Assessment of the massive hemorrhage in placenta accreta spectrum with magnetic resonance imaging

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Abstract. The aim of the present study was to evaluate whether MRI features are able to predict massive hemorrhage of patients with placenta accreta spectrum (PAS). A total of 40 patients with suspected PAS after ultrasound examination were subjected to MRI. Of these, 29 patients were confirmed as having PAS. MRI data were analyzed independently by two radiologists in a blinded manner. Inter-observer agreement was determined. The 29 confirmed patients were divided into two groups (moderate and massive hemorrhage) according to the estimated blood loss (EBL) and blood transfusion, and the MRI features were compared between the two groups. The EBL, as well as blood transfusion, between the patients with and without each MRI feature were compared. The inter-observer agreement between the two radiologists for the 11 MRI features had statistical significance (P<0.05). Intra-placental thick dark bands and markedly heterogeneous placenta were the most important MRI features in predicting massive hemorrhage and blood transfusion (P<0.05). The difference in EBL between the patients with and without focal defect of the uteroplacental interface (UPI) was significant (P<0.05). The differences in blood transfusion between the patients with and without myometrial thinning, disruption of the inner layer of the UPI, increased placental vascularity and increased vascularity at the UPI were significant (P<0.05). These results indicate that MRI features may predict massive hemorrhage of patients with PAS, which may be helpful for pre-operative preparation of PAS patients.

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Introduction

Placenta accreta spectrum (PAS), which represents a clinical challenge in obstetrics, is defined as myometrial involvement by the fetal trophoblast (1,2). It may lead to uncontrollable bleeding and threaten the lives of mother and baby. Its prevalence has markedly increased in China over the past 50 years, primarily due to the increasing number of pregnant females undergoing primary and repeat cesarean sections (3). Obstetricians have implemented various methods to improve the massive hemorrhage caused by placenta implantation, including ascending uterine artery ligation (AUAL), uterine artery embolization (UAE) and prophylactic abdominal aorta balloon occlusion (ABO), but the therapeutic effects are varied (4). Interventional radiology is commonly applied and placement of prophylactic balloon catheters in the common or internal iliac arteries are commonly used to help control massive hemorrhage (5,6). Development of an effective way to prenatally predict massive hemorrhage may allow for appropriate pre-operative preparation, including the arrangement for treatment by a skilled surgical team.

There have been several reports on the association between clinical information or therapeutic schedule and the risk of massive hemorrhage (7,8). Wright *et al* (8) reported an association among PAS (placenta accreta, increta or percreta), gestational age of <34 weeks at delivery and estimated blood loss (EBL)≥5,000 ml. It was noted that patients with placenta previa, who delivered at an earlier gestational age, were more likely to require ≥10 units of blood. Shamshirsaz *et al* (7) reported that a standardized approach for patients with morbidly adherent placentation provided by a specific multidisciplinary team was associated with improved maternal outcomes compared with a more traditional non-multidisciplinary approach. There are several reports on sonographic evaluation for predicting the risk of massive bleeding. For

instance, Hasegawa *et al* (9) reported that advanced maternal age, previous cesarean section and presence of sponge-like tissue in the cervix were risk factors of massive bleeding during cesarean section in cases of placenta previa, regardless of whether placental adherence was present. Baba *et al* (10) reported that anterior placentation was a risk factor of massive hemorrhage during cesarean section for placenta previa.

Chen *et al* (11) reported that low signal intensity bands on T2-weighted imaging may be a predictor of poor maternal outcome in patients with invasive placenta previa. However, studies on the association between MRI features and hemorrhage of patients with PAS are currently limited. The present study investigated whether MRI features are able to predict massive hemorrhage of patients with PAS. The results may be helpful for pre-operative preparation.

Materials and methods

Patients. The present study was a retrospective study. A total of 40 patients who underwent ultrasonography (US) and placenta MRI examination from March 2015 to May 2018 were enrolled. The inclusion criteria were as follows: (a) Patients with suspected PAS or inconclusive results on US, (b) patients at high risk of PAS with one or more of the following: Maternal age >35 years, grand multiparity, previous uterine interventional procedures (e.g. cesarean section, dilatation and curettage and myomectomy) and placenta previa (12). The exclusion criteria were as follows: (a) Medical records not available, (b) only MRI data of post-partum placenta implantation available, (c) early pregnancy, (d) patients who had induced labor rather than cesarean section due to stillbirth in utero. The patients were first diagnosed with suspected or inconclusive PAS using US, based on the detection of any of the following: Loss/irregularity of the echolucent area between uterus and placenta, thinning or interruption of the hyperechoic interface between uterine serosa and bladder wall, the presence of turbulent placental lacunae with high-velocity flow (>15 cm/sec), hypervascularity of the uterine serosa-bladder wall interface and irregular intraplacental vascularization (13). All patients received cesarean section and only one patient underwent subtotal hysterectomy due to uncontrollable bleeding. The final diagnosis of PAS was made based on intra-operative observation for 39 patients and by histopathology for one patient who was treated by subtotal hysterectomy. Finally, 29 patients (72.5%, 29/40) were confirmed as having PAS (average age, 33.5±4.2 years), and 11 patients were confirmed as non-PAS (average age, 32.8±3.2 years).

The retrospective study was performed in accordance with the standards set out in the Code of Ethics of the World Medical Association (Declaration of Helsinki) and the research procedures were approved by the ethics review board of Shandong Provincial Hospital (Jinan, China). Informed consent was obtained from each patient.

MRI examination. All MRI examinations were performed with a 1.5-T system (HDxt; GE Healthcare). An eight-channel pelvic phased-array surface coil was used for signal reception. All patients were imaged in the supine or left lateral position depending on tolerability for each case. The MRI protocol included axial, sagittal and coronal fast imaging employing

steady-state acquisition with the following settings: Repeat time (TR), 3.6 msec; echo time (TE), 1.6 msec; matrix size, 224x256; thickness, 5-7 mm; intersection gap, 1 mm; and field of view (FOV), 400x400 mm^2, as well as single-shot fast spin-echo T2-weighted imaging (TR, 1,800 msec; TE, 81 msec; matrix size, 288x192; thickness, 5-6 mm; intersection gap, 1 mm; FOV, 380x380-400x400 mm^2) and liver acquisition with volume acceleration (TR, 3.9 msec; TE, 1.8 msec; matrix size, 288x200; thickness, 2.5 mm; intersection gap, 0.5 mm; and FOV, 400x400 mm^2).

MRI data analysis. MRI data were analyzed independently by two radiologists (JZ with five years and HX with ten years of experience in evaluating the placenta using MRI) blinded to the patients' history, US examination results, presence of PAS and intra-operative findings. MRI data were interpreted on a PACS view station (Centricity RIS CE V2.0; GE Healthcare). A total of 11 MRI features were evaluated, including placenta previa, focal defect of the uteroplacental interface (UPI), myometrial thinning, disruption of the inner layer of the UPI, intraplacental thick dark bands, focal defect of the interval between the bladder and uterus, increased placental vascularity, markedly heterogeneous placenta, uterine bulge, increased uterine vascularity and increased vascularity in the UPI (14). A complete description of the MRI features is provided in Supplemental Table SI. In case of any disagreement, a third radiologist (QL) with 15 years of experience in evaluating the placenta using MRI was consulted.

Clinical diagnosis of PAS. The reference standard for determining the actual status of the placenta was established by one obstetrician (CZ with 20 years of experience in obstetrics) according to intra-operative findings recorded in the electronic medical records of most patients (n=39). The diagnostic criteria were as follows (15): Placenta accreta: i) No placental tissue invading through the surface of the uterus. ii) Incomplete separation with uterotonics and gentle cord traction and manual removal of the placenta was required for the remaining placenta. iii) Bleeding cannot be controlled autonomously. Placenta increta: i) No placental tissue invading through the surface of the uterus. ii) Placental tissue implanted in myometrium of uterus requiring to be removed by forceps curettage. Placenta percreta: Macroscopically, the whole layer of the uterus (including the serosal surface), even the surrounding organs, was invaded by placental tissues.

Hemorrhage analysis. The EBL was estimated by an experienced obstetrician who participated in the operation based on the operative report, which included fluid volume in the negative pressure aspirator, dressing weight and other operative findings. The blood volume in the mixture of blood and amniotic fluid was calculated according to the total fluid volume, hematocrit of the mixture and prenatal hematocrit. The EBL was estimated and documented during surgery. Packed red blood cell (PRBC) transfusion and plasma transfusion were also documented. Moderate hemorrhage was defined as EBL<2,000 ml and PRBC transfusion <10 units. Massive hemorrhage was defined as EBL≥2,000 ml or PRBC transfusion ≥10 units (7,8). The patients were divided into two groups

Table I. Demographic and clinical information of all patients.

Item	Non-PAS (n=11)	PAS (n=29)	P-value	Moderate hemorrhage (n=19)	Massive hemorrhage (n=10)	P-value
Maternal age (years)	32.8±3.2 (28-40)	33.5±4.2 (27-40)	0.635	34.5±4.4 (28-40)	31.6±3.1 (27-36)	0.076
Gestational age (days)	239±26 (192-272)	241±30 (126-280)	0.864	242±23 (189-269)	237±42 (126-280)	0.716
EBL (ml)	586±358 (300-1,400)	1286±855 (300-3,500)	0.001	816±347 (300-1,600)	2180±824 (800-3,500)	<0.001
PRBC transfusion (units)	1.95±2.76 (0-8)	4.59±4.36 (0-14)	0.07	2.11±2.05 (0-6)	9.32±3.57 (4-14)	<0.001
Plasma transfusion (ml)	127±205 (0-600)	405±408 (0-1,200)	0.008	166±197 (0-550)	860±299 (400-1,200)	<0.001
Interval time	12.3±17.1 (0-47)	9.6±13.2 (0-65)	0.604	11.3±15.5 (1-65)	6.5±6.9 (0-21)	0.366
RBC (10^{12}/l) (normal range 3.8-5.1)	3.47±0.35 (2.94-4.03)	3.7±0.42 (2.91-4.64)	0.11	3.71±0.43 (3.14-4.64)	3.69±0.41 (2.91-4.48)	0.912
Hemoglobin (g/l) (normal range 115-150)	99.7±13.7 (83-123)	105.4±15.7 (74-137)	0.295	105.5±16.6 (74-137)	105.3±14.8 (81-127)	0.971
Hematocrit (%) (normal range 35-45)	30.4±3.6 (26.5-37.9)	32.1±4.0 (24-39)	0.215	31.9±4.0 (24-39)	32.6±4.1 (27-38.2)	0.636
PT (sec) (normal range 10.7-14.0)	12.8±0.8 (11.4-14.1)	12.6±1.7 (10.3-19)	0.761	12.3±1.1 (10.3-14.5)	13.3±2.5 (10.4-19)	0.263
INR (normal range 0.8-1.2)	1.00±0.06 (0.94-1.10)	1.02±0.14 (0.87-1.62)	0.633	1.00±0.06 (0.87-1.11)	1.06±0.22 (0.9-1.62)	0.449
APTT (sec) (normal range 21-35)	31.6±3.2 (25-34.3)	30.1±4.7 (21.9-39)	0.338	29.1±5.4 (21.9-39)	32.0±2.1 (28.3-36.3)	0.045
Cesarean sections per patient			0.361			0.897
None	0	3		2	1	
Once	10	24		16	8	
Twice	1	2		1	1	
Abortions per patient			0.126			0.677
None	2	8		5	3	
Once	1	11		8	3	
Twice	6	9		5	4	
≥Three times	2	1		1	0	
Hemostatic methods			0.437			0.035
ABO	1	7		2	5	
UAE	0	2		0	2	
AUAL	9	27		18	9	

The data values are expressed as mean ± standard deviation (range) or n. PAS, placenta accreta spectrum; EBL, estimated blood loss; PRBCs, packed red blood cells; Interval time, interval time between MRI and cesarean section; RBC, red blood cell; PT, Prothrombin time; INR, prothrombin time international normalized ratio; APTT, activated partial thromboplastin time; ABO, prophylactic abdominal aorta balloon occlusion; UAE, uterine artery embolization; AUAL, ascending uterine artery ligation.

Table II. Inter-observer agreement for MRI features.

MRI feature	κ-all[a]	P-value	κ-PAS[a]	P-value
Placenta previa	0.787	<0.001	0.886	<0.001
Focal defect of the UPI	0.615	<0.001	0.557	0.002
Myometrial thinning	0.593	<0.001	0.551	0.003
Disruption of the inner layer of the UPI	0.627	<0.001	0.514	0.005
Intraplacental thick dark bands	0.725	<0.001	0.703	<0.001
Focal defect of the IBU	0.481	<0.001	0.473	0.003
Increased placental vascularity	0.654	<0.001	0.623	0.001
Markedly heterogeneous placenta	0.908	<0.001	0.901	<0.001
Uterine bulge	0.375	0.018	0.426	0.017
Increased uterine vascularity	0.714	<0.001	0.703	<0.001
Increased vascularity in UPI	0.644	<0.001	0.519	0.005

[a]κ-values of 0.00-0.20, poor agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, good agreement; 0.81-0.99, excellent agreement; 1.00, perfect agreement. UPI, uteroplacental interface; κ-all, κ-values for the 40 patients with suspected PAS; κ-PAS, κ-values for the 29 patients with confirmed PAS; IBU, interval between the bladder and uterus; PAS, placenta accreta spectrum.

Table III. Association between involvement depth and hemorrhage.

Involvement depth	Patients (n)	EBL (ml)	PRBCs transfusion (units)	Plasma transfusion (ml)
Placenta accreta	6	717±299	1.33±2.07	67±103
Placenta increta	16	1,275±801	4.09±3.72	350±322
Placenta percreta	7	1,800±854	8.54±4.58	821±428
P-value		0.070	0.005	0.001

The data values are expressed as mean ± standard deviation (range) or n. EBL, estimated blood loss; PRBCs, packed red blood cells.

(moderate hemorrhage and massive hemorrhage) according to EBL and PRBC transfusion.

Statistical analysis. Statistical analysis was performed with SPSS for Windows, version 17.0 (SPSS, Inc.). Placenta previa is a five-valued variable (without placenta previa, low-lying placenta, marginal placenta previa, partial placenta previa or complete placenta previa). The other 10 MRI features are binary variables (with or without the MRI feature). Inter-observer agreement regarding categorical data between the first two radiologists was assessed using a Kappa test. Demographic profiles of numerical data [including age, gestational age, EBL, PRBC transfusion, plasma transfusion, interval time between MRI and operation, RBCs, hemoglobin, hematocrit, prothrombin time, prothrombin time international normalized ratio (INR) and activated partial thromboplastin time (APTT)] of non-PAS and PAS patients, as well as moderate hemorrhage and massive hemorrhage patients, were compared using the independent-samples t-test. The numbers of cesarean sections and abortions of the non-PAS and PAS patients, as well as the number of patients with moderate and massive hemorrhage, were compared using the Mann-Whitney U-test. The hemostatic methods for the non-PAS and PAS patients, as well as the moderate hemorrhage and massive hemorrhage patients, were compared using a χ^2 test.

The MRI features between the moderate and massive hemorrhage patients were compared using the χ^2 test. The EBL, PRBC transfusion and plasma transfusion between patients with and without each MRI feature were compared using the independent-samples t-test. The EBL, PRBC transfusion and plasma transfusion among different subtypes of placenta previa were compared using one-way analysis of variance. For all statistical analyses, P<0.05 was considered to indicate statistical significance.

Results

Patients. As presented in Table I, the clinical information of the patients was compared. The EBL and plasma transfusion for the PAS patients were significantly higher than those for the non-PAS patients (P<0.01). The differences in the other demographic characteristics between the non-PAS and the PAS patients were not significant (P>0.05). There were 19 cases of moderate hemorrhage (including 6 cases of placenta accreta, 11 cases of placenta increta and 2 cases of placenta percreta), 10 cases of massive hemorrhage (including 5 cases of placenta increta and 5 cases of placenta percreta). The EBL, PRBC transfusion and plasma transfusion for the patients in the massive hemorrhage group were significantly
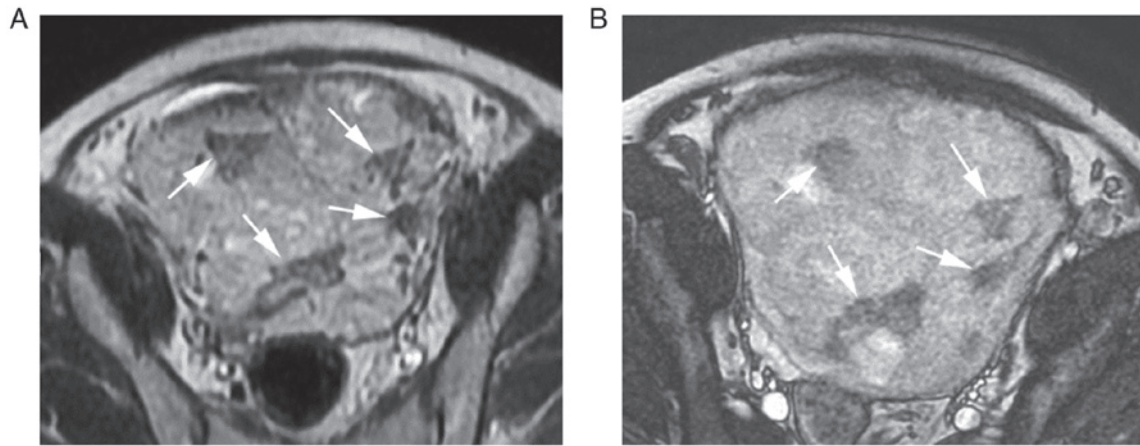
Figure 1. Intraplacental thick dark bands of a 30-year-old female at 34 weeks plus 4 days of gestation with complete placenta previa and placenta percreta. The amounts regarding estimated blood loss, packed red blood cell transfusion and plasma transfusion were 3,000 ml, 12 units and 1,200 ml, respectively. (A) The axial single-shot fast spin echo T2-weighted and (B) fast imaging employing steady-state acquisition images indicate intraplacental thick dark bands (arrows), displaying as hypointense in the two images.

higher than those for the patients in the moderate hemorrhage group (P<0.001). The mean APTT for the massive hemorrhage group was significantly longer than that for the moderate hemorrhage group (P<0.05), but the mean APTT of the two groups was in the normal range. A total of three hemostatic methods have been applied for the patients (Table I). One of the two PAS patients treated with UAE underwent pre-operative UAE, while the others underwent post-operative UAE. One of the 27 PAS patients treated with AUAL underwent unilateral AUAL, while the other 26 patients underwent bilateral AUAL. The difference in hemostatic methods between the moderate hemorrhage group and the massive hemorrhage group was significant (P<0.05). The proportion of patients who underwent ABO in the massive hemorrhage group was larger than that in the moderate hemorrhage group. However, the blood loss and transfusion in the massive hemorrhage group were still higher than those in the moderate hemorrhage group. Other hemostatic methods, including the use of oxytocin, tourniquet, local suture ligation, uterine packing hemostasis and placement of hemostatic gauze, were applied according to the intra-operative conditions. Each patient was treated using multiple hemostasis methods.

All patients underwent planned cesarean section and no emergency surgery was performed in the present study. One PAS patient underwent subtotal hysterectomy. A total of 4 PAS patients delivered with broken placentae. The other 35 patients delivered with almost complete placentae. No maternal mortality occurred. There was no case of bladder invasion. One stillborn fetus was delivered.

Inter-observer agreement. Interobserver agreement was excellent for one of the eleven MRI features (markedly heterogeneous placenta, κ>0.8), good for three MRI features (intraplacental thick dark bands, increased placental vascularity, increased uterine vascularity, κ>0.6) and moderate for two MRI features (myometrial thinning, focal defect of the interval between the bladder and uterus, κ>0.4). For the remaining five MRI features (placenta previa, focal defect of the UPI, disruption of the inner layer of the UPI, uterine

bulge and increased vascularity in UPI), the κ-values for the 40 patients with suspected PAS (κ-all) and for the 29 patients with confirmed PAS (κ-PAS) were not in the same interval, but the inter-observer agreement was statistically significant. The detailed κ-values of each MRI feature are provided in Table II. Inter-observer agreement was fair (κ-all=0.375) only for the MRI feature of uterine bulge.

Association between involvement depth and hemorrhage. There were 6 cases of placenta accreta (20.7%), 16 cases of placenta increta (55.2%) and 7 cases of placenta percreta (24.1%). EBL, PRBC transfusion and plasma transfusion of patients with placenta accreta, increta and percreta are compared in Table III. The EBL exhibited an increasing trend along with the implant depth, but without significant difference (P>0.05). The differences in PRBC transfusion, as well as plasma transfusion, among the three groups were significant (P<0.05). The differences in PRBC transfusion and plasma transfusion between the placenta accreta and placenta percreta groups, as well as that between the placenta increta and placenta percreta groups, were significant (P<0.05). However, there was no significant difference between the placenta accreta and the placenta increta groups (P>0.05).

Association between MRI features and hemorrhage Differentiation between moderate and massive hemorrhage group. To differentiate between the moderate and massive hemorrhage groups, the MRI features of the two groups were compared. Among the 29 PAS patients, the differences between the two groups (moderate vs. massive hemorrhage group) were significant in two MRI features (intraplacental thick dark bands, P=0.005; markedly heterogeneous placenta, P=0.020). The two MRI features are provided in Figs. 1 and 2, respectively. The differences in the other 9 MRI features between the two groups were not significant (i.e. placenta previa, P=0.081; focal defect of the UPI, P=0.173; myometrial thinning, P=0.059; disruption of the inner layer of the UPI, P=0.054; focal defect of the interval between the bladder and uterus, P=0.64; increased placental vascularity, P=0.198;
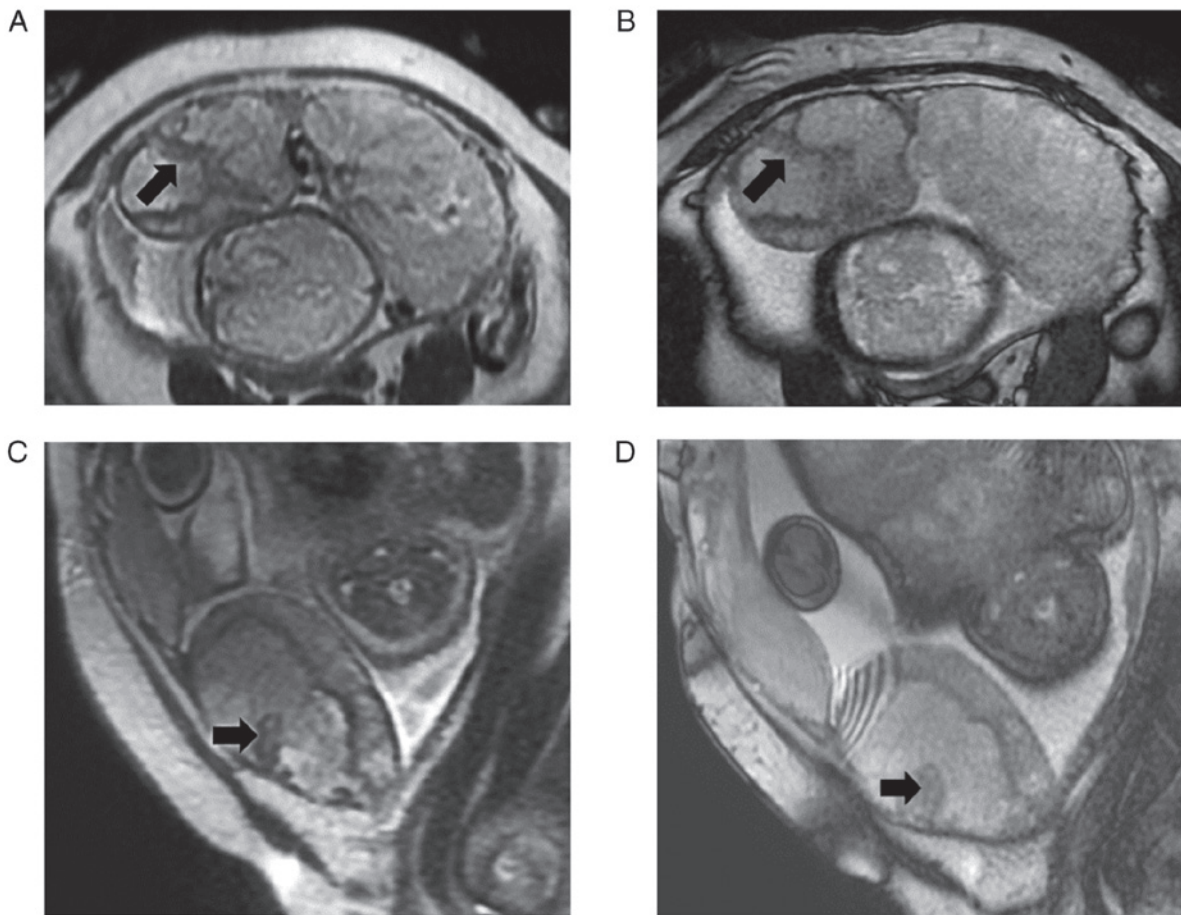
Figure 2. Intraplacental thick dark bands of a 40-year-old female at 36 weeks plus 6 days of gestation with complete placenta previa and placenta percreta at the anterior lower uterine segment. The amounts regarding estimated blood loss, packed red blood cell transfusion and plasma transfusion were 1,600 ml, 6 units and 550 ml, respectively. (A) A markedly heterogeneous placenta containing intraplacental thick dark bands, as indicated by black arrows, was shown in an axial SSFSE T2-weighted image; (B) axial FIESTA image; (C) sagittal SSFSE T2-weighted image; and (D) sagittal FIESTA image. SSFSE, single-shot fast spin echo; FIESTA, fast imaging employing steady-state acquisition.

uterine bulge, P=0.777; increased uterine vascularity, P=0.596; increased vascularity in UPI, P=0.206; Tables IV and V). These results indicated that the MRI features of intraplacental thick dark bands and markedly heterogeneous placenta may be helpful in predicting massive hemorrhage.

MRI features as grouping variables. The differences in EBL, PRBC transfusion and plasma transfusion were compared between the patients with and without each MRI feature (Table VI). There were no significant differences in EBL and blood transfusion among the different subtypes of placenta previa (Table IV). The differences in EBL between the patients with and without the three MRI features were significant (i.e., focal defect of the UPI, intraplacental thick dark bands, markedly heterogeneous placenta; P<0.05). The three MRI features are presented in Fig. 3. The differences in PRBC transfusion and plasma transfusion between the patients with and without the six MRI features were significant (P<0.05). The six MRI features included myometrial thinning, disruption of the inner layer of the UPI, intraplacental thick dark bands, increased placental vascularity, markedly heterogeneous placenta and increased vascularity in UPI (Table VI). Representative images of the six MRI features are displayed in Figs. 1-3.

Discussion

In the present study, not only all of the PAS patients but also all the non-PAS patients had placenta previa and/or a history of at least one prior cesarean section and/or one abortion. There was a large proportion of PAS (72.5%, 29/40) in the present study. This may be due to inclusion of patients with suspicious PAS or inconclusive findings on US who are at high risk of PAS.

There is an emphasis in China on uterine-sparing management. Therefore, the diagnosis of PAS for most patients was confirmed according to intra-operative findings. There is a recent International Federation of Gynecology and Obstetrics (FIGO) system of clinical classification based on clinical findings (16). The diagnosis of placenta accreta and percreta in the present study was basically consistent with that of the FIGO system. In the present study, the diagnosis of placenta increta was based on the placenta separation method of forceps curettage. Although the diagnosis of placenta increate was described differently, the meaning was consistent with that of the FIGO system.

The EBL is notoriously subjective and subject to error, particularly when the volume is very low or very high (17). EBL was estimated by an experienced obstetrician in this

Table IV. EBL and blood transfusion in the patients with PAS with different subtypes of placenta previa.

Subtype of placenta previa	Moderate hemorrhage	Massive hemorrhage	Total	EBL (ml)	Transfused PRBC (units)	Transfusion of plasma (ml)
Without	1	0	1	600±0 (600-600)	2.00±0.00 (2.00-2.00)	0±0 (0-0)
Low-lying	4	0	4	1,050±412 (600-1,600)	3.00±2.58 (0.00-6.00)	238±281 (0-550)
Marginal	4	0	3	633±321 (400-1,000)	0.00±0.00 (0.00-0.00)	0±0 (0-0)
Partial	1	1	2	1,250±1,061 (500-2,000)	3.88±5.48 (0.00-7.75)	500±707 (0-1,000)
Complete	10	9	19	1,479±941 (300-3,500)	5.87±4.53 (0.00-14.00)	516±402 (0-1,200)
Total	19	10	29	P=0.477	P=0.206	P=0.187

The data values are expressed as mean ± standard deviation (range) or n. EBL, estimated blood loss; PAS, placenta accreta spectrum; PRBCs, packed red blood cells.

Table V. Differentiation between moderate and massive hemorrhage group of PAS patients with MRI features.

MRI feature	Moderate hemorrhage (n=19)	Massive hemorrhage (n=10)	P-value
Focal defect of the UPI	13	9	0.173
Myometrial thinning	11	9	0.059
Disruption of the inner layer of the UPI	15	10	0.054
Intraplacental thick dark bands	1	5	0.005
Focal defect of IBU	1	1	0.640
Increased placental vascularity	2	3	0.198
Markedly heterogeneous placenta	2	5	0.020
Uterine bulge	3	2	0.777
Increased uterine vascularity	4	3	0.596
Increased vascularity in UPI	5	5	0.206

The data values are expressed as mean ± standard deviation (range) or n. PAS, placenta accreta spectrum; UPI, uteroplacental interface; IBU, interval between the bladder and uterus.
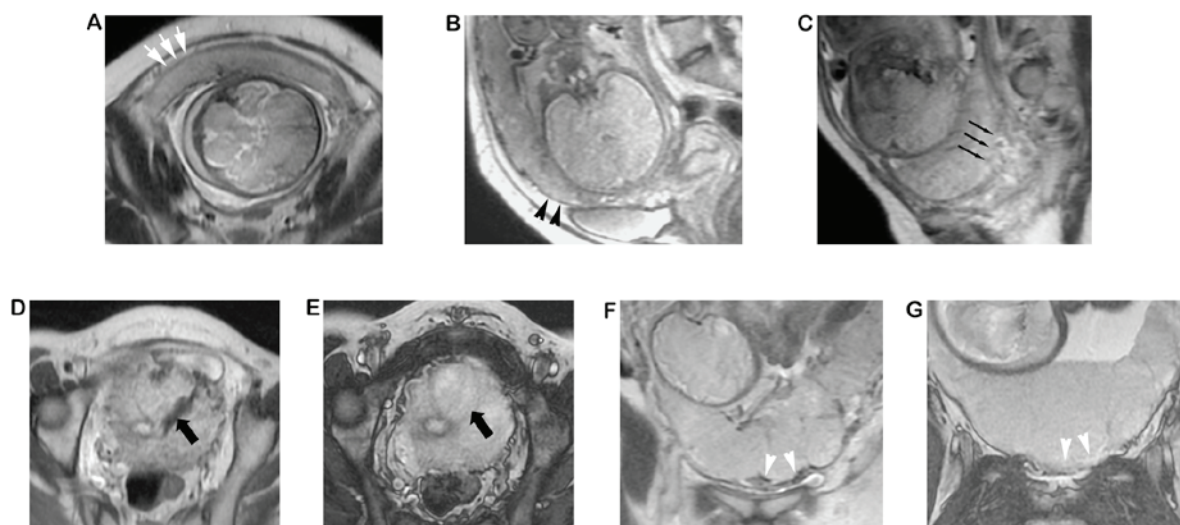

Figure 3. MRI images from five different patients. (A) Image obtained from patient 1, where focal defects of the UPI were indicated by white arrows. Thickness, 2.2 mm. The three layers of the myometrium could not be displayed clearly. (B) Patient 2, displaying myometrial thinning (black arrowheads; thickness, 1.7 mm) and focal defect of the UPI; (C) Patient 3, displaying disruption on the inner layer of the UPI (black thin arrows), where the inner layer of the UPI was interrupted; (D and E) Patient 4, exhibiting increased placental vascularity (black thick arrows). (D) The vessel exhibited a lack of flow on the single-shot fast spin echo T2-weighted image and was isointense on the (E) fast imaging employing steady-state acquisition image. (F and G) Patient 5, where increased vascularity was observed at the UPI. (F) A lack of flow on the SSFSE T2-weighted image and (G) isointense on the FIESTA image (white arrowheads). SSFSE, single-shot fast spin echo; FIESTA, fast imaging employing steady-state acquisition; UPI, uteroplacental interface.

Table VI. Differences in EBL, PRBC transfusion and plasma transfusion between the patients with and without each MRI feature.

MRI feature	EBL (ml)			PRBC transfusion (Units)			Plasma transfusion (ml)		
	No	Yes	P-value	No	Yes	P-value	No	Yes	P-value
Placenta previa	-	-	0.477	-	-	0.206	-	-	0.187
Focal defect of the UPI	843±326 (600-1,500)	1,427±926 (300-3,500)	0.018	2.86±3.44 (0.00-10.00)	5.15±4.54 (0.00-14.00)	0.232	200±365 (0-1000)	470±407 (0-1,200)	0.129
Myometrial thinning	922±689 (300-2,500)	1,450±887 (400-3,500)	0.126	2.17±2.60 (0.00-7.50)	5.69±4.59 (0.00-14.00)	0.015	156±219 (0-600)	518±427 (0-1,200)	0.006
Disruption of the inner layer of the UPI	750±520 (300-1,500)	1,372±874 (400-3,500)	0.181	1.00±1.15 (0.00-2.00)	5.17±4.42 (0.00-14.00)	0.001	50±100 (0-200)	462±411 (0-1,200)	0.000
Intraplacental thick dark bands	965±552 (300-2,500)	2517±679 (1,600-3,500)	0.001	3.47±3.81 (0.00-14.00)	8.92±3.77 (4.00-14.00)	0.004	304±366 (0-1000)	792±341 (400-1,200)	0.007
Focal defect of the IBU	1,248±873 (300-3,500)	1,800±283 (1,600-2,000)	0.388	4.19±4.10 (0.00-14.00)	10.00±5.66 (6.00-14.00)	0.068	370±391 (0-1,200)	875±460 (550-1,200)	0.092
Increased placental vascularity	1,154±845 (300-3,500)	1,920±638 (1,000-2,500)	0.067	3.55±3.60 (0.00-12.00)	9.60±4.56 (4.00-12.00)	0.003	325±381 (0-1,200)	790±325 (400-1,200)	0.017
Heterogeneous placenta	964±565 (300-2,500)	2,300±845 (1,000-3,500)	0.000	3.44±3.90 (0.00-14.00)	8.21±3.91 (4.00-14.00)	0.009	300±374 (0-1,000)	736±345 (400-1,200)	0.011
Uterine bulge	1,254±864 (400-3,500)	1,440±891 (300-2,500)	0.667	4.13±4.10 (0.00-14.00)	6.80±5.40 (0.00-14.00)	0.220	375±397 (0-1,200)	550±477 (0-1,200)	0.393
Increased uterine vascularity	1,172±770 (300-3,000)	1,643±1,069 (500-3,500)	0.211	4.42±4.20 (0.00-14.00)	5.14±5.15 (0.00-14.00)	0.710	389±411 (0-1,200)	457±428 (0-1,200)	0.706
Increased vascularity in UPI	1,142±820 (300-3,500)	1,560±896 (500-3,000)	0.217	3.33±2.85 (0.00-10.00)	7.00±5.75 (0.00-14.00)	0.028	295±315 (0-1,000)	615±494 (0-1,200)	0.042

The data values are expressed as mean ± standard deviation (range) or n. EBL, estimated blood loss; PRBCs, packed red blood cells; UPI, uteroplacental interface; IBU, interval between the bladder and uterus; No, without the MRI feature; Yes, with the MRI feature.

study. Different obstetricians may have different estimates. Therefore, the association between PRBC transfusion and plasma transfusion, as well as MRI features, was evaluated in the present study. There were no significant differences in red blood cells, hemoglobin, hematocrit, prothrombin time and INR between the massive hemorrhage group and the moderate hemorrhage group. There was a significant difference in APTT between the two groups, but the APTT of each group was in the normal range. They were therefore unlikely to have influenced the PRBC and plasma transfusion.

The κ-all and κ-PAS values exhibited certain differences, which may be due to the small number of patients, resulting in the low robustness of the κ-values. The inter-observer agreement for most MRI features was equal to or superior to moderate. The inter-observer agreement for only uterine bulge (κ-all) was fair. The inter-observer reliability may be influenced in part by the differences in the experience of the radiologists interpreting the images. The eleven MRI features in the present study were proved to have a role in differentiating PAS from normal placentae or determining implant depth (14,18-22).

The EBL exhibited a trend to increase along with the placental implant depth in the present study. However, there was no significant difference among the three groups (P=0.070). Of note, the EBL does not always increase with the increase of the implant depth; however, studies on the association between MRI features and hemorrhage of PAS patients prior to delivery are limited. Chen et al (11) defined blood loss of >1,000 ml during surgery as significant hemorrhage. Poor maternal outcome was defined as parturient with significant hemorrhage or emergency hysterectomy. They reported that low signal intensity bands on T2-weighted imaging may be a predictor of poor maternal outcome after UAE-assisted cesarean section in patients with invasive placenta previa. The intraplacental thick dark bands and markedly heterogeneous placenta were reported to be important MRI features not only in predicting massive hemorrhage but also the differentiating factors for EBL, PRBC transfusion and plasma transfusion. Intra-placental thick dark bands were the result of fibrin deposition (14). In certain previous studies, intra-placental thick dark bands can differentiate between PAS and non-PAS (14,18,22). In the present study, intra-placental thick dark bands were observed more frequently in the massive hemorrhage group than in the moderate hemorrhage group. Fibrin deposition may result in narrowed intervillous space (18,23). The maternal vessels (spiral arteries and draining veins) may be dilated or increased to enhance blood flow to the placenta. Increased and/or dilated vessels may result in more hemorrhage when the placenta is manually removed.

A markedly heterogeneous placenta is associated with invasive placentation (18,19). Lax et al (19) and Ueno et al (22) indicated that a markedly heterogeneous placenta was more frequently observed in cases of PAS than in normal placentae. Bour et al (14) reported that a markedly heterogeneous placenta was not significantly associated with the diagnosis of PAS, but more frequently observed in patients with placenta percreta than in those with placenta accreta. In the present study, it was observed that a markedly heterogeneous placenta was more frequent in the massive hemorrhage group than in the moderate hemorrhage group. It was indicated that the characterization of markedly heterogeneous placenta partly depended on the presence of intraplacental thick dark bands and increased placental vascularity.

Bour et al (14) reported that thinning or focal defect of the UPI was significantly associated with the diagnosis of invasive placenta and was the single independent predictor of invasive placenta. This study suggested that the EBL of patients with focal defect of the UPI was more than that of the patients without this MRI feature. However, the blood transfusion difference between the patients with and without the MRI feature was not significant.

Most PAS patients have the MRI feature of myometrial thinning, but this feature is not unique, as numerous maternal patients with a normal placenta also have such a feature (22). The disruption of the inner layer of the UPI had 81% sensitivity for the diagnosis of PAS (14). Increased placental vascularity was significantly associated with PAS (18,22,24). Increased vascularity in UPI was identified as a novel MRI feature in the present study. The maternal spiral arteries at the myometrium-placenta interface run parallel to the villous branches of the chorionic arteries and perpendicular to the decidua surface. The vessels at the UPI may be prone to rupture when the placenta is manually removed. Although the difference in EBL between the patients with and without the four MRI features was not significant, the difference in blood transfusion was significant, which may reflect blood loss to a certain extent.

The present study had several limitations. First, it was a retrospective study. The hemostasis methods were not arranged in advance. The proportion of patients who underwent ABO in the massive hemorrhage group was greater than that in the moderate hemorrhage group, but the ABO was more effective (25). Therefore, the hemostasis method of ABO should not influence the results. In addition, patients who underwent MRI had already been screened by US, and there was already suspicion for PAS, particularly suspicion for placenta increta and percreta. The diagnostic accuracy was therefore biased prior to interpretation. However, the radiologists were blinded to the EBL, PRBC transfusion and plasma transfusion. Therefore, any bias made during PAS diagnosis were unlikely to have affected the results. A further limitation is the inaccurate estimation of blood loss, particularly in those patients with massive hemorrhage (8,17). To minimize this bias, EBL and blood transfusion were analyzed and the hemostatic methods that may affect blood loss were recorded. In addition, the size of the PAS cohort was small, which may influence the results of the statistical analysis. Finally, the present study was a retrospective single-center study and selection bias may have been present. Further multiple-center studies with larger samples are warranted.

In conclusion, two MRI features, intraplacental thick dark bands and markedly heterogeneous placenta, are helpful in predicting massive hemorrhage in patients with PAS. Focal defect of the UPI, myometrial thinning, disruption of the inner layer of the UPI, increased placental vascularity and increased vascularity at the UPI may also contribute to predicting hemorrhage to a certain extent. Patients with these MRI features may have a higher risk of massive hemorrhage and pre-operative preparations should be arranged for them in advance.

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Availability of data and materials

The data used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

All authors of this manuscript have made substantial contributions to this work. All authors have read and approved the final manuscript. The specific contribution of each author is listed as follows: Study design: YL, ZH;Study conception: CZ, YL, JZ. Case collection: JZ, ZH, HX, QL. Statistical analysis: JZ. Image capture: YX, ZL; US operation: XH; Clinical supervision: CZ, YL; Manuscript preparation: JZ, YL,ZH; Manuscript revision: QL, ZH, XH.

Ethics approval and consent to participate

The study was performed in accordance with the standards set out in the Code of Ethics of the World Medical Association (Declaration of Helsinki) and the research procedures were approved by the ethics review board of Shandong Provincial Hospital (Jinan, China). Informed consent was obtained from each patient.

Patient consent for publication

Not applicable.

Competing interests

All authors declare that they have no competing interests.

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