DATABASE ANALYSIS

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Received: Accepted: Available online: Published:	2021.04.18 2021.07.11 2021.07.30 2021.10.22		Comparison of Magnetic Resonance Imaging of the Lower Uterine Segment in Pregnant Women with Central Placenta Previa with and without Placenta Accreta Spectrum from a Single Center						
Authors' Data Statisti Data Int Manuscript Litera Fund:	Received: 2021.04.18 Accepted: 2021.07.11 vailable online: 2021.07.30 Published: 2021.10.22 Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G F 4 C 5 ACE 1 Corresponding Author: Financial support: Background: Material/Methods:		Shunyu Hou* Ye Song* Jiahui Wu Liping Zhou Suya Kang Xi Chen Lei Zhang Yanli Lu Yongfei Yue	 Department of Obstetrics and Gynecology, The Affiliated Suzhou Hospital or Nanjing Medical University, Suzhou Municipal Hospital, Suzhou, Jiangsu, PR Department of Infectious Diseases, Children's Hospital of Soochow Universi Suzhou, Jiangsu, PR China Department of Ultrasound, Sichuan Provincial Maternity and Child Health C Hospital, Chengdu, Sichuan, PR China Department of Endocrinology and Metabolism, Xinghua People's Hospital Affiliated to Kangda College of Nanjing Medical University, Xinghua, Jiangsu PR China Department of Medical Imaging, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Suzhou, Jiangsu, PR China 					
			* Shunyu Hou and Ye Song contributed equally to this work Yongfei Yue, e-mail: yueyongfeiyyf @163.com This study was supported by Suzhou Municipal Hospital Gynecological Clinical Trial and Improvement Project (SLT201955), the Clinical Medical Expert Team Project of Suzhou (SZYJTD201709), Suzhou Science and Technology Development Project (SYSD2020133), and Suzhou Science and Technology Project for Youth (KJXW2017026)						
-	Back Material/N	kground: Aethods:	Placenta accreta spectrum (PAS) includes placenta in to abnormal decidualization and can lead to severe a with central placental previa (CPP). This study from a imaging (MRI) changes in the lower uterine segment This retrospective study includes 90 pregnant womer ticipants were confirmed to have CPP by MRI. Eight I patal outcomes for mothers and newborns.	creta, placenta percreta, and placenta accreta. PAS is due maternal hemorrhage and occurs in up to 3% of women single center aimed to compare the magnetic resonance in pregnant women with CPP, with and without PAS. n with PAS and 66 pregnant women without PAS. All par- MRI parameters were assessed and compared with peri-					
Results: Conclusions:		Results: clusions:	The pregnancies in the non-PAS group had less operative time (P =0.001), less intrapartum hemorrhage (P <0.001), and less blood transfusion than the PAS group (P <0.001). The 8 MRI variables with different odds ratios were placenta thickness (4.20), cervical lengths (3.27), placental dark T2 bands area (5.10), cervical marginal sinus (3.04), bladder bulge (3.55), myometrial thinning (6.41), lower uterine segment bulge (4.61), and placental signals in the cervix (9.14). The sensitivity and specificity of MRI in the diagnosis of PAS were 82.22% and 91.09%, respectively, by the combined 8 MRI features, and the area under the curve (AUC) was 0.816. The findings from this study showed that MRI of the lower uterine segment had high sensitivity and specificity for the diagnosis of PAS in pregnant women with CPP.						
	Ке	ywords:	Magnetic Resonance Imaging • Placenta Accreta •	Placenta Previa					
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Background

Placenta accreta spectrum (PAS) includes placenta increta, placenta percreta, and placenta accreta, and was formerly known as morbidly adherent placenta. PAS is due to abnormal decidualization and can lead to severe maternal hemorrhage [1]. PAS has been reported to occur in up to 3% of women with central placental previa with no prior cesarean deliveries [2]. Placenta previa (PP) is classified into 4 categories based on the distance from placental edge to the internal cervix: lowlying placenta, marginal placenta, partial placenta, and complete placenta previa (CPP). PAS has a high incidence among patients with CPP, which is considered a severe life-threatening obstetric disease and may be associated with bladder injury and massive intraoperative and postpartum hemorrhage [3]. PAS is associated with a number of causes, including PP, miscarriage, cesarean section, smoking, and history of uterine surgery [4]. The incidence of PAS has risen from 0.8% in the 1980s to 3% in the 2010s [5]. During cesarean section, most PAS patients need blood transfusions or even hysterectomies.

Ultrasound is the first-line imaging modality. However, in recent years, magnetic resonance imaging (MRI) is increasingly widely used in obstetrics and benefits from the experience of functional MRI, which allows the assessment of PAS and abnormalities around the lower uterine segment. It has been found that MRI has high sensitivity and specificity in the diagnosis of PAS [6,7]. PP is mostly located in the lower uterine segment, where the muscle tissue is thinner than in the body of the uterus. Placental villi are prone to implant in the uterine wall in order to obtain enough nutrients for fetal growth. In the third trimester, the uterine wall in the lower uterine segment is thinner and there is a high probability of placental villi penetrating the uterine wall and implanting in the bladder. The bleeding spots are in the uterine body and lower uterine segment in partial and marginal PP women, while bleeding spots are often in the lower uterine segment and cervical canal in CPP patients. The uterine body is free and completely exposed to the field of vision, so we can use figure 8 suturing, uterine artery ligation, B-Lynch, and other methods to stop the hemorrhage in the uterine body. In front of the lower segment of the uterus is the bladder, behind is the rectum, and on both sides is the ureter. Moreover, the cervical canal space is narrow, which creates great difficulty for surgical hemostasis.

The antenatal diagnosis of PAS is helpful for obstetricians to make adequate preoperative preparation and reduce hemorrhagic morbidity [8]. There are abundant studies on evaluation of PAS by MRI, but there is no uniform standard for PAS and severity assessment. Therefore, this study from a single center aimed to compare the sensitivity and specificity of MRI changes in the lower uterine segment in pregnant women with CPP, with and without PAS.

Material and Methods

Patient Selection

Informed consents were signed by pregnant women and the study was approved by the ethics review board of our hospital. From August 2014 to October 2020, a total of 156 pregnant women with CPP diagnosed by MRI examinations were included in our study at our hospital. All patients had a prenatal ultrasound before MRI evaluation. We included 90 pregnant women with PAS and 66 women without PAS. Inclusion criteria were CPP patients with gestational age between 32 and 37 weeks, and complete pelvic MRI images. All of the participants had at least 1 previous cesarean section. Patients with multiple pregnancies, marginal placenta previa, partial placenta previa, did not undergo MRI examination, or delivered in other hospitals were excluded. The PAS were diagnosed after laparotomy, which was based on Collins's three-step diagnostic method [9]. The detailed exclusion criteria and the flow chart of the study design are shown in Figure 1.

Patient and Public Involvement

Patients or public were not involved in this study.

MRI Data Acquisition

Before cesarean delivery, all patients underwent pelvic MRI using the 3.0 T MRI system (Siemens Medical Solutions, Erlangen, Germany). Sedation and intravenous gadolinium injection were not used for any patients. Patients were in the supine or left lateral decubitus position with moderately full bladder. The MRI protocol comprised T1WI and T2WI images in sagittal, coronal, and axial orientations. The scanning time was less than 1 s/image, and the entire MRI study was completed within 30 min. In this study, we used the following MRI signs in the lower uterine segment to evaluate PAS: placenta thickness, cervical lengths, placental dark T2 bands area, cervical marginal sinus, bladder bulge, myometrial thinning, lower uterine segment bulge, and placental signals in the cervix.

The measurement of placental thickness was the shortest distance from the interior cervix orifice to the fetal surface of placenta (**Figure 2A**). The length of cervical canal was measured from the interior cervix orifice to the external cervix orifice (**Figure 2A**). Three MRI features (placental dark T2 bands, myometrial thinning, and lower uterine segment bulge) were derived from the lower uterine segment, which we defined in our study as follows: The tangent line at the internal cervix (line A), parallel line 5 cm from line A (line B), the lower uterine segment (white arrow) between line A and line B is the area that we studied (**Figure 2B**). The cervix was thicker than normal with varicosities suggests that the cervix was rich in

(Microsoft office word 2007, Microsoft,

USA).



blood supply (Figure 2C (white circle)). We defined uterine wall partial defect or even placental tissue signals seen in myometrium as myometrial thinning by MRI (Figure 2C (red circle). When the placenta was located entirely in the lower uterine segment, the lower uterine segment was often enlarged and dilated (Figure 2D). MRI signs consistent with placental tissue were seen in the cervix, which means that the placenta might be invaded into the cervix (Figure 2D (white circle)). The MRI images were analyzed by 2 experienced radiologists on female pelvic MRI. Radiologists were blinded to all clinical information, ultrasonoscopy imaging, and the impressions of the other radiologists. Any disagreement in the process of interpretation was resolved by the senior radiologist.

Statistics Analysis

Continuous variables are expressed as mean (standard deviation) or median (interquartile range) depending on the underlying distribution of the data, and nominal data are expressed in the form of frequency (percentage). The sensitivity and specificity of MRI examination were calculated. Kappa statistics for different radiologist's reliability were calculated for each sign. The chi-squared test, Fisher's exact test, or Mann-Whitney U test were used to evaluate the significance of clinical factors between the 2 groups. Receiver operating characteristic curve (ROC) was used to evaluate the diagnostic value of different MRI features. A P value <0.05 was considered statistically significant. The graph of odds ratios was constructed using GraphPad Prism 8.0 software. All statistical analyses were performed by using SPSS 23.0 statistics software.

Results

Clinical Characteristics of the Patients

We included 156 women in the study, and the clinical characteristics of CPP are presented in Table 1. Ninety of 156 patients had evidence of PAS intraoperatively (accreta/increta, n=57; percreta, n=33). In all patients, cesarean section was performed. No statistically significant relation could be detected as regards age, BMI, previous placenta pervia, bladder injury, cesarean hysterectomy, or Apgar score in correlation to the type of PAS. No maternal deaths were recorded.

The gestational weeks of delivery (35.56±1.14 vs 36.38±1.06; P<0.001) and MRI examination (33.82±2.35 vs 34.62±1.42; P=0.015) in the PAS group were significantly smaller than those in the non-PA group, and more newborns in the PAS group were admitted to the NICU (83.33% vs 60.61%; P=0.001). The number of prior cesareans was greater in patients with PAS than that in patients without the disease (1.33±0.64 vs 0.92±0.56; P<0.001). The operating times were longer in the PAS group than in the non-PAS placenta group (91.88±31.73 vs 72.82±36.49; P=0.001). When considering the clinical outcome, 3 (3.33%) parturient underwent emergency hysterectomy due to massive bleeding (>5000 ml) and unstable vital signs.

Interrater Agreement

The level of agreement between the 2 radiologists was basically satisfactory for the identification of each of the MRI signs, with kappa values ranging from 0.795 to 0.967. Interpretation of kappa scores was evaluated according to the following definitions: 1.0 perfect agreement, 0.91 to 0.99 almost perfect agreement, 0.81 to 0.90 substantial agreement, 0.71 to 0.80



Figure 2. Different imaging characteristics of magnetic resonance imaging (MRI) in central placenta previa patients (Sagittal T2-weighted). (Microsoft office PowerPoint 2007, Microsoft, USA). (A) Placenta thickness: Placental thickness was measured from the internal cervix (red arrow); Cervical length: White arrow indicate the measurement of cervical length. (B) Placental dark T2 bands: The tangent line at the internal cervix (line A), parallel line 5 cm from line A (line B), the dark band (white arrow) between line A and line B is the area that we studied. (C). Cervical marginal sinus: Assessment of cervical marginal sinus signs using MRI (white circle); Myometrial thinning: The myometrium was partially defective, and placental tissue signals were seen in myometrium (red circle). (D). Placental signals in the cervix: Signs consistent with placental tissue were seen in the cervix, which means that the placenta may be inserted into the cervix (white circle); Lower uterine segment bulge: The placenta located entirely in the lower uterine segment, the lower uterine segment was enlarged and dilated.

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Parameter	Placenta accreta (n=90)	Non-placenta accreta(n=66)	p-value
Age at delivery(years)	32.09±3.87	31.03±3.84	0.092
BMI before delivery (kg/m ²)	26.28±3.31	26.60±4.70	0.628
Gravidity	3.39±1.38	2.92±1.27	0.033
Parity	1.88±0.54	1.67±0.59	0.021
Prior cesareans	1.33±0.64	0.92 <u>±</u> 0.56	<0.001
GA at delivery (week)	35.56±1.14	36.38±1.06	<0.001
GA by MRI (week)	33.82±2.35	34.62±1.42	0.015
Previous placenta pervia	7 (7.78%)	2 (3.03%)	0.209
Operative time	91.88±31.73	72.82 <u>+</u> 36.49	0.001
IPH (ml)	1717.70±992.69	1152.98±772.26	<0.001
Amount of transfusion (ml)	1760.18±866.93	943.98±451.46	<0.001
Bladder injury	5 (5.56%)	1 (1.52%)	0.195
Caesarean hysterectomy	3 (3.33%)	0 (0.00%)	0.134
Birth weight (gram)	2461.11±388.01	2694.70±346.09	<0.001
APGAR Scores			
1 st min	10 (9, 10)	10 (9, 10)	0.563
5 th min	10 (10, 10)	10 (10, 10)	0.628
NICU admission	75 (83.33%)	40 (60.61%)	0.001

Table 1. Clinical characteristics of pregnant women with placenta previa (PP).

APGAR Scores were expressed as median (interquartile range). GA – gestational age; IPH – intrapartum hemorrhage.

Table 2. Interobserver reliability of magnetic resonance imaging (MRI) in the diagnosis of placenta accreta spectrum (PAS).

MRI features	Either	Both	Agree	Карра	Interpertation		
Placenta thickness	43 (27.564)	41 (26.282)	98.718	0.967	Almost perfect		
Cervical lengths	28 (17.949)	24 (15.385)	97.436	0.908	Almost perfect		
Placental dark T2 bands area	73 (46.795)	63 (40.385)	93.590	0.870	Substantial		
Cervical marginal sinus	32 (20.213)	27 (17.308)	96.795	0.895	Substantial		
Bladder bulge	23 (14.744)	16 (10.256)	95.513	0.795	Moderate		
Myometrial thinning	47 (30.128)	36 (23.077)	92.949	0.819	Substantial		
Lower uterine segment bulge	52 (33.333)	43 (27.564)	94.231	0.864	Substantial		
Placental signals in the cervix	26 (16.667)	22 (14.103)	97.436	0.902	Almost perfect		

Presented here as No. (%). Number (and proportion) of studies in which either radiologist or both radiologists reported a finding. Percentage of studies in which they agreed.

	No.(%) of patients				Sensitivity	Specificity	PPV	NPV	AUC	D
MRI feature		PAS		on-PAS	(%)	(%)	(%)	(%)	AUC	P
Placenta thickness (>50 mm)					36.67	87.88	80.49	50.43	0.592	0.001
Yes	33	(36.67)	8	(12.12)						
No		(63.33)	58	(87.88)						
Cervical lengths (<25 mm)					21.11	92.42	79.17	46.21	0.639	0.021
Yes	19	(21.11)	5	(7.58)						
No	71	(78.89)	61	(92.42)						
Placental dark T2 bands area			55.56	80.30	79.37	56.99	0.615	<0.001		
Yes	50	(55.56)	13	(19.70)						
No	40	(44.44)	53	(80.30)						
Cervical marginal sinus					23.33	90.91	77.78	46.51	0.556	0.020
Yes	21	(23.33)	6	(9.09)						
No	69	(76.67)	60	(90.91)						
Bladder bulge					14.44	95.45	81.25	45.00	0.542	0.044
Yes	13	(14.44)	3	(4.55)						
No	77	(85.56)	63	(95.45)						
Myometrial thinning					34.44	92.42	86.11	50.83	0.634	<0.001
Yes	31	(34.44)	5	(7.58)						
No	59	(65.56)	61	(92.42)						
Lower uterine segment bulge				38.89	87.88	81.40	51.33	0.634	<0.001	
Yes	35	(38.89)	8	(12.12)						
No	55	(61.11)	58	(87.88)						
Placental signals in the cervix			22.22	96.97	90.91	47.76	0.588	0.001		
Yes	20	(22.22)	2	(3.03)						
No	70	(77.78)	64	(96.97)						
Combination of all 8 MRI features		-		-	82.22	91.09	-	-	0.816	<0.001

Table 3. Diagnostic indexes for the association of magnetic resonance imaging (MRI) features with placenta accreta spectrum (PAS).

PAS – placenta accreta spectrum; PPV – positive predictive value; NPV – negative predictive value; AUC – area under the curve.

moderate agreement, 0.61 to 0.70 fair agreement, and <0.6 slight agreement. The detailed results are shown in **Table 2**.

Comparison of MRI Features Between PA and Non-PA Patients

Significant differences were found in the 8 depicted MRI features between PAS pregnancies and non-PAS pregnancies (P<0.05). The single MRI feature has lower sensitivity (from 14.44% to 55.56%) and higher specificity (from 80.30% to 96.97%), but the combination of 8 indicators has higher sensitivity (82.22%) and specificity (91.09%) at the same time (**Table 3**). According to our results, the predictive value of a single MRI feature on PA is limited (AUC from 0.542 to 0.639), but the presence of 8 MRI signs have a good predictive effect for PA, with an area under the curve (AUC)=0.816 (**Table 3**, **Figure 3**). **Figure 4** shows MRI characteristics in central placenta previa patients with and without placenta accreta (sagittal T2-weighted). We found much thicker placenta, much shorter cervix, heterogeneous placenta, the dilated lower part of the

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Figure 3. Receiver operating characteristic curve (ROC) of different magnetic resonance imaging (MRI) features for all patients. (SPSS 23.0 statistics software, IBM America).

uterus, and myometrium defect (**Figure 4A**). **Figure 5** shows the ORs concerning the prediction of PAS in relation to 8 MRI features. The odds ratio using the 8 above MRI findings ranged from 3.04 to 9.14. CPP patients with MRI sign (placental signals in the cervix) had the highest odds ratio (9.14, 95% CI: 2.06-40.67, *P*=0.001) for PAS. The placental thickness in PAS patients were significantly thicker than those in non-PAS patients (5.28 ± 1.23 cm vs 4.05 ± 1.22 cm; *P*<0.001). Compared with patients in non-PAS group, the cervical lengths of patients with PAS were significantly shorter (2.74 ± 0.53 cm vs 3.28 ± 0.40 cm; *P*<0.001) (**Figure 6**).

Discussion

Ultrasound is widely used in the diagnosis of PP, but MRI can accurately assess placenta position and whether the placenta invades surrounding organs, and is not affected by maternal fat thickness. In recent years, MRI has played an increasingly important role in the diagnosis of PP and PAS [10]. MRI provides multiplane imaging and high soft-tissue resolution, and



Figure 4. Magnetic resonance imaging (MRI) characteristics in central placenta previa patients with and without placenta accreta (Sagittal T2-weighted). (Microsoft Office PowerPoint 2007, Microsoft, USA). (**A**) Central placenta previa with placenta accrete: Placenta thickness is 12.3 centimeters; The cervical canal is almost completely eroded by the placenta and we can hardly see a clear cervix; The placental signal is heterogeneous and many dark T2 bands are seen in the placenta (white arrow); The whole placenta is located in the lower part of the uterus, which is dilated; A partial myometrium defect can be seen at the uterine and placental interface (white circle); (**B**) Central placenta previa without placenta accrete: Placenta thickness is 3.2 centimeters; We can see a clear cervix (white arrow); Placenta signals are homogeneous; The boundary between the uterine myometrium and placenta is clear (red arrow).

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Figure 6. (A) The mean placenta thickness in cases with and without placenta accreta spectrum. (B) The mean cervical length in cases with and without placenta accreta spectrum. (SPSS 23.0 statistics software, IBM, USA).

it can more accurately assess the presence of PAS and bladder invasion compared with ultrasound [11,12]. The danger of CPP is largely determined by PAS in the lower uterine segment and the cervical canal, so our study focused on MRI features in this part of the uterus.

Multiple studies have shown an association between PAS and more prior cesarean deliveries [13]. All pregnant women in our study had a history of at least 1 cesarean section. As many reports described, previous cesarean deliveries and/ or PP were independent clinical risk factors of PAS [14,15]. In our study, the gravidity and parity in PAS group were significantly higher than that in the control group. CPP with PAS is a potential life-threatening obstetric disease that needs a multidisciplinary approach for appropriate management. CPP accompanied by PAS had a higher hysterectomy rate in order to save maternal life; however, the hysterectomy rate (3.33% in PAS group) was low in our study, mainly due to adequate preoperative evaluation and skilled surgical procedures (uterine artery ligation, anti-arcuate compression suturing, and B-lynch suturing) [16]. The uterus is thin in the third trimester, so PAS lacks specificity determined by direct signs of MRI. Sometimes, we can only judge PAS by some indirect signs of placenta in the lower uterine segment. Identification the site of PAS is very important because it requires different surgical procedures for therapy. We can easily remove the placenta and suture the local bleeding point if the site of PAS is in the body of the uterus. However, when the placenta is implanted in the lower uterine segment, we need to carefully remove the placenta and stop bleeding, otherwise the surrounding bladder and ureters may be damaged. It was very thin and lacked blood supply in the lower uterine segment of pregnant women with a history of cesarean section, the placental villi easily proliferates and implant, and even penetrates the uterine wall to get more blood nutrients.

Over the past few years, many studies have been reported that some of MRI signs (eg, focal myometrial interruption, dark placental bands, uterine bulge, and placental heterogeneity) were associated with PAS [17,18]. The placenta thickness in PAS group was much thicker than non-PAS group (OR, 4.20; 95% CI, 1.79-9.87), which indicates proliferation of placental villi, and even PAS. Shortening of the cervical was an important sign of PAS and can make the cesarean section more

difficult [19]. Our results showed that patients with the PAS had shorter cervical lengths than the patients without PAS. Abnormal vascularity and percretism signs were the 2 most predictive MRI features of PAS [20]. Our study found that placental signal in the cervix was the highest risk sign (OR, 9.14; 95% CI, 2.06-40.67) for placental implantation and it is difficult to stop bleeding in the cervix. Many researches have demonstrated that the dark intraplacental band on T2WI was a useful MRI feature for predicting PAS [21,22]. The signs of dark intraplacental bands, focal outward bulging of the placenta, and abnormal placental vascularity are reliable signs of PAS [23]. The dark intraplacental band on T2WI usually represents fibrin deposition or placental infarction, which was associated with placental invasion [24]. Uterine bulging was another useful MRI feature, which indicated that extensive growth of placental villus leads to PAS [25]. Our study results suggested that PAS had a higher risk in women with lower uterine segment bulge (OR, 4.61; 95%CI, 1.97-10.82). The value of a single MRI feature for PAS prediction was limited; however, the sensitivity and specificity of predicting PAS were 82.22% and 91.09%, respectively, by using the combination of these 8 MRI features.

However, there were some potential limitations in our study. The scale of the study, which included 156 pregnant women with CPP, was not large enough. Therefore, we need a largersample and multi-center study to further verify our conclusions.

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Conclusions

MRI features of the lower uterine segment have high sensitivity and specificity for the diagnosis of PAS in pregnant women with CPP. The placental signals in the cervix, myometrial thinning and placental dark T2 bands area, are the most useful signs for the diagnosis of PAS. We found they may play an important role in assessing the risk of disease in pregnant women and making adequate preoperative preparation for obstetricians.

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Conflict of Interest

None declared.

Declaration of Figure Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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