













Performance of antenatal imaging to predict placenta accreta spectrum degree of severity

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ABSTRACT

Introduction: In cases of placenta accreta spectrum, a precise antenatal diagnosis of the suspected degree of invasion is essential for the planning of individual management strategies at delivery. The aim of this work was to evaluate the respective performances of ultrasonography and magnetic resonance imaging for the antenatal assessment of the severity of placenta accreta spectrum disorders included in the database. The secondary objective was to identify descriptors related to the severity of placenta accreta spectrum disorders.

Material and methods: All the cases included in the database for which antenatal imaging data were available were analyzed. The rates of occurrence of each ultrasound

Abbreviations: IS-PAS, International Society of Placenta Accreta Spectrum; MRI, magnetic resonance imaging; PAS, placenta accreta spectrum; US, ultrasound.

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and magnetic resonance imaging descriptor were reported and compared between the Group “Accreta-Increta” (FIGO grades 1 & 2) and the Group “Percreta” (FIGO grade 3).

Results: Antenatal imaging data were available for 347 women (347/442, 78.5%), of which 105 were included in the Group “Accreta – Increta” (105/347, 30.2%) and 213 (213/347, 61.4%) in the Group “Percreta”. Magnetic resonance imaging was performed in addition to ultrasound in 135 women (135/347, 38.9%). After adjustment for all ultrasound descriptors in multivariate analysis, only the presence of a bladder wall interruption was associated with a significant higher risk of percreta (Odds ratio 3.23, Confidence interval 1.33–7.79). No magnetic resonance imaging sign was significantly correlated with the degree of severity.

Conclusions: The performance of ultrasound and magnetic resonance imaging to discriminate mild from severe placenta accreta spectrum disorders is very poor. To date, the benefit of additional magnetic resonance imaging has not been demonstrated.

KEYWORDS

abnormal invasive placenta, magnetic resonance imaging, placenta accreta spectrum, severity, ultrasound

1 | INTRODUCTION

Prenatal screening of placenta accreta spectrum (PAS) has a major impact on peripartum management.¹ It has been shown that morbidity related to PAS disorders was reduced when the condition was diagnosed during the antenatal period in comparison with intrapartum diagnosis. Chantraine et al. reported in 2013 a PAS case series comparing 40 women who had antenatal diagnosis with 26 women in whom diagnosis was not known before delivery.² In women with antenatal diagnosis, the rates of emergency hysterectomies (12% vs. 69%, $p = 0.0004$) & massive transfusions (20% vs. 46%, $p = 0.025$) were significantly lower. In a previous report, Tikkanen et al. also observed a reduction in peripartum blood loss (4500 ml vs. 7800 ml, $p = 0.012$) and number of units of packed of red blood cells transfused (7 vs. 13.5, $p = 0.026$) in women with antenatal diagnosis.³

Much remains to be done, PAS still being diagnosed at the time of delivery in a half to two-thirds of the cases in recent cohort studies.^{4–6} Thus, ultrasound (US) screening of PAS by experienced operators is recommended in women presenting with a low-lying placenta or previa if they had a previous caesarean delivery. This screening policy must be mandatory if these women are to be appropriately referred for management in referrals centers of expertise. The role of magnetic resonance imaging (MRI) is more controversial, and this technique is only currently recommended as an adjuvant to US for evaluating the degree of extension where there is doubt on US or areas not accessible with US such as posterior PAS or in cases of severely raised body mass index.^{7–9}

Although screening relies on US and more marginally MRI, the descriptors of PAS remain controversial in terms of interpretation, reproducibility, predictive value and even their terminology.

Key message

The performance of ultrasonography and MRI to discriminate the most severe PAS disorders is very poor. In ultrasound, only the presence of bladder wall interruption is associated with a higher risk of percreta. To date, the benefit of additional MRI has not been demonstrated.

Our society recently published proposals for standardization.^{8,9} As previously described, these standardized descriptors were reported in the International Society for Placenta Accreta Spectrum (IS-PAS) database for all the women who had antenatal diagnosis.¹⁰

The vast majority of publications on antenatal imaging focus on the screening sensitivity and specificity of US and/or MRI to predict the existence or absence of a PAS disorder. It would have been very interesting to compare the performance of different screening policies between 15 expert centers from different countries, but as cases with antenatally suspected PAS but normal placentas at the time of delivery were not systematically recorded in the database it was not possible to evaluate the screening value of antenatal imaging with this international cohort.

The severity of PAS, rated 1–6, was however precisely recorded for the 442 cases included in the database.¹¹ In case of placenta accreta spectrum, a precise diagnosis of the degree of invasion is essential for the planning of individual management strategies at the time of delivery.¹² The respective values of US and MRI for the assessment of PAS severity are poorly reported and previous publications rely on non-consensual classifications of degrees of

invasiveness. There is no publication in the field of PAS antenatal imaging based on such precise grading, to our knowledge.¹³

The aim of this study was to evaluate the respective performances of US and MRI for the antenatal assessment of the severity of PAS disorders. The secondary objective was to identify descriptors related to the severity of PAS.

2 | MATERIAL AND METHODS

The IS-PAS database contains both retrospectively and prospectively collected obstetric and surgical data of pregnant patients with antenatally suspected and/or clinically or pathologically proven PAS. Fourteen European and one non-European center (USA) provided cases retrospectively treated between 2008 and 2014 and prospectively from 2014 to 2019. In total, 442 cases were included in the database.

Data was collected via chart review using a standardized, secured and password-protected online data collection platform (FetView, Zeitgeist Health SE, Prague, Czech Republic) which contains structured case data and reports, but no images. The IS-PAS Grading used in the database had been proposed by the FIGO 2018 before the FIGO classification for the clinical diagnosis of PAS disorders was published. A perinatal clinical and pathological confirmation of PAS facilitates further classification of our cases according to the FIGO grading system (correspondence in Table 1). Knowing that variable depth may be seen in a single specimen, PAS were classified in our study according to their greatest depth of invasion. All patients with PAS from all participating centers were included and none excluded and only expert imagers in the field of PAS included cases. The patients reported were not chosen. All the cases included in the database for which antenatal diagnosis has been achieved were analyzed in this study. The 95 cases for which data was missing or that had been discovered at the time of delivery were excluded. Antenatally suspected PAS and peripartum uncomplicated third stage of labor, i.e. "false positive cases" were excluded for this analysis. Performance of MRI was at the discretion of each center and performed according to the protocol of each center: MRI was always

performed preoperatively in 53% of the centers in cases with suspected PAS and in 27% of centers only in selected cases.

In order to evaluate the performance of US & MRI to assess the severity of PAS with abnormally invasive disorders, the cases were grouped into two degrees of severity. Grades 2 & 3 of the IS-PAS, corresponding to grades 1 & 2 of the FIGO consensus guidelines^{11,13} were included in the Group "Accreta-Increta", i.e. the less severe cases. Grades 4 to 6 of the IS-PAS, corresponding to grade 3 of the FIGO, were included in the Group "Percreta", i.e. the most severe conditions. The indications for MRI were analyzed in terms of correlation with the degree of severity of PAS. The presence or absence of each US or MRI descriptor were detailed in the database. US descriptors were loss clear zone, myometrial thinning, abnormal placenta lacunae, bladder wall interruption, placental bulge, focal exophytic mass, uterovesical and sub placental hypervascularity, bridging vessels, feeder vessels and parametrial involvement.⁹ MRI descriptors were heterogeneous placenta placental bulge, dark intra placental bands, placental infarction, loss retroplacental dark zone, myometrial thinning, bladder wall interruption and abnormal vascularization placental bed.⁸

Statistical analysis was performed with Stata version 13.0 (Stata Corporation). The rates of occurrence of each US & MRI descriptor were reported and compared between both Groups with a Chi² or Fisher's exact test, as appropriate. A multivariate analysis with a logistic regression model was performed to identify descriptors significantly associated with a higher risk of percreta. All US descriptors highlighted in the univariate analysis ($p < 0.15$) were included in the logistic regression model. Significance was set at 5%.

2.1 | Ethical approval

Local Ethical Committee/IRB approval and Data Use Agreements were obtained according to local policies by each center. Details of these can be found in the online Supporting Information contained in the second Commentary of this supplement.¹⁰

3 | RESULTS

Over the 442 total cases included in the IS-PAS database, antenatal imaging data were available for 347 women (347/442, 78.5%). A normal placentation was found at the time of delivery for 29 cases (29/347, 8.3%), which were excluded from further analysis. A focal placenta accreta or increta (grade 2 IS-PAS) was found in 49 women (49/347, 14.1%), a diffuse (involving the entire placental bed) placenta accreta or increta (Grade 3 IS-PAS) in 56 (56/347, 16.1%). A total of 105 women were included in the Group "Accreta - Increta" (105/347, 30.2%) and 213 (213/347, 61.4%) in the Group "Percreta".

MRI was performed in addition to US in 135 women (135/347, 38.9%), including 119 in the confirmed cases. The distribution of US and additional MRI examinations according to severity grades is reported in Table 1. No significant correlation was found between

TABLE 1 Distribution of ultrasound and additional magnetic resonance imaging examinations according to severity grades

IS-PAS grades	FIGO class	US only N = 199	Additional MRI N = 119
2	1	31 (15.6)	18 (15.1)
3	2	38 (19.1)	18 (15.1)
4	3a	76 (38.2)	59 (49.6)
5	3b	34 (17.1)	16 (13.4)
6	3c	20 (10.0)	8 (6.7)

Data are expressed in N (%). The 29 cases IS-PAS grade 1 were excluded from further analysis.

Abbreviations: IS-PAS, International Society of Placenta Accreta Spectrum; MRI, magnetic resonance imaging.

severity grades and MRI indication rate. MRI was performed on average at 28±5 gestational week (12–39 GW) with injection of contrast agents in 55.6% of cases (75/135).

The presence of descriptors related to the severity of PAS (Group “Accreta-Increta & Group “Percreta”) is reported in Table 2 for US and Table 3 for MRI. The significantly more frequently observed US signs in percreta were loss of clear zone (96.2% vs. 86.6%), myometrial thinning (96.7% vs. 72.9%), bladder wall interruption (52.2% vs. 24.0%), placental bulge (59.9% vs. 28.7%), uterovesical hypervascularity (90.8% vs. 66.7%), bridging vessels (67.3% vs. 40.0%) and parametrial involvement (11.8% vs. 4.4%). The sensitivity, specificity, positive and negative predictive values as well as the likelihood ratios for the US signs are presented in Table 4 and in Table 5 for MRI signs. The risk of percreta according to the US descriptors is presented in Table 6. After adjustment for all US descriptors in multivariate analysis, only the presence of a bladder wall interruption was associated with a significant higher risk of percreta (Adjusted Odds Ratio 3.23, Confidence Interval CI 1.33–7.79). No MRI sign was significantly correlated with the degree of severity.

4 | DISCUSSION

To our knowledge, this is the first largest international multicenter cohort study assessing the performance of antenatal imaging for the prediction of PAS degree of severity. This is an observational study of practices relying on a consensual nomenclature that had been defined and diffused to all centers before the start of inclusions. The data collected in the database has the great interest of reflecting the real practice of expert centers.

With US, almost every descriptor was significantly more frequently observed in percreta cases, apart from the lacunae, the sub-placental hypervascularity and the presence of feeder vessels (no significant difference). But the only sign that remained significantly associated on multivariate analysis with a peripartum diagnosis of percreta was the bladder wall interruption, with a relatively low calculated adjusted odds ratio of 3.23 (Confidence Interval CI 1.33–7.79).

The results for MRI were even worse, with no descriptor in this series being significantly correlated with a higher degree of severity. It has to be noted that MRI remained an optional examination in the

	Accreta-Increta Group (N = 105)	Percreta Group (N = 213)	p value
Loss clear zone	84/97 (86.6)	177/184 (96.2)	0.03
Myometrial thinning	62/85 (72.9)	173/179 (96.7)	<0.001
Abnormal placenta lacunae	72/95 (75.8)	133/174 (76.4)	0.905
Bladder wall interruption	23/96 (24.0)	82/157 (52.2)	<0.001
Placental bulge	25/87 (28.7)	94/157 (59.9)	<0.001
Focal exophytic mass	8/88 (9.1)	27/159 (17.0)	0.062
Uterovesical hypervascularity	58/87 (66.7)	157/173 (90.8)	<0.001
Sub placental hypervascularity	65/86 (75.6)	122/161 (75.8)	0.973
Bridging vessels	32/80 (40.0)	101/150 (67.3)	<0.001
Feeder vessels	37/83 (44.6)	87/158 (55.1)	0.122
Parametrial involvement	4/90 (4.4)	20/170 (11.8)	0.038

TABLE 2 Ultrasound signs related to the severity of placenta accreta spectrum disorders

Data are expressed as n/N* (%). N* and N can be different in case of missing data.

	Accreta-Increta Group (N = 36)	Percreta Group (N = 83)	p value
Heterogeneous placenta	12/17 (70.6)	25/40 (62.5)	0.394
Placental bulge	9/25 (36.0)	32/56 (57.1)	0.064
Dark intra placental bands	16/26 (61.6)	33/47 (70.2)	0.450
Placental infarction	2/13 (15.4)	4/35 (11.4)	0.524
Loss retroplacental dark zone	8/17 (47.1)	25/43 (58.1)	0.311
Myometrial thinning	21/25 (84.0)	55/62 (88.7)	0.391
Bladder wall interruption	2/22 (9.1)	13/53 (24.5)	0.111
Abnormal vascularization placental bed	3/20 (15.0)	11/48 (22.9)	0.352

TABLE 3 Magnetic resonance imaging signs related to the severity of placenta accreta spectrum disorders

Data are expressed as n/N* (%). N* and N can be different in case of missing data.

TABLE 4 Sensitivity, specificity, predictive values and likelihood ratio for the ultrasound signs for the detection of severity of placenta accreta spectrum disorders (FIGO grade 3)

	Sensitivity	Specificity	PPV	NPV	LR+
Loss clear zone	96.2	13.4	67.8	65.0	1.11
Myometrial thinning	96.7	27.1	73.6	79.3	1.32
Abnormal placenta lacunae	76.4	24.2	64.9	35.9	1.00
Bladder wall interruption	52.2	76.1	78.1	49.3	2.18
Placental bulge	59.9	71.3	79.0	49.6	2.08
Focal exophytic mass	17.0	90.9	77.1	37.7	1.86
Uterovesical hypervascularity	90.8	33.3	73.0	64.4	1.36
Sub placental hypervascularity	75.8	24.4	65.2	35.0	1.00
Bridging vessels	67.3	60.0	75.9	49.5	1.68
Feeder vessels	55.1	55.4	70.2	39.3	1.23
Parametrial involvement	11.7	95.6	83.3	36.4	2.64

Abbreviations: LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

TABLE 5 Sensitivity, specificity, predictive values and likelihood ratio for the magnetic resonance imaging signs for the detection of severity of placenta accreta spectrum disorders (FIGO grade 3)

	Sensitivity	Specificity	PPV	NPV	LR +
Heterogeneous placenta	62.5	29.4	67.6	25.0	0.88
Placental bulge	57.1	64	78.0	40.0	1.58
Dark intra placental bands	70.2	38.5	67.3	41.6	1.14
Placental infarction	11.4	84.6	66.7	26.2	0.74
Loss retroplacental dark zone	58.1	52.9	75.6	33.3	1.23
Myometrial thinning	88.7	16	72.4	36.4	1.05
Bladder wall interruption	24.5	90.9	86.7	33.3	2.69
Abnormal vascularization placental bed	22.9	85	78.6	31.5	1.52

Abbreviations: LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

TABLE 6 Risk of percreta according to the ultrasound descriptors in multivariate analysis (Adjusted OR)

	Adjusted ^a OR	95%CI
Loss clear zone	1.24	0.37–4.11
Myometrial thinning	3.02	0.98–9.28
Bladder wall interruption	3.23	1.33–7.79
Placental bulge	1.27	0.52–3.11
Focal exophytic mass	0.38	0.11–1.29
Uterovesical hypervascularity	1.54	0.59–3.99
Bridging vessels	1.48	0.58–3.72
Feeder vessels	0.97	0.44–2.16
Parametrial involvement	1.18	0.31–4.48

Abbreviations: CI, confidence interval; OR, odds ratio.

^aAdjustment for all factors associated with “risk of percreta” in the univariate analysis ($p < 0.15$).

majority of prenatally suspected cases, having been performed in only 38.9% of women.

As this cohort consists of cases either antenatally suspected or discovered at delivery, it does not allow traditional analysis of

performance of imaging for screening for PAS. Indeed, very few suspected cases which were ultimately normal at the time of delivery (false-positive screening) were included in the database so it was impossible to correctly evaluate the negative predictive value of US. Furthermore, no information was available regarding the true negatives. This makes assessment of absolute ability to diagnose PAS from normal placentation impossible from this data. As the images were not included in the clinical multicenter database, it was not possible to evaluate the intra- and inter-observer reproducibility from this data.

Therefore, the data was analyzed with the intention of assessing the discriminatory value for each US and MRI sign between PAS which was contained within the uterus (accreta/increta) and the more severe and surgically challenging part of the spectrum where the placenta has reached the serosa or invaded beyond it, percreta. However, there is no score with a fixed cut-off that defines affected cases. Each observer, trained in PAS imaging in accordance with the IS-PAS descriptors, had to propose a diagnosis on the basis of the presence or absence of the different signs. We did, however, evaluate the level of correlation of each descriptor with the degree of severity of each case included. The low levels

of correlation between severity and each individual descriptor that we found confirms that, currently, it is not possible to develop a simple scoring system.

Determining before delivery the severity and degree of invasion of PAS is another main goal of the prenatal management of these women in order to better anticipate and determine the optimal management during delivery that may differ between mild and severe PAS. The lack of ability of the imaging signs to differentiate severity of the PAS is disappointing. However, these results are in agreement with the previously published reports. In a recent metanalysis, Pagani et al concluded that "US had an overall good diagnostic accuracy in recognizing the depth of placental invasion".¹⁴ Their conclusion relied on an indirect comparison of the sensitivity, specificity and diagnostic odds ratios of each US descriptor. But these data were only provided separately for each degree of severity of PAS (i.e. accreta - increta - percreta) and no multivariate analysis had been performed. It was therefore incorrect to make such a statement.

Other recent reports all confirmed the unreliability of antenatal imaging for the diagnosis of severity of invasion. As observed in our series, Jauniaux et al noted in a 2017 meta-analysis that positive correlations were found between the cumulative rates of the more invasive PAS disorders and US imaging sensibility & specificity but not with diagnostic odds ratio.¹⁵ Although some descriptors are more often associated with percretas, no sign or combination of signs appear to be specific to the severity of invasion. The severity can be assessed in two main ways. First, the pathological severity. This work relied on the FIGO classification, which was consensually used within our network. Second, the clinical severity in terms of consequences for both mother and child. Our group has chosen not to use this concept for the evaluation of the predictive value of imagery. Indeed, the clinical impact depends on the pathological severity but also on the management strategy (cesarean section hysterectomy, conservative approach, resection, type of anesthesia, recourse to interventional radiology, etc.). As our submission is from a collection of data from an international network of teams with different practices, clinical severity couldn't be used.

Regarding MRI, our results also confirm the previously reported lack of demonstrated utility. We failed to identify any publication in which the ability of MRI to discriminate severe from less severe PAS disorders had been investigated. Indeed, unlike the few publications on US included in the metanalysis of Jauniaux,¹⁵ the diagnostic odds ratio was never reported for MRI. As with US, even if some descriptors are more often observed in case of percretas, none is specific to this condition.

Our data, as well as those reported by Einerson in 2018, challenge the idea that MRI might be a useful adjunct to US in the diagnosis of PAS severity.¹⁶ In addition to the notion of the absence of a sign or combination of signs specifically correlated with severe forms, it was shown in their study that when MRI resulted in a change in the US diagnosis, it was incorrect in 37% of the cases. Finally, all the data available for MRI are retrospective and of low scientific quality, in particular because of the very inhomogeneous

nature of the image acquisition protocols. MRI could better perform than US in describing the topography of invasion. However, this information was not collected in the version of the databases used for this study. The next database version will collect this information for US and MRI. A research group in Nancy, France has recently started a prospective, standardized study for the MRI diagnosis of PAS (DIANE study, clinical trial registration NCT04328532) which aims to answer these questions.

Although the database was built and populated by obstetricians, with priority given to the techniques used and peripartum outcomes, detailed imaging information was available for a very large proportion of patients. Furthermore, thanks to previous work published by the IS-PAS (when it was originally the European working group - EW-AIP), the terminology of the descriptors described was common to all centers for both US and MRI. The grading of the severity of the cases was also pre-defined and rigorously applied. All analyses were based on the local interpretation of the imaging performed, US and MRI. Images were not uploaded in the database & as a consequence were not subsequently reviewed. Obstetricians & radiologists who performed the exams, however, were all experienced & fully trained for PAS imaging in accordance with the nomenclature of the study. It is therefore unlikely that the observed lack of correlation in findings may be significantly explained by variations in applying the visual findings to the prescribed nomenclature or imaging protocols.

However, ultimately this is an analysis of data reported by each center and despite the joint effort to define the descriptors and grades, interpretation bias may have persisted. The potentially different performances between centers may represent a potential bias, although only referrals centers of expertise included cases. It couldn't be evaluated due to the small number of cases per center, of approximately 20–25. A review of each case and each imaging test by several experts would be the only way to avoid such vagaries.

One limitation is that the diagnostic accuracy of both US and MRI may be partially dependent upon the incidence of the most severe cases and this study included only patients from referrals centers of expertise. As a consequence, the respective rates of accreta-increta & percreta cases might differ from those of the general population.

Nevertheless, such a methodology has so far never been applied in the field of PAS antenatal diagnosis. The data reported here are therefore of very high quality compared to much of the available literature.

5 | CONCLUSION

Performance of antenatal imaging to discriminate the more severe cases and determine the degree of invasion remains low. To date, the benefit of additional MRI has not been demonstrated. Recently, much effort has been made to clarify the clinical diagnosis of the various degrees of invasion and standardize the terminology for the description of imaging signs. The IS-PAS is fully committed to this

rigorous approach and is continually aiming to improve the quality of the data collected. Following this initial analysis improvements have been made to the IS-PAS database which should further enhance the imaging data collected in future. However, there is no doubt that prospective research protocols with appropriate control groups will certainly be necessary to progress our understanding of how these signs fully relate to findings at delivery.

CONFLICTS OF INTEREST

Loïc Sentilhes carried out consultancy work and was a lecturer for Ferring Laboratories in the previous 3 years. The other authors have no conflict of interest to declare.

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