with sensitivity and specificity of 87.9% and 71.9%, respectively; increasing volume of intraplacental dark bands on T2-weighted imaging is a promising predictor of greater risk for significant hemorrhage associated with UAE-assisted CS in patients with invasive placenta previa. Our study demonstrated that the low signal intensity bands on T2-weighted imaging might be a high-risk factor that potentially correlates with poor maternal outcome after UAE-assisted CS in patients with invasive placenta previa.

Table 4. Multiple logistic regression analysis results of potential predictors for poor outcome after UAE-assisted cesarean section

<table>
<thead>
<tr>
<th>Variable</th>
<th>P</th>
<th>Odds ratio (95% CI)</th>
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<tbody>
<tr>
<td>Low signal intensity bands on T2WI</td>
<td>0.020</td>
<td>14.79 (1.03–185.84)</td>
</tr>
<tr>
<td>Placental cervical protrusion sign</td>
<td>0.212</td>
<td>17.48 (0.21–1453.19)</td>
</tr>
<tr>
<td>The tenting of the bladder and/or infiltration of the pelvic organ</td>
<td>0.999</td>
<td>–</td>
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UAE, uterine-artery embolization; CI, confidence interval; T2WI, T2-weighted imaging.

There are several reports on sonographic evaluation for predicting the risk of massive bleeding in patients with invasive placenta previa (8–12). Hasegawa et al. (8) determined advanced maternal age (≥35 years old), previous CS, and sponge-like sonographic findings in the cervix as risk factors for massive bleeding during CS in cases of placenta previa. Baba et al. (9) reported anterior placenta position as a risk factor of massive hemorrhage during CS for placenta previa. Choi et al. (10) reported complete placenta previa as one of the risk factors for massive hemorrhage and peripartum hysterectomy. Recently, MRI has gained popularity in the evaluation of abnormal placenta. In the last two decades, UAE has become the first-line alternative treatment in controlling intractable peripartum hemorrhage, with a success rate of >90% (4–6, 20). This study focused on the preoperative evaluation of placental MRI features that can potentially predict high risk for significant hemorrhage associated with UAE-assisted CS in patients with invasive placenta previa. Our study demonstrated that the low signal intensity bands on T2-weighted imaging might be a high-risk factor that potentially correlates with poor maternal outcome after UAE-assisted CS in patients with invasive placenta previa. Low signal intensity bands on T2-weighted imaging is a promising predictor of greater blood loss or hysterectomy after UAE-assisted CS. The cervical protrusion sign and placenta percreta were potential risk factors for poor maternal outcome in univariate analysis; however, their significance was lost in the multivariate analysis. To the best of our knowledge, our study was the first to use the MRI features to predict the maternal outcome after UAE-assisted CS in patients with invasive placenta previa.
significant hemorrhage in patients with placenta previa during the UAE-assisted CS (3, 4, 23, 24), which is consistent with our findings (P = 0.001).

Placental cervical protrusion sign was also regarded as a useful novel MRI finding for predicting placenta invasion by Ueno et al. (16), which is a known risk factor for the poor outcome of patients with placenta previa after CS. The potential reason for this might be related to the blood supply of the cervix. It is well known that not only the uterine artery but also internal pudendal arteries supply the cervix, which is different from the blood supply of the uterus (25). Therefore, just uterine artery embolization would not be sufficient to control the intractable bleeding from cervix-placenta adherent interface. Another possible reason for this is that the cervical stroma is mainly composed of connective tissue, resulting in weakness of contraction and intractable hemorrhage on the adherent surface of placenta accreta or increta. In our study, placental cervical protrusion sign was associated with poor maternal outcome in the univariate analysis. However, the significant association was lost during multivariate analysis. We speculate that this might be due to the limited number of patients. Further studies with larger sample sizes would be needed to clarify the value of cervical protrusion sign for predicting the poor outcome.

Placenta percreta is the most severe form of abnormal placental adherence, and the incidence is the lowest, accounting for only 7% of placenta invasion (26). The patient always experiences a significant hemorrhage during delivery when placenta removal is attempted. Highly aggressive and specialized surgical treatment is often required in patients with placenta percreta (27). Clausen et al. (28) reviewed 119 patients with placenta percreta, 66 of whom were managed by hysterectomy as the initial procedure. Yu et al. (3) mentioned that emergency hysterectomy was performed in two of four patients with placenta percreta due to massive hemorrhage in spite of the prophylactic uterine artery embolization. Grace Tan et al. (29) mentioned that in patients with placenta percreta, emergency hysterectomy must be considered if refractory hemorrhage is encountered. In our cohort of patients, we identified four patients with placenta percreta on MRI preoperatively, all of whom underwent hysterectomies in spite of the utility of prophylactic UAE procedure. In multivariate analysis, the sample size of patients with placenta percreta was too small to reach a statistically association with treatment outcome due to the rare incidence.

The treatment efficacy of prophylactic catheter placement is not uniform. Some authors advocate placement of arterial catheters before delivery because of the possibility of intractable hemorrhage (3–6); however, this is not a systematic procedure and only restricted to specific situations because of the risk of catheter displacement and because less than 50% of women with invasive placenta actually require transcatheter arterial embolization (30). In our department, the prophylactic UAE procedure was selectively performed on those patients who were suspected to experience significant hemorrhage due to invasive placenta previa. National guidelines do not recommended prophylactic balloon catheter placement because this approach conveys a risk of permanent sciatic nerve ischemia, arterial dissection, arterial rupture, and inferior leg ischemia (31). Should the prophylactic balloon catheter be used, it should be placed in the common iliac arteries instead of internal iliac arteries (32).

Previous studies revealed anterior placentation and complete placenta previa as independent risk factors for massive hemorrhage during CS (9, 10, 26); however, in the present study, they were not associated with significant hemorrhage possibly due to the added value of occlusion of the blood supply to the uterus and placenta by the UAE procedure.

In addition to its retrospective nature, there are some limitations to our study. First, the small number of the enrolled patients limited the power of statistical analysis. Given the rare incidence of patients with placenta percreta, it is difficult to gather large numbers of patients in short term. In our opinion, our study could serve as a preliminary finding for further studies with larger sample sizes. Second, our study focused only on the MRI findings of placenta abnormalities; MRI manifestations were not compared with pathologic findings to determine whether there is an underlying pathologic foundation for the low signal intensity bands on T2-weighted imaging.

In conclusion, our study demonstrates that the low signal intensity bands on T2-weighted imaging might reflect a high risk of significant hemorrhage after UAE-assisted CS in patients with invasive placenta previa. When this finding is identified preoperatively on MRI, effective management strategies should be prepared for potential significant intraoperative bleeding or hysterectomy.

Conflict of interest disclosure
The authors declare no conflicts of interest.

References
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