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Diagnostic accuracy of ultrasound in detecting the depth of invasion in women at risk of abnormally invasive placenta: A prospective longitudinal study

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Abstract

Introduction: The aim of this study was to assess the diagnostic accuracy of ultrasound in detecting the depth of abnormally invasive placenta in women at risk.

Material and methods: Prospective longitudinal study including women with placenta previa and at least one prior cesarean delivery or uterine surgery. Depth of abnormally invasive placenta was defined as the degree of trophoblastic invasion through the myometrium and was assessed with histopathological analysis. The ultrasound signs explored were: loss of clear zone, placental lacunae, bladder wall interruption, uterovesical hypervascularity, and increased vascularity in the parametrial region.

Results: In all, 210 women were included in the analysis. When using at least one sign, ultrasound had an overall sensitivity of 100% (95% CI 96.5-100) and overall specificity of 61.9 (95% CI 51.9-71.2) for all types of abnormally invasive placenta. Using two ultrasound signs increased the diagnostic accuracy in terms of specificity (100%, 95% CI 96.5-100) but did not affect sensitivity. When stratifying the analysis according to the depth of placental invasion, using at least one sign had a sensitivity of 100% (95% CI 93.7-100) and 100% (95% CI 92.6-100) for placenta accreta/increta and percreta, respectively. Using three ultrasound signs improved the detection rate for placenta percreta with a sensitivity of 100% (95% CI 92.6-100) and a specificity of 77.2% (95% CI 69.9-83.4).

Conclusions: Ultrasound has a high diagnostic accuracy in detecting the depth of placental invasion when applied to a population with specific risk factors for anomalies such as placenta previa and prior cesarean delivery or uterine surgery.

KEYWORDS

abnormally invasive placenta, increta, percreta, placenta accreta, prenatal diagnosis, ultrasound

Abbreviations: AIP, abnormally invasive placenta; CD, cesarean delivery; CI, confidence intervals; DOR, diagnostic odds ratio; LR^+, positive likelihood ratio; LR^-, negative likelihood ratio; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value.

1 | INTRODUCTION

The rise in cesarean delivery (CD) rates in the last three decades has led to a massive increase in the incidence of abnormally invasive placenta (AIP) disorders.[1-4]

Accurate prenatal diagnosis is fundamental in order to reduce the burden of maternal morbidities associated with these anomalies, such as massive hemorrhage, damage to adjacent organs, and admission to intensive care unit, by allowing a pre-planned treatment in centers with high level of expertise in surgical management.[5,6] Ultrasound is the primary tool used to diagnose AIP and prenatal magnetic resonance imaging (MRI) is usually performed to confirm the diagnosis and delineate the severity of placental invasion.[7,8]

Depth of placental invasion is one of the major determinants in predicting the outcome of women affected by AIP.[2] This refers to the degree of infiltration of the trophoblastic tissue through the myometrium and uterine serosa and classified as placenta accreta, increta or percreta. A recent systematic review reported that ultrasound has an overall good diagnostic accuracy in detecting the depth of placental invasion, and that myometrial thinning, bladder wall interruption, and uterovesical hypervascularity are the ultrasound signs associated with the most severe types of AIP.[9]

Despite this, the small number of studies, retrospective design, heterogeneity in ultrasound signs explored, and gestational ages at assessment did not allow a comprehensive estimate of the actual diagnostic accuracy of ultrasound in identifying the severity of AIP.

The primary aim of this study was to assess the diagnostic accuracy of ultrasound in detecting the severity of AIP, expressed as the depth of placental invasion, in a prospective cohort of women at risk for these anomalies.

Key Message

Ultrasound has a high diagnostic accuracy in detecting the depth of abnormally invasive placenta when applied to a population with specific risk factors for such anomalies.

2 | MATERIAL AND METHODS

This is a prospective study including women with placenta previa and at least one prior CD or uterine surgery referred to the Department of Obstetrics and Gynecology, Arnas Civico Hospital, Palermo, Italy, a referral regional center for AIP, between 2007 and 2017. All women had a longitudinal assessment in the second and third trimester of pregnancy to detect AIP as per local guidelines.

The ultrasound signs explored in this study are shown in Figure 1 and Appendix S1[10]:

(1) Loss of clear zone, defined as a loss, or irregularity, of hypoechoic plane in myometrium underneath the placental bed ("clear zone").
(2) Placental lacunae, defined as the presence of numerous lacunae, often containing turbulent flow visible on gray-scale or color Doppler ultrasound.
(3) Bladder wall interruption, defined as loss or interruption of bright bladder wall (hyperechoic band or "line" between uterine serosa and bladder lumen).
(4) Uterovesical hypervascularity, defined as a striking amount of color Doppler signal seen between myometrium and posterior wall of bladder, including vessels appearing to extend from placenta, across myometrium, and beyond serosa into bladder or other organs; often running perpendicular to myometrium.

Furthermore, we explored the diagnostic performance of a recently described ultrasound sign, increased vascularity in the parametrial region, defined as the presence of hypervascularity extending beyond the lateral uterine walls and involving the region of the parametria, in detecting the presence and depth of placental invasion in affected women (Figure 1).[11]

Ultrasound assessment was performed via transvaginal and transabdominal ultrasound in all cases. All examinations were originally performed using a 4.0-6.0 MHz curved transabdominal or 5.0-7.0 MHz transvaginal transducer (GE Voluson® 730, General Electrics and Samsung WS80A with Elite, Samsung); when using color Doppler ultrasound, the pulsed rate frequency (PRF) was initially set at 1.3 KHz, but this was lowered to identify the presence of placental lacunar flow.

Depth of AIP was defined as the degree of trophoblastic invasion through the myometrium and was assessed on histopathological analysis of the removed uterus. Placenta accreta was diagnosed when anchoring placental villi were attached to myometrium rather than decidua, but without completely invading it. Placenta increta was diagnosed when chorionic villi penetrated the myometrium, and the diagnosis of placenta percreta was considered when chorionic villi penetrated through the myometrium to the uterine serosa and/or adjacent organs.[4] All uterine specimens were assessed by the same research pathologist blinded to the ultrasound and surgical findings. In addition, because different degrees of placental invasion may co-exist in the same uterus, every case was labeled according to the maximum depth of placental invasion observed.

In this study, women affected by AIP were divided in two different sub-groups: placenta accreta/increta and placenta percreta; this choice was based on the fact that placenta percreta is associated with the higher rate of peri-surgical complications compared with placenta accreta and increta.[12]

2.1 | Statistical analyses

The distribution of the different ultrasound signs in women affected vs those not affected by AIP was ascertained using the Chi-square test for categorical variables. Binary logistic regression analysis was

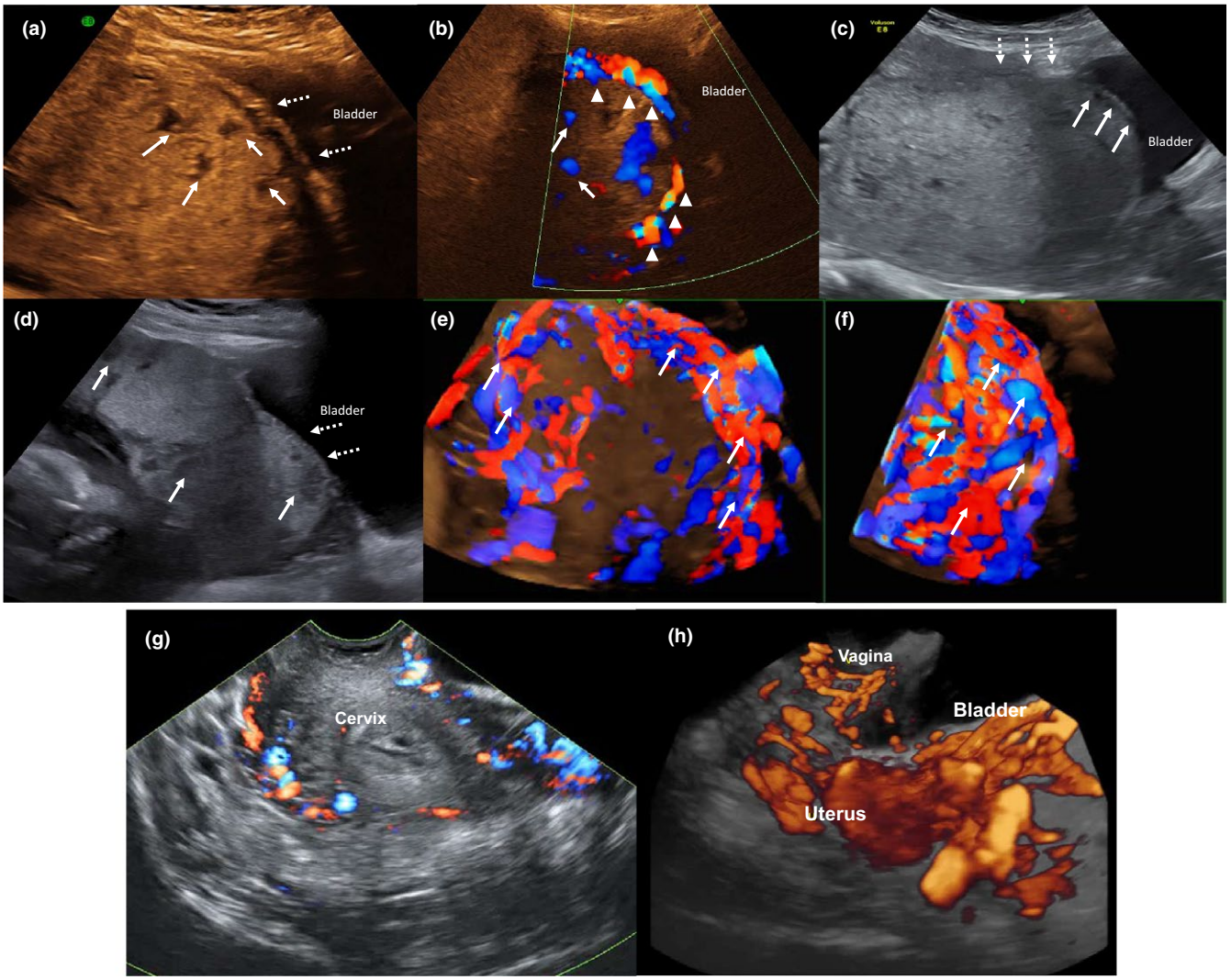

FIGURE 1 Ultrasound signs of abnormally invasive placenta (AIP). A and B, Intra-placental lacunae (white arrows) seen at gray scale (A) and color Doppler ultrasound. B, Focal interruption of the bladder wall (dotted arrows) and increased sub-placental vascularity (arrowheads) C, Loss of the retro-placental hypoechoic clear space. AIP is associated with the loss (dotted arrows) of the hypoechoic space (white arrows), which is thought to represent the decidua basalis, D, Intra-placental lacunae (white arrows) and loss of the hypoechoic space at gray-scale ultrasound. E and F, Hypervascularity of the uterine placental interface and presence of multiple tortuous vessels indicating high degrees of AIP. G, Increased vascularity in the parametrial region; axial plane at the level of the cervix showing increased vascularity extending laterally towards the parametria. H, Sagittal view showing massive vascularization involving vessels from the vagina, uterus, and bladder. [Color figure can be viewed at wileyonlinelibrary.com]

then performed to explore the strength of association between different pregnancy and ultrasound characteristics and AIP. Furthermore, the overall diagnostic accuracy of ultrasound and different ultrasound signs in detecting the depth of AIP was assessed by computing summary estimates of sensitivity, specificity, positive and negative predictive values (PPV and NPV), positive and negative likelihood ratios (LR^+ and LR^-), and diagnostic odds ratio (DOR). Finally, receiver operating characteristics curve (ROC) analysis was performed to estimate the diagnostic accuracy of ultrasound, expressed as number of signs, in identifying all AIP, placenta accreta/increta and placenta percreta, respectively. The DOR is defined as the ratio of the odds of the test being positive if the patient/woman has a disease, relative to the odds of the test being positive if the patient/woman does not have the disease (LR^+/LR^-); it may range from zero to infinity, with higher DOR being indicative of better test performance.[13]The 95% confidence intervals (CI) for specificity and sensitivity and for PPV and NPV were computed according to the efficient-score method (corrected for continuity) described by Newcombe.[14] STARD guidelines for studies on diagnostic accuracy were followed.[15] Statistical significance was defined as a two-sided *P*-value <.05, and all analyses were performed using STATA 13.1 (StataCorp, College Station, TX, USA).

2.2 | Ethical approval

This study was approved by the Arnas Civico Hospital Local Ethical Committee (Reference No: 1711) and all women provided written informed consent.

3 | RESULTS

In all, 210 women with placenta previa and at least one prior CD or uterine surgery were included in the analysis.

General characteristics of the population analyzed in the study are reported in Table 1. Major placenta previa, defined as placenta completely covering the internal cervical os, was found in 92.9% of the women (95% CI 88.5-95.9; 195/210), and minor previa, defined as partial, marginal or low-lying placenta, in 7.1% (95% CI 4.1-11.5; 15/210).[4] All placenta previa were anterior; there were no cases of AIP arising from a posterior placenta. In all, 86.7% (95% CI 81.3-91.0; 182/210) of women had had a prior CD, and 13.3% (95% CI 9.0-18.7; 28/210) myomectomy or uterine curettage. Maternal age (34.4 ± 4.2 vs 29.6 ± 5.3, $P = 0.0001$), parity (2 [2-3] vs 2 [0-2], $P = 0.0001$), and the number of previous CDs (2 [1-2] vs 2 [0-2], $P = 0.0006$) were higher in women affected than unaffected by AIP (Table 1). The incidence of AIP in the study population was 50.0% (95% CI 43.3-56.7; 105/210); placenta accreta/increta occurred in 27.1% (95% CI 21.3-33.7; 57/210) and placenta percreta in 22.9% (95% CI 17.4-29.1; 48/210) of all cases of AIP, respectively. There was no case of AIP outside the study population in the time period considered.

When assessing the distribution of the different ultrasound signs of AIP between the second and third trimester of pregnancy, there was no difference in the incidence of loss of the clear zone (88.6% vs 92.4%, $P = 0.48$), placental lacunae (100% vs 100%, $P = 1.00$), bladder wall interruption (87.6% vs 87.6%, $P = 1.00$), uterovesical hypervascularity (79.1 vs 79.1, $P = 1.00$), or increased vascularity in the parametrial region (47.6 vs 50.5, $P = 0.68$) throughout gestation. Therefore, we decided to report the diagnostic performance of ultrasound and different ultrasound signs of a scan performed in the third trimester of pregnancy.

Table S1 reports the incidence of the different ultrasound signs suggestive of AIP in cases affected vs those not affected by AIP. Loss of the clear zone, placental lacunae, bladder wall interruption, uterovesical hypervascularity or increased vascularity in the parametrial region were more common in cases affected by different types of AIP than those not affected ($P < 0.0001$ for all comparisons) (Table S1). Furthermore, the incidence of each of the ultrasound signs explored was higher in cases affected by placenta percreta than by placenta accreta/increta (Table S1). On logistic regression analysis, loss of the clear zone, bladder wall interruption, uterovesical hypervascularity, and increased vascularity in the parametrial region were independently associated with AIP (Table S2).

Ultrasound had an area under the curve (AUC) of 100 (95% CI 100-100) in detecting all types of AIP; when the depth of invasion was considered, AUC was 0.755 (95% CI 0.69-0.82) for placenta accreta/increta and 0.923 (95% CI 0.89-0.94) for placenta percreta (Figure 2). Table 2 reports the diagnostic accuracy of the different ultrasound signs in detecting AIP during the third trimester of pregnancy. Overall, loss of the clear zone had a good diagnostic accuracy in detecting all types of AIP, with a sensitivity of 90.5% (95% CI 83.2-95.3), a specificity of 81.0 (95% CI 72.1-88.0), a PPV of 82.6% (95% CI 74.4-89.0), an NPV of 89.5% (95% CI 81.5-94.8), an LR^+ of 4.8

TABLE 1 Overall characteristics of the sample and univariate analyses comparing the incidence of abnormally invasive placenta (AIP) by each potential predictor. All analyses were also stratified by type of AIP (placenta accreta/increta or placenta percreta)

	Overall sample (n = 210)	No AIP (n = 105)	All AIP (n = 105)	p^{aA}	Placenta accreta/increta (n = 57)	p^{aB}	Placenta percreta (n = 48)	p^{aC}
Maternal age in years, mean (SD)	32.1 (5.4)	29.6 (5.3)	34.6 (4.1)	<.0001	34.6 (4.4)	<.0001	34.5 (3.9)	<.0001
Gestational age at delivery in weeks, mean (SD)	35.3 (2.2)	36.3 (1.1)	34.3 (2.6)	<.0001	35.1 (1.5)	<.0001	33.4 (3.3)	<.0001
Previous cesarean delivery, median (interquartile range)	2 (1-2)	2 (0-2)	2 (1-2)	<.0001	2 (1-2)	0.04	2 (1-2)	<.0001
Number of detected signs, median (interquartile range)	1.5 (2-5)	0 (0-1)	5 (2-5)	<.0001	4 (3-5)	<.0001	5 (2-5)	<.0001

[a]Chi-square test for categorical variables; *t* test and Kruskal-Wallis test for normally distributed and non-normally distributed continuous variables, respectively: All *P*-values are referred to the comparisons between healthy women (no AIP) and: [A] all women with a diagnosis of AIP; [B] women with a diagnosis of placenta accreta or increta only; [C] women with a diagnosis of placenta percreta only.

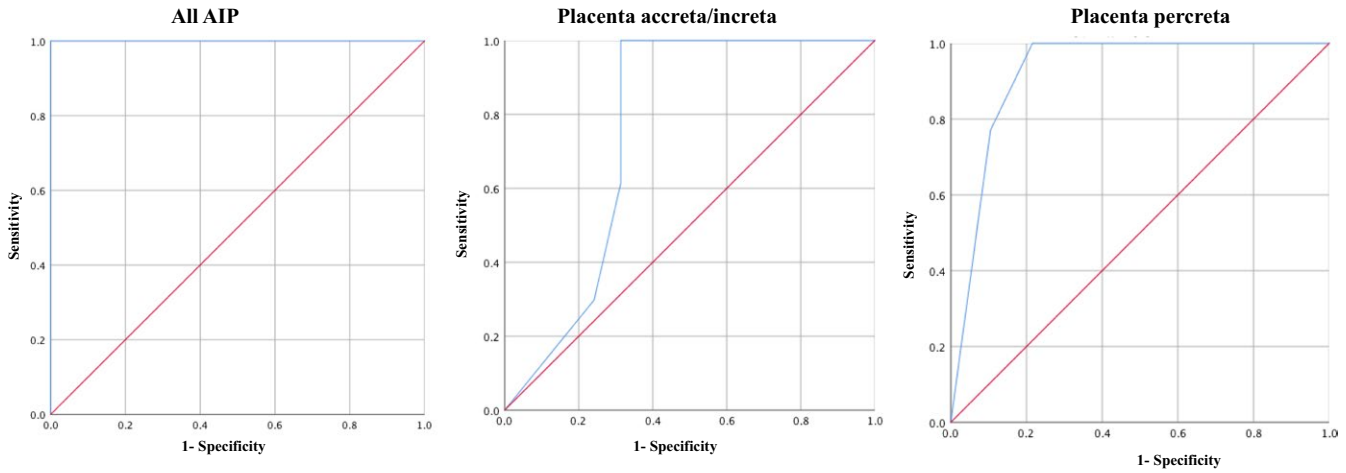

FIGURE 2 Receiver operating characteristic (ROC) curve showing the diagnostic accuracy of ultrasound in detecting different types of AIP. [Color figure can be viewed at wileyonlinelibrary.com]

(95% CI 3.2-7.1), an LR^- of 0.12 (95% CI 0.1-0.2), and a DOR of 40.4 (95% CI 18.0-90.3). When stratifying the analysis according to the depth of placental invasion, loss of the clear zone had a high sensitivity of 82.5% (95% CI 70.1-91.3) and 100% (95% CI 92.6-100) for placenta accreta/increta and percreta, respectively; however, the specificity was low (55.6% and 58.6%).

Placental lacunae had a sensitivity of 100% in detecting all types of AIP, placenta accreta/increta and percreta, but a specificity of 81% (95% CI 72.1-88.0), 55.6% (95% CI 47.3-63.6), and 58.6 (95% CI 50.7-66.3), respectively.

Bladder wall interruption had a high diagnostic accuracy in detecting all types of AIP, with a sensitivity of 90.5% (95% CI 83.2-95.3), a specificity of 99.0% (95% CI 94.8-100), a PPV of 99.0% (94.3-100), an NPV of 91.2% (95% CI 84.5-95.7), an LR^+ of 63.7 (13.0-612), an LR^- of 0.10 (95% CI 0.2-0.2), and a DOR of 634 (95% CI 112-3585). When stratifying the analysis according to the depth of AIP, sensitivity and specificity were respectively 82.5% (95% CI 70.1-91.3) and 68.0% (95% CI 60.0-75.3) for placenta accreta/increta and 100% (95% CI 92.6-100) and 70.4% (95% CI 62.7-77.3) for placenta percreta.

Uterovesical hypervascularity, defined as the presence of abnormal vascularization at the uterine bladder interface, often consisting of aberrant vessels running across myometrium and beyond the uterine serosa, had a sensitivity of 79.0% (95% CI 70.0-86.4) and a specificity of 100% (95% CI 96.5-100) in detecting all AIP. However, sensitivity improved when only cases of placenta percreta were considered (100%, 95% CI 90.8-100).

Increased vascularity in the parametrial region is a recently described ultrasound sign mainly suggestive of the placenta percreta, defined as the presence of hypervascularity extending beyond the lateral uterine walls and involving the region of the parametria, which can be appreciated in a transverse view of the lower uterine segment and cervix (Figure 1). Increased vascularity in the parametrial region had a low sensitivity of 51.4% (95% CI 41.5-61.3) but a high specificity of 100 (95% CI 96.5-100) in detecting all types of AIP; however, its diagnostic performance improved in terms of sensitivity when cases affected by placenta percreta were considered (77.1%, 95% CI 62.7-88.0).

The diagnostic performance of ultrasound in detecting AIP according to the number of imaging signs used is shown in Table 3. No case of either placenta accreta/increta or percreta was missed during the study period. Overall, when using at least one sign, ultrasound had a sensitivity of 100% (95% CI 96.5-100) and a specificity of 62.9 (95% CI 52.9-72.1). Using two ultrasound signs to label a case as positive, increased the diagnostic accuracy in terms of specificity (100%, 95% CI 96.5-100) but did not affect sensitivity. Finally, when three ultrasound signs were used, sensitivity for all types of AIP was 81.0% (95% CI 72.1-88.0) but specificity remained the same (100%, 95% CI 96.5-100) (Table 3).

When stratifying the analysis according to the depth of placental invasion, using at least one sign resulted in a sensitivity of 100% (95% CI 93.7-100) and 100% (95% CI 92.6-100) for placenta accreta/increta and percreta, respectively. The specificity for placenta accreta/increta was 43.1% (95% CI 35.2-51.4) when using only one ultrasound sign and 68.6% (95% CI 60.6-75.9) when using two to label a case as positive; the corresponding figures for placenta percreta were 40.8% (95% CI 33.1-48.7 when using one sign) and 64.8%, (95% CI 56.9-72.1 when using at least two signs). The relatively low specificity of ultrasound in identifying the depth of placental invasion was due to the poorer performance of ultrasound in discriminating between placenta accreta/increta and percreta rather than between cases affected and not affected by AIP.

Finally, using three signs to label a case as affected by AIP improved the diagnostic accuracy of ultrasound in detecting placenta percreta with a sensitivity of 100% (95% CI 92.6-100) and a specificity of 77.2% (95% CI 69.9-83.4).

We also explored the diagnostic performance of different combinations of ultrasound signs in detecting AIP during the third trimester of pregnancy (Table S3). The presence of placental lacunae and loss of the

TABLE 2 Diagnostic accuracy of each ultrasound sign to predict a diagnosis of abnormally invasive placenta (AIP): summary estimates of sensitivity, specificity, positive and negative predictive values (PPV and NPV), positive and negative likelihood ratios (LR^+ and LR^-), and diagnostic odds ratios (DOR) were computed either for all AIP diagnoses or stratified by each degree of AIP (placenta accreta/increta or placenta percreta)

Ultrasound signs	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	LR^+ (95% CI)	LR^- (95% CI)	DOR (95% CI)
All AIP							
Loss of the clear zone	90.5 (83.2-95.3) (95/105)	81.0 (72.1-88.0) (85/105)	82.6 (74.4-89.0)	89.5 (81.5-94.8)	4.75 (3.19-7.08)	0.12 (0.06-0.21)	40.4 (18.0-90.3)
Placental lacunae	100 (96.5-100) (105/105)	81.9 (73.2-88.7) (86/105)	84.7 (77.1-90.5)	100 (95.8-100)	5.41 (3.62-8.08)	0.01 (0.00-0.09)	936 (55.7-15726)
Bladder wall interruption	90.5 (83.2-95.3) (95/105)	99.0 (94.8-100) (104/105)	99.0 (94.3-100)	91.2 (84.5-95.7)	63.7 (13.0-612)	0.10 (0.06-0.18)	634 (112-3585)
Uterovesical hypervascularity	79.0 (70.0-86.4) (83/105)	100 (96.5-100) (105/105)	100 (95.7-100)	82.7 (75.0-88.8)	167 (10.5-2657)	0.21 (0.15-0.31)	783 (46.8-13099)
Increased vascularity in the parametrial region	51.4 (41.5-61.3) (53/105)	100 (96.5-100) (105/105)	100 (93.4-100)	67.3 (59.3-74.6)	109 (6.82-1742)	0.49 (0.40-0.59)	223 (13.5-3688)
Placenta accreta/increta							
Loss of the clear zone	82.5 (70.1-91.3) (47/57)	55.6 (47.3-63.6) (85/153)	40.9 (31.8-50.4)	89.5 (81.5-94.8)	1.85 (1.5-2.3)	0.32 (0.2-0.5)	5.83 (2.7-13.9)
Placental lacunae	100 (93.7-100) (57/57)	56.2 (48.0-64.2) (86/153)	46.0 (37.0-55.2)	100 (95.8-100)	2.28 (1.9-2.7)	∞ (0-0.1)	∞ (18.1-∞)
Bladder wall interruption	82.5 (70.1-91.3) (47/57)	68.0 (60.0-75.3) (104/153)	49.0 (38.6-59.4)	91.2 (84.5-95.7)	2.57 (2.0-3.4)	0.26 (0.1-0.4)	9.9 (4.5-23.8)
Uterovesical hypervascularity	61.4 (47.6-74.0) (35/57)	68.6 (60.6-75.9) (105/153)	42.2 (31.4-53.5)	82.7 (75.0-88.8)	1.96 (1.4-2.7)	0.56 (0.4-0.8)	3.5 (1.8-6.9)
Increased vascularity in the parametrial region	29.8 (18.4-43.4) (17/57)	75.8 (68.2-82.4) (116/153)	31.5 (19.5-45.6)	74.4 (66.8-81.0)	1.23 (0.7-2.0)	0.93 (0.7-1.1)	1.3 (0.6-2.7)
Placenta percreta							
Loss of the clear zone	100 (92.6-100) (48/48)	58.6 (50.7-66.3) (95/162)	41.7 (32.6-51.3)	100 (96.2-100)	2.42 (2.0-2.9)	∞ (0-0.1)	∞ (16.8-∞)
Placental lacunae	100 (92.6-100) (48/48)	53.1 (45.1-61.0) (86/162)	38.7 (30.1-47.9)	100 (95.6-100)	2.1 (1.8-2.5)	∞ (0-0.1)	∞ (13.4-∞)
Bladder wall interruption	100 (92.6-100) (48/48)	70.4 (62.7-77.3) (114/162)	50.0 (39.6-60.4)	100 (96.8-100)	3.38 (2.7-4.2)	∞ (0-0.1)	∞ (27.8-∞)
Uterovesical hypervascularity	100 (90.8-100) (48/48)	78.4 (71.3-84.5) (127/162)	57.8 (46.5-68.6)	100 (97.1-100)	4.63 (3.5-6.2)	∞ (0-0.1)	∞ (41.7-∞)
Increased vascularity in the parametrial region	77.1 (62.7-88.0) (37/48)	89.5 (83.7-93.8) (145/162)	68.5 (54.5-80.5)	93.0 (87.7-96.4)	7.35 (4.6-11.8)	0.26 (0.1-0.4)	27.9 (11.5-73.0)

CI, Confidence interval.

TABLE 3 Diagnostic accuracy of ≥1 and ≥2 ultrasound signs, to predict a diagnosis of abnormally invasive placenta (AIP): summary estimates of sensitivity, specificity, positive and negative predictive values (PPV and NPV), positive and negative likelihood ratios (LR^+ and LR^-), and diagnostic odds ratios (DOR) were computed either for all AIP diagnoses or by each degree of AIP (placenta accreta/increta or placenta percreta)

Ultrasound signs	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	LR^+ (95% CI)	LR^- (95% CI)	DOR (95% CI)
All AIP							
≥1 sign	100 (96.5-100) (105/105)	62.9 (52.9-72.1) (66/105)	72.9 (64.9-80.0)	100 (94.6-100)	2.69 (2.1-3.5)	∞ (0-0.6)	∞ (43.1-∞)
≥2 signs	100 (96.5-100) (105/105)	100 (96.6-100) (105/105)	100 (96.6-100)	100 (96.6-100)	∞ (28.2-∞)	∞ (0-0.04)	∞ (1468.6-∞))
≥3 signs	81.0 (72.1-88.0) (85/105)	100 (96.6-100) (105/105)	100 (95.8-100)	84.0 (76.4-89.9)	∞ (22.9-∞)	0.19 (0.1-0.3)	∞ (103.0-∞)
Placenta accreta/increta							
≥1 sign	100 (93.7-100) (57/57)	43.1 (35.2-51.4) (66/153)	39.6 (31.6-48.1)	100 (94.6-100)	1.76 (1.5-2.0)	∞ (0-0.1)	∞ (10.7-∞)
≥2 signs	100 (93.7-100) (57/57)	68.6 (60.6-75.9) (105/153)	54.3 (44.3-64.4)	100 (96.6-100)	3.19 (2.5-4.0)	∞ (0-0.1)	∞ (30.5-∞)
≥3 signs	64.9 (51.1-77.1) (37/57)	68.6 (60.6-75.9) (105/153)	43.5 (32.8-54.7)	84.076.4-898.9)	2.07 (1.5-2.8)	0.51 (0.3-0.7)	4.05 (2.0-8.1)
Placenta percreta							
≥1 sign	100 (92.6-100) (48/48)	40.7 (33.1-48.7) (66/162)	33.8 (26.2-42.1)	100 (94.6-100)	1.69 (1.5-1.9)	∞ (0-0.2)	∞ (8.3-∞)
≥2 signs	100 (92.6-100) (48/48)	64.8 (56.9-72.1) (105/162)	45.7 (36.0-55.7)	100 (96.6-100)	2.84 (2.3-3.5)	∞ (0-0.1)	∞ (21.7-∞)
≥3 signs	100 (92.6-100) (48/48)	77.2 (69.9-83.4) (125/162)	56.5 (45.3-67.2)	100 (97.1-100)	4.38 (3.3-5.8)	∞ (0-0.1)	∞ (38.9-∞)

clear zone or bladder wall interruption had a sensitivity and a specificity of 90.5% (95% CI 83.2-95.3) and 100% (95% CI 96.6-100), respectively, in detecting AIP; the corresponding figures for bladder wall interruption and placental lacunae or uterovesical hypervascularity were 87.4% (95% CI 79.0-93.3) and 100% (95% CI 96.6-100). When stratifying the analysis to the most severe type of AIP, a combination of loss of the clear zone with placental lacunae, bladder wall interruption or uterovesical hypervascularity resulted in a sensitivity of 100% (95% CI 92.6-100) in detecting placenta percreta. Visualization of an increased vascularity in the parametrial region did not add anything in terms of sensitivity for placenta percreta but increased specificity when combined with loss of the clear zone, placental lacunae, bladder wall interruption or uterovesical hypervascularity (89.5%, 95% CI 88.4-93.8).

4 | DISCUSSION

Depth of placental invasion is one of the major determinants of surgical outcome in women with AIP;[2] thus, accurate prenatal identification is fundamental to plan the optimal surgical approach. Despite this, the actual diagnostic performance of ultrasound in identifying the depth of placental invasion has not been consistently explored. With the small number of cases included in previously published studies, their retrospective design, and lack of longitudinal assessment of women at risk, it was not possible to extrapolate robust evidence to guide management. Furthermore, the large majority of these studies did not report the number or type of ultrasound signs used to label a case as affected. Finally, computation of diagnostic accuracy was mainly based on retrospective analysis of stored images, thus limiting the reliability of the results.

The present study is one of the largest prospective series to date on the role of prenatal ultrasound in detecting the depth of placental invasion. The findings from this study show that, when applied to a population with specific risk factors, ultrasound has an excellent diagnostic accuracy for all AIP, with a sensitivity and a specificity of 100%. More importantly, the diagnostic performance of ultrasound in detecting AIP was improved compared with that reported in the last the decade, especially in terms of specificity. Esakoff et al reported a sensitivity and a specificity of 89.5% and 91.0% for all AIP and the corresponding figures in the study by Chou et al were 82.4% and 96.8%, respectively.[16,17] A better understanding of the pathophysiology of AIP, identification of women at high risk, and improvement in ultrasound equipment and operator skills likely accounts for such results. The major contributor to such improvement was the smaller rate of false-positive diagnoses and the subsequent higher PPV compared with the previously published literature. This is fundamental because a high PPV may reduce inappropriate interventions in women with false-positive diagnoses, such as iatrogenic preterm delivery or use of interventional radiology techniques.

Despite this, the specificity of ultrasound in discriminating between placenta accreta/increta and percreta was low (Table 3). To overcome this limitation, we explored the diagnostic performance of a recently described ultrasound sign, increased vascularity in the parametrial region, in identifying the depth of placental invasion. High degrees of AIP are characterized by the presence of a rich vascular anastomotic system in the bladder, uterus, and vagina, involving the superior, medial and inferior vaginal arteries, and the lower vesical arteries.[18] Under normal circumstances, these connections are microscopic and not of hemodynamic significance. However, in the presence of AIP, the increased production of antigenic factors leads to a massive recruitment and thus enlargement of these vessels, which turn into high flow-low resistance reservoirs.[18] We have recently reported that this anastomotic system can be appreciated on ultrasound, especially in women with the most severe types of AIP, such as placenta percreta (Figure 1).[11] In the present study, vascular invasion of the parametria was an ultrasound sign more specific for placenta percreta than other sub-types of AIP, although it did not substantially affect sensitivity.

We have previously shown that ultrasound signs suggestive of AIP were present in a large majority of affected women already since the first trimester of pregnancy and that there was no difference in the distribution of such signs between the second and third trimester, even in cases with placenta percreta.[19] Despite this, longitudinal assessment of women at risk for AIP through the third trimester is fundamental in order to delineate more accurately the extent and topography of placental invasion, which may become evident only later on in gestation. The topography of placental invasion has been mainly reported using fetal MRI and there is still limited evidence on its reproducibility on ultrasound. In this study, we did not assess the diagnostic accuracy of ultrasound in identifying the topography of invasion and further evidence is needed before integrating such a classification in the ultrasound assessment of women at risk of AIP. Until then, it may be reasonable to perform MRI to delineate the site and extension of placental invasion if severe types of AIP, such has placenta percreta, are suspected on ultrasound.[20]

The diagnostic accuracy of ultrasound in detecting AIP is also dependent upon the number of ultrasound signs used to label a case as affected. It might be speculated that a reduction in the number of sonographic criteria needed to label a scan as suggestive for AIP may increase the sensitivity; however, this is likely to reduce the specificity of the test. Conversely, an increase in the number of criteria needed to label a case as positive would reduce sensitivity but improve specificity. The findings from this study show that the diagnostic accuracy of ultrasound increases in terms of specificity when at least two imaging signs suggestive of AIP are used, and sensitivity. is not affected. The use of three ultrasound signs was associated with a better specificity for placenta percreta.

A high incidence of AIP in the present cohort, lack of stratification of the analysis according to the type of placenta previa (complete vs marginal), number of previous CDs, and consideration of placenta accreta and increta separately represent the major weaknesses of this study. Furthermore, the results of this study are applicable only to women with anterior placenta previa and prior CD or uterine surgery, because all cases of AIP in our population occurred in women with such risk factors. Finally, we did not explore the diagnostic accuracy of recently reported ultrasound signs suggestive

of AIP, such as residual myometrial thickness, grading of placental lacunae, and the topography of placental invasion, because they were not consistently reported in the published literature at the time the study was designed.

A prospective design, assessment of a homogeneous population with objectively recognized risk factors for AIP and evaluation of the diagnostic performance of different combinations of ultrasound signs in detecting AIP represent the major strengths of this study.

5 | CONCLUSION

Further large studies are needed to explore the diagnostic performance of ultrasound in describing the topography of placental invasion and to ascertain whether integrating different combinations of ultrasound signs, pregnancy, and maternal characteristics can improve the diagnostic accuracy of ultrasound in identifying the depth of placental invasion in women affected by AIP.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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