

Intracervical lakes as sonographic marker of placenta accreta spectrum disorder in patients with placenta previa or low-lying placenta

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KEYWORDS: Cesarean hysterectomy; parametrial invasion; PAS; percreta; placenta accreta spectrum; ultrasound

CONTRIBUTION

What are the novel findings of this work?

This study introduces a new ultrasound sign, intracervical lakes (ICL), associated with placenta accreta spectrum disorder in women with placenta previa or low-lying placenta, which potentially represents a marker of deep villus invasion.

What are the clinical implications of this work?

Presence of ICL seems to be an independent predictor of placenta percreta and its incorporation into ultrasound examination may increase the diagnostic accuracy for Cesarean hysterectomy and major postpartum hemorrhage in women with placenta previa or low-lying placenta.

ABSTRACT

Objective To evaluate the diagnostic accuracy of a new ultrasound sign, intracervical lakes (ICL), in predicting the presence of placenta accreta spectrum (PAS) disorder and delivery outcome in patients with placenta previa or low-lying placenta.

Methods This was a retrospective multicenter study of women with placenta previa or low-lying placenta at ≥ 26 weeks' gestation, who were referred to three Italian tertiary units from January 2015 to September 2018. The presence of ICL, defined as tortuous anechoic spaces within the cervix which appeared to be hypervascular on color Doppler, was evaluated on ultrasound images obtained at the time of referral. The primary aim was to explore the diagnostic accuracy of ICL in detecting the presence and depth of PAS disorder. The secondary

aim was to explore the accuracy of this sign in predicting total estimated blood loss, antepartum bleeding, major postpartum hemorrhage at the time of Cesarean section and need for Cesarean hysterectomy. The diagnostic accuracy of ICL in combination with typical sonographic signs of PAS disorder, was assessed by computing summary estimates of sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios and diagnostic odds ratios (DOR).

Results A total of 332 women with placenta previa or low-lying placenta were included in the analysis, with a median maternal age of 33.0 (interquartile range, 29.0–37.0) years. ICL were noted in 15.1% of patients. On logistic regression analysis, the presence of ICL was associated independently with major postpartum hemorrhage (odds ratio (OR), 3.3 (95% CI, 1.6–6.5); $P < 0.001$), Cesarean hysterectomy (OR, 7.0 (95% CI, 2.1–23.9); $P < 0.001$) and placenta percreta (OR, 2.8 (95% CI, 1.3–5.8); $P \leq 0.01$), but not with the presence of any PAS disorder (OR, 1.6 (95% CI, 0.7–3.5); $P = 0.2$). Compared with the group of patients without ultrasound signs of PAS disorder, the presence of at least one typical sonographic sign of PAS disorder in combination with ICL had a DOR of 217.2 (95% CI, 27.7–1703.4; $P < 0.001$) for placenta percreta and of 687.4 (95% CI, 121.4–3893.0; $P < 0.001$) for Cesarean hysterectomy.

Conclusion ICL may represent a marker of deep villus invasion in women with suspected PAS disorder on antenatal sonography and anticipate the occurrence of severe maternal morbidity. Copyright © 2019 ISUOG. Published by John Wiley & Sons Ltd.

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INTRODUCTION

Placenta accreta spectrum (PAS) disorders encompass a wide spectrum of conditions, characterized by an abnormal adherence of the placenta to the implantation site. Although the pathophysiology of PAS has not yet been completely elucidated, placenta previa and prior Cesarean section (CS) represent the main risk factors for the occurrence of these anomalies, while the depth and topography of placental invasion are the major determinants of maternal morbidity^{1,2}. Prenatal diagnosis of PAS has been associated with reduced hemorrhagic morbidity, compared with cases in which such anomalies are detected at delivery, by allowing planned treatment in centers with expertise in surgical management of this condition^{3,4}.

Ultrasound represents the gold standard for antenatal evaluation of women at risk for PAS disorder, while magnetic resonance imaging is usually performed to define the depth and topography of placental invasion, particularly in cases of posterior low-lying placenta^{5–11}. However, a significant proportion of cases with PAS disorder still remain undiagnosed before surgery¹². There is large heterogeneity in the reported diagnostic performance of ultrasound in detecting PAS disorder^{13,14}. A multitude of ultrasound signs for PAS disorder have been reported, but it is yet to be ascertained which one can provide the optimal combination of sensitivity and specificity¹⁵. More importantly, the large majority of studies report the diagnostic performance of different ultrasound signs merely in detecting the presence of PAS disorder, but did not explore whether they could predict the severity of the condition^{16,17}.

On these grounds, the introduction of new imaging signs for PAS disorders seems crucial to improve the performance of ultrasound in identifying women affected by the most severe types of these conditions, in order to minimize the risk of adverse outcome.

The purpose of the present study was to evaluate the role of a new ultrasound sign, named intracervical lakes (ICL), in predicting the presence of PAS disorder and delivery outcome in patients with placenta previa or low-lying placenta.

METHODS

This was a retrospective multicenter study of women with placenta previa or low-lying placenta at ≥ 26 weeks' gestation, who were referred to one of three Italian tertiary units (Brescia, Parma and Palermo) between January 2015 and September 2018. The study was approved by the ethics committee of the three centers and the patients had provided written informed consent for their data to be used for research purposes.

Only women with delivery outcome and histopathological results available were included. All patients underwent transabdominal and transvaginal ultrasound examination using two-dimensional grayscale imaging, color Doppler and three-dimensional power Doppler,

with a 4.0–6.0-MHz curved transabdominal or a 5.0–7.0-MHz transvaginal transducer (Voluson E10 (GE Healthcare, Zipf, Austria); Samsung WS80A 'with Elite' (Samsung Healthcare, Samsung Electronics, Milan, Italy); and Philips iU22 (Philips Healthcare Systems, Bothell, WA, USA)).

The placenta was defined as placenta previa when it was lying directly over the internal os and as low-lying when it was situated < 20 mm from the internal os¹¹. Antenatal diagnosis of PAS disorder was based on the following typical ultrasound signs¹⁸: loss of the clear zone, defined as loss of the hypoechoic plane between the placenta and the underlying myometrium; presence of placental lacunae, defined as irregular vascular spaces within the placental parenchyma, showing turbulent flow within, on grayscale or color Doppler ultrasound; bladder-wall interruption, defined as loss or interruption of the echogenic bladder border; and uterovesical hypervascularity, defined as the presence of vessels visualized by color Doppler crossing the myometrium and extending from the placenta to the posterior bladder wall or to other organs, often running perpendicular to the myometrium.

Ultrasound images obtained during the first examination at the time of referral were reviewed by a select group of expert sonographers (T.G., G.C., F.P., N.F., F.F and T.F.), all with more than 10 years of experience in prenatal diagnosis, to evaluate qualitatively and reach a consensus regarding the presence/absence of the new sonographic marker, ICL. ICL was defined as tortuous anechoic spaces within the cervix, which appeared to be hypervascular on color Doppler, using a pulsed-rate frequency < 1.3 kHz (Figure 1).

The primary aim of the present study was to explore the strength of association and diagnostic accuracy of ICL in detecting, first, any type of PAS disorder and, second, placenta percreta. The secondary aim was to explore the accuracy of this new sonographic sign in predicting the following clinical outcomes: total estimated blood loss (EBL); antepartum bleeding (defined as the occurrence of any hemorrhagic event before the time of delivery); major postpartum hemorrhage (EBL ≥ 1000 mL); and need for Cesarean hysterectomy.

In women undergoing hysterectomy, the reference standard for PAS disorder was the histopathological assessment performed by a pathologist blinded to the ultrasound and surgical findings. Furthermore, every case was labeled according to the maximum depth of placental invasion observed. Placenta accreta was diagnosed when anchoring placental villi were attached to the myometrium without completely invading it. Placenta increta was diagnosed when chorionic villi penetrated the myometrium, while the diagnosis of placenta percreta was considered when chorionic villi penetrated through the myometrium to the uterine serosa and/or adjacent organs. In women not undergoing hysterectomy, the presence of PAS disorder at the time of scheduled Cesarean delivery was defined according to the grading system originally proposed by Collins *et al.*¹⁸ and modified by the International Federation of Gynecology and Obstetrics (FIGO)¹⁹.

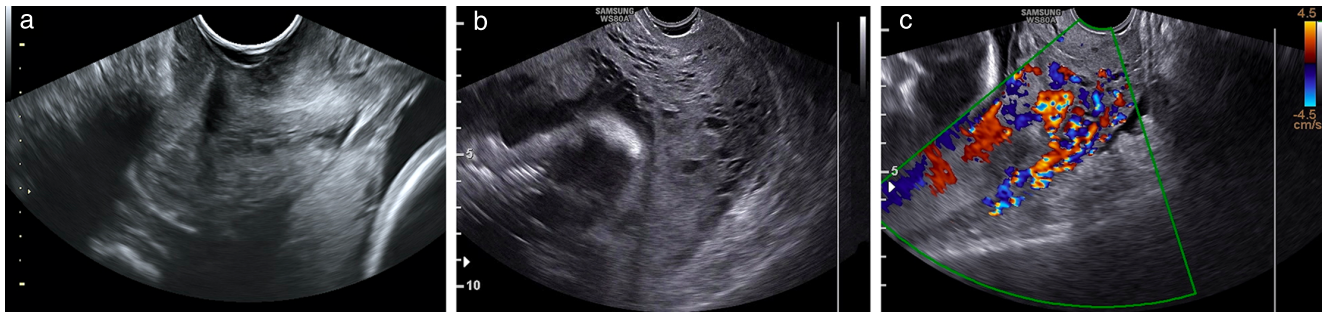


Figure 1 (a) Grayscale ultrasound image of normal cervix in woman with posterior placenta previa. Grayscale (b) and color Doppler (c) images of cervix with intracervical lakes in woman with posterior, low-lying placenta.

Timing of delivery was tailored according to the antenatal symptoms and the sonographic findings. For women with low-lying placenta or apparently uncomplicated placenta previa, delivery was planned between 36+0 and 37+0 weeks of gestation. Late preterm (34+0 to 36+0 weeks) delivery was considered for women presenting with a history of vaginal bleeding or for those with suspected PAS disorder.

In the latter case, management was planned by a local surgical team based on clinical and perioperative scenarios which included: Cesarean hysterectomy with the placenta left *in situ*, if placental removal by administration of uterotonic drugs and a controlled cord traction failed; conservative surgical management, including partial myometrial resection and the use of balloon tamponade, when the extent of the placenta accreta was limited in depth and surface area and the entire placental implantation area was accessible and visualized²⁰; and use of interventional radiology techniques.

There was no change in the management of women according to the presence of ICL, with regard to prenatal follow-up, timing of delivery and the surgical technique used.

Statistical analysis

Statistical analysis was performed using SPSS v21.0 (IBM SPSS Statistics for Windows, Version 21.0, 2012; IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to assess the normality of the distribution of the data. For comparison between more than two groups, ANOVA and the Kruskal–Wallis test were used for normally and non-normally distributed data, respectively. Binomial logistic regression analysis was performed to explore the strength of association between different pregnancy and ultrasound characteristics and primary and secondary outcomes. *P*-values < 0.05 were considered statistically significant. The diagnostic accuracy of ICL was assessed by computing summary estimates of sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, positive and negative likelihood ratios and diagnostic odds ratios (DOR)²¹. The study was performed following the STARD guidelines for studies on diagnostic accuracy²².

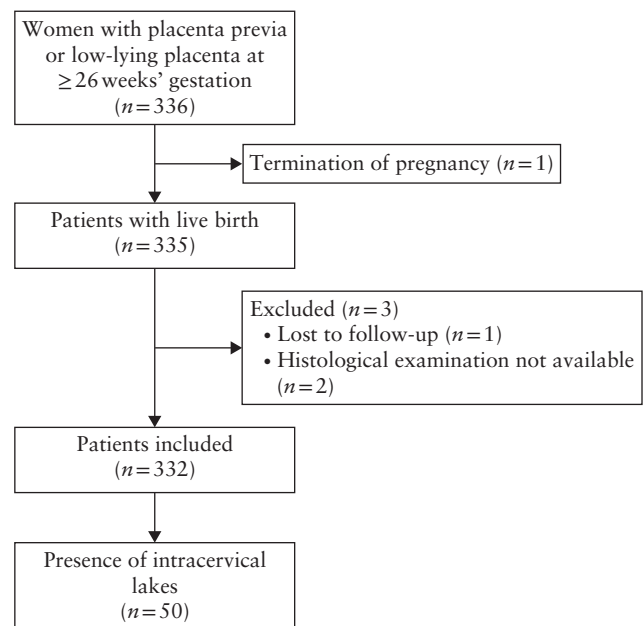


Figure 2 Flowchart showing inclusion in study of women with low-lying placenta or placenta previa at ≥ 26 weeks' gestation.

RESULTS

Three-hundred and thirty-two consecutive women with a prenatal diagnosis of placenta previa or low-lying placenta were included in the analysis (Figure 2). General characteristics and delivery outcome of the population included in the analysis are described in Table 1. Median maternal age was 33.0 (interquartile range (IQR), 29.0–37.0) years, while median prepregnancy body mass index was 24.2 (IQR, 21.7–26.6) kg/m². Overall, 63.3% of women had at least one previous CS. The incidence of PAS disorders was 53.0% (176/332), while placenta percreta was present in 42.0% (74/176) of these women. The presence of ICL was noted in 50 (15.1%) patients and in 43 of these, other typical ultrasound signs of PAS disorder were present. Ninety-two (27.7%) women had major postpartum hemorrhage during delivery and 132 (39.8%) underwent Cesarean hysterectomy.

Background and delivery characteristics of the study population, according to the presence of ultrasound

signs of PAS disorder, including the new sonographic marker, are described in Table 2. Women with ICL associated with at least one typical ultrasound sign of PAS disorder had a significantly higher incidence of major postpartum hemorrhage ($P < 0.001$), Cesarean

hysterectomy ($P < 0.01$) and placenta percreta ($P < 0.01$) compared to the groups of women without signs of PAS disorder and those with typical ultrasound signs of PAS disorder but no ICL.

On logistic regression analysis, presence of ICL was associated independently with major postpartum hemorrhage (odds ratio (OR), 3.3 (95% CI, 1.6–6.5); $P < 0.001$), Cesarean hysterectomy (OR, 7.0 (95% CI, 2.1–23.9); $P < 0.001$) and placenta percreta (OR, 2.8 (95% CI, 1.3–5.8); $P \leq 0.01$), but not with the presence of any PAS disorder (OR, 1.6 (95% CI, 0.7–3.5); $P = 0.2$) (Table 3).

The sensitivity, specificity, PPV and NPV of ICL for the prediction of Cesarean hysterectomy were, respectively, 30.3% (95% CI, 22.6–39.0%), 95.0% (95% CI, 91.0–97.6%), 80.0% (95% CI, 66.3–90.0%) and 67.4% (95% CI, 61.6–72.8%). The respective values for the detection of placenta percreta were 35.1% (95% CI, 24.4–47.1%), 91.0% (95% CI, 86.5–93.9%), 58.0% (95% CI, 39.9–63.9%) and 83.0% (95% CI, 80.4–85.3%).

Compared with the group with placenta previa or low-lying placenta without ultrasound signs of PAS disorder, the presence of at least one typical sonographic sign of PAS disorder was associated with a DOR of 72.5 (95% CI, 9.8–534.9) for placenta percreta and of 129.5 (95% CI, 30.7–545.7) for Cesarean hysterectomy. The presence of at least one typical sonographic sign of PAS disorder in combination with ICL had a DOR of 217.2 (95% CI, 27.7–1703.4; $P < 0.001$) for placenta percreta and of 687.4 (95% CI, 121.4–3893.0; $P < 0.001$) for Cesarean hysterectomy (Table 4).

Table 1 Background and delivery characteristics in 332 women with low-lying placenta or placenta previa at ≥ 26 weeks' gestation

Parameter	Value
Maternal age (years)	33.0 (29.0–37.0)
Prepregnancy BMI (kg/m ²)	24.2 (21.7–26.6)
GA at delivery (weeks)	36.1 (35.0–37.0)
Gravidity	3 (2–4)
Parity	1 (0–2)
Number of previous Cesarean sections	
1	65 (19.6)
2	92 (27.7)
≥ 3	53 (16.0)
Previous myomectomy	13 (3.9)
Previous curettage	64 (19.3)
Placenta previa	293 (88.3)
Low-lying placenta	39 (11.7)
Anterior placenta	275 (82.8)
Antenatal bleeding	63 (19.9)
Total EBL (mL)	700.0 (500.0–1000.0)
Major PPH*	92 (27.7)
Cesarean hysterectomy	132 (39.8)
Any PAS disorder	176 (53.0)
Placenta percreta	74 (22.3)

Data are given as median (interquartile range) or n (%). *Estimated blood loss (EBL) ≥ 1000 mL. BMI, body mass index; GA, gestational age; PAS, placenta accreta spectrum; PPH, postpartum hemorrhage.

Table 2 Maternal and delivery characteristics in 332 women with low-lying placenta or placenta previa at ≥ 26 weeks' gestation, according to presence of at least one typical sonographic sign of placenta accreta spectrum (PAS) disorder and/or intracervical lakes (ICL)

Parameter	No PAS sign (n = 143)	ICL only (n = 7)	Typical PAS sign only (n = 139)	Typical PAS sign + ICL (n = 43)	Overall P	Between-group P
Maternal age (years)	32.0 (27.0–36.5)	32.0 (27.0–32.0)	34.0 (30.0–38.0)	34.0 (30.5–36.5)	0.02	0.03 ^{a,c,d}
BMI (kg/m ²)	23.8 (21.1–26.5)	24.5 (23.4–30.2)	24.4 (22.1–26.6)	24.5 (22.5–27.0)	0.15	NS
Gravidity	2.0 (1.0–3.0)	2.0 (1.5–3.0)	3.0 (2.0–4.0)	3.0 (3.0–4.0)	< 0.001	< 0.001 ^{a,b} , 0.047 ^d
Parity	1.0 (0–2.0)	1.0 (0.5–2.0)	2.0 (1.0–2.0)	2.0 (1.0–3.0)	< 0.001	< 0.001 ^{a,b}
Number of previous CS						
1	20 (14.0)	2 (28.6)	29 (20.9)	14 (32.6)	< 0.05	< 0.05 ^b
2	23 (16.1)	2 (26.8)	51 (36.7)	16 (37.2)	< 0.001	< 0.001 ^{a,b}
≥ 3	10 (7.0)	1 (14.3)	31 (22.3)	11 (25.6)	< 0.01	< 0.001 ^a , < 0.01 ^b
Previous myomectomy	10 (6.9)	0 (0)	3 (2.1)	0 (0)	0.07	NS
Previous curettage	31 (21.7)	0 (0)	26 (18.7)	7 (16.3)	0.49	NS
Placenta previa	110 (76.9)	7 (100)	134 (96.4)	42 (97.7)	< 0.001	< 0.001 ^a , 0.001 ^b
Anterior placenta	93 (65.0)	7 (100)	133 (95.7)	42 (97.7)	< 0.001	< 0.001 ^{a,b}
Antenatal bleeding	40 (28.0)	2 (28.6)	19 (13.6)	2 (4.6)	0.001	0.001 ^a , < 0.01 ^b
Total EBL (mL)	600 (400–1000)	600 (550–800)	700 (500–900)	1000 (800–1200)	< 0.001	0.02 ^a , < 0.001 ^{b,e} , 0.001 ^d
Major PPH*	35 (24.5)	0 (0)	33 (23.7)	24 (55.8)	< 0.001	< 0.001 ^{b,e} , 0.01 ^d
Cesarean hysterectomy	2 (1.4)	1 (14.3)	90 (64.7)	39 (90.7)	< 0.001	< 0.001 ^{a,b,d} , 0.01 ^c , < 0.01 ^e
Any PAS disorder	42 (29.4)	0 (0)	97 (69.8)	37 (86.0)	< 0.001	< 0.001 ^{a,b,c,d}
Placenta percreta	1 (0.7)	0 (0)	47 (33.8)	26 (60.5)	< 0.001	< 0.001 ^{a,b} , < 0.01 ^e

Data are given as median (interquartile range) or n (%). *Estimated blood loss (EBL) ≥ 1000 mL. ^aNo PAS sign vs typical PAS sign only. ^bNo PAS sign vs typical PAS sign + ICL. ^cICL only vs typical PAS sign only. ^dICL only vs typical PAS sign + ICL. ^eTypical PAS sign only vs typical PAS sign + ICL. BMI, prepregnancy body mass index; CS, Cesarean section; NS, not significant; PPH, postpartum hemorrhage.

Table 3 Binomial logistic regression analysis of association of maternal characteristics and sonographic signs with diagnosis of placenta percreta, any placenta accreta spectrum (PAS) disorder, Cesarean hysterectomy and major postpartum hemorrhage (PPH), in women with low-lying placenta or placenta previa at ≥ 26 weeks' gestation

Parameter	Placenta percreta	Any PAS disorder	Cesarean hysterectomy	Major PPH*
Maternal age (in years)	1.1 (1.0–1.1)	1.1 (1.1–1.2)	1.2 (1.1–1.3)	1.1 (1.0–1.2)
Number of previous CS	1.2 (0.9–1.6)	0.9 (0.7–1.2)	1.5 (0.9–2.2)	0.7 (0.5–0.9)
Parity ≥ 1	7.5 (0.9–63.3)	2.8 (1.3–5.9)	11.3 (2.0–64.7)	1.7 (0.8–3.5)
Intracervical lakes	2.8 (1.3–5.8)	1.6 (0.7–3.5)	7.0 (2.1–23.9)	3.3 (1.6–6.5)
At least one typical US sign of PAS	45.7 (6.1–342.6)	5.3 (3.0–9.6)	72.9 (20.6–258.2)	1.4 (0.7–2.5)
Anterior placenta	19.5 (2.7–143.6)	1.2 (0.7–2.2)	23.9 (5.7–100.1)	0.4 (0.2–0.8)

Data are given as odds ratio (95% CI). *Estimated blood loss ≥ 1000 mL. CS, Cesarean section; US, ultrasound.

Table 4 Diagnostic performance of presence of at least one typical sonographic sign of placenta accreta spectrum (PAS) disorder alone or in combination with intracervical lakes (ICL) for prediction of major postpartum hemorrhage (PPH), Cesarean hysterectomy, any PAS disorder and placenta percreta in women with low-lying placenta or placenta previa at ≥ 26 weeks' gestation, using as reference population with low-lying placenta or placenta previa with no sonographic sign of PAS disorder

Adverse outcome/ predictor	Sensitivity (% (95% CI))	Specificity (% (95% CI))	PPV (% (95% CI))	NPV (% (95% CI))	DOR (95% CI)	LR+ (95% CI)	LR– (95% CI)
Major PPH*							
Typical PAS sign + ICL	40.7 (28.1–54.2)	85.0 (77.6–90.1)	55.8 (42.9–68.0)	75.5 (71.2–79.4)	3.9 (1.9–7.9)	2.7 (1.6–4.6)	0.7 (0.6–0.9)
Typical PAS sign	48.5 (36.2–61.0)	50.5 (43.6–57.4)	23.7 (19.0–29.2)	75.5 (70.3–80.1)	0.9 (0.6–1.7)	1.0 (0.7–1.3)	1.02 (0.8–1.3)
Cesarean hysterectomy							
Typical PAS sign + ICL	95.1 (83.5–99.4)	97.2 (93.1–99.2)	90.7 (77.9–97.4)	98.6 (95.0–99.8)	687.4 (121.4–3893.0)	34.5 (13.8–88.4)	0.05 (0.01–0.2)
Typical PAS sign	97.8 (92.4–99.7)	74.2 (67.2–80.2)	64.7 (56.2–72.6)	98.6 (94.7–99.6)	129.5 (30.7–545.7)	3.8 (3.0–4.9)	0.03 (0.01–0.1)
Any PAS disorder							
Typical PAS sign + ICL	46.8 (35.5–58.4)	94.4 (88.2–97.9)	86.0 (72.1–95.0)	70.6 (62.4–77.9)	14.9 (5.8–37.8)	8.4 (3.8–18.6)	0.6 (0.44–0.67)
Typical PAS sign	69.8 (61.4–77.3)	70.6 (62.4–77.9)	69.8 (63.7–75.3)	70.6 (64.7–76.0)	5.6 (3.3–9.3)	2.4 (1.8–3.2)	0.4 (0.3–0.6)
Placenta percreta							
Typical PAS sign + ICL	96.3 (81.0–99.9)	89.3 (83.4–93.7)	60.5 (44.4–75.0)	99.3 (96.2–100.0)	217.2 (27.7–1703.4)	9.0 (5.8–14.3)	0.04 (0.01–0.2)
Typical PAS sign	97.9 (88.9–100.0)	60.7 (54.1–67.0)	33.8 (26.0–42.3)	99.3 (96.2–99.9)	72.5 (9.8–534.9)	2.5 (2.1–3.0)	0.03 (0.006–0.2)

*Estimated blood loss ≥ 1000 mL. DOR, diagnostic odds ratio; LR–, negative likelihood ratio; LR+, positive likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

DISCUSSION

The findings of this study showed that presence of ICL in women with a low-lying placenta or placenta previa is associated independently with major postpartum hemorrhage, Cesarean hysterectomy and placenta percreta. Presence of both ICL and at least one typical sonographic sign of PAS disorder yielded a higher prediction of these complications compared with presence of typical sonographic signs of PAS disorder alone.

In the most severe forms of PAS disorder, there is progressive invasion of the myometrium by the trophoblastic tissue and massive production of angiogenic factors leading to increased vascularity in the area invaded by the placenta²³. In this scenario, ICL can be considered as the consequence of massive trophoblastic invasion of the uterine cervix leading to an intracervical disruption process. Together with the lower uterus and upper vagina, the cervix is considered part of the S2 area, according to the

invasion topography described by Palacios-Jaraquemada *et al.*²⁴. Assessing the trophoblastic invasion of this area is crucial to planning an appropriate surgical strategy^{25–27}. According to a recently proposed ultrasound staging system for PAS disorders, all cases of placenta previa with evidence of increased vascularity in the inferior part of the lower uterine segment, potentially extending into the parametrial region (PAS3 in the proposed system), had been categorized as Stage 6 according to the FIGO postnatal clinical grading system, with good correlation between this ultrasound finding and surgical outcome²⁸. However, the assessment of this finding on color Doppler ultrasound is highly subjective and technically challenging, especially beyond 30 weeks of gestation²⁷.

Almost 90% of women diagnosed prenatally with placenta previa accreta have an elective or emergency Cesarean hysterectomy; however, an emergency peripartum hysterectomy is associated with considerable morbidity and mortality¹². Near-miss cases of PAS disorder

are associated mostly with placenta percreta invading the lower bladder segment and parametria²⁹. Given the overall low specificity and PPV of ultrasound for diagnosis of placenta percreta and prediction of Cesarean hysterectomy⁸, ICL could be used as a second-step ultrasound sign in patients with at least one typical sonographic sign of PAS disorder.

A number of previous studies have tried to explore whether ultrasound can stratify the surgical risk of women affected by PAS disorder. A recent prospective study by Cali *et al.*²⁷ reported a high sensitivity of ultrasound in detecting placenta percreta, ranging between 80% and 100%. In the same study, however, the presence of at least one ultrasound sign of PAS disorder showed a high sensitivity (77–100%) but a low specificity (40–77%) in detecting placenta percreta; in the presence of at least two signs, the specificity was improved, but the PPV remained at about 55%.

The easier visualization of newly formed vessels in the cervical tissue may represent a marker of parametrial vascularization and indicate placental trespassing of the lower uterine segment. Transvaginal sonographic assessment of the cervix in women with placenta previa has been suggested recently by some authors. Bertucci *et al.*³⁰ introduced a new sonographic sign for the prediction of maternal morbidity in women with abnormally invasive placenta previa, the so-called jellyfish sign, defined as the absence of the normal linear demarcation between the placenta previa and the cervix. Although based on a small number of cases, their pilot study yielded a high specificity for both PAS disorder (95%) and need for Cesarean hysterectomy (96.2%).

Our series included a large proportion of women (about 35%) without a previous uterine surgery. While the typical ultrasound signs of PAS disorder are associated mostly with previous uterine surgery, ICL might potentially represent a standalone marker for morbidly adherent placenta, and their presence may anticipate PAS disorder in women with placenta previa, low-lying placenta or posterior placenta, but with intact uterus.

Finally, the presence of isolated ICL in the absence of other typical ultrasound signs of PAS disorder was observed in only a small group of patients, not allowing a definitive conclusion on this subject.

Strengths and limitations

The main strengths of this study include the large sample size, inclusion of consecutive patients, evaluation of different clinical outcomes and assessment of the ultrasound images by expert examiners in the prenatal diagnosis of PAS disorder. The retrospective unblinded assessment of ICL and the lack of evaluation of the intra- and interobserver variability of the explored signs represent the major weaknesses of the present study.

Inclusion of only women affected by placenta previa or low-lying placenta represents another limitation of the study. A significant proportion of PAS disorders has been shown to occur in women with no recognizable risk

factors for these anomalies³¹. In this scenario, the findings from this study are applicable only to women presenting with placenta previa or low-lying placenta.

In this preliminary study, the number and distribution of the ICL were not assessed because our main outcome was to assess the clinical significance of this new sign and to assess its association with the risk of PAS disorder. Furthermore, we did not perform a longitudinal assessment of the changes of the ICL following the first diagnosis, and absence/presence of the sign was not reassessed on the images collected at subsequent ultrasound examinations prior to delivery.

Finally, given the lack of a prospective protocol for the pathological assessment of cervical vascularization, we were unable to correlate the sonographic assessment of ICL with any histological measure of neovessel formation.

Conclusions

ICL may represent a marker of deep villus invasion in women with suspected PAS disorder on antenatal ultrasound and anticipate the occurrence of severe maternal morbidity. Further studies are needed in order to evaluate the reproducibility of this sign and to elucidate whether its introduction into ultrasound screening of women at risk of PAS disorder may improve the identification of patients at higher risk of adverse outcome.

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Los espacios intracervicales como marcador ecográfico de trastornos del espectro de la placenta acreta en pacientes con placenta previa o placenta baja

RESUMEN

Objetivo Evaluar la precisión del diagnóstico de un nuevo indicio de ultrasonido, los espacios intracervicales (EIC), para predecir la presencia de trastornos del espectro de la placenta acreta (EPA) y el resultado del parto en pacientes con placenta previa o placenta baja.

Métodos Este fue un estudio multicéntrico retrospectivo de mujeres con placenta previa o placenta baja a ≥ 26 semanas de gestación, que se remitieron a tres unidades terciarias italianas desde enero de 2015 a septiembre de 2018. Se evaluó la presencia de EIC, definida como espacios anecoicos tortuosos dentro del cuello uterino que parecían ser hipervasculares en el Doppler a color, en imágenes de ecografías obtenidas en el momento de la remisión. El objetivo principal fue estudiar la precisión del diagnóstico mediante EIC en la detección de la presencia y la profundidad de un trastorno del EPA. El objetivo secundario fue explorar la precisión de este indicador para predecir la pérdida total estimada de sangre, la hemorragia antes del parto, la hemorragia puerperal importante en el momento de la cesárea y la necesidad de una histerectomía por cesárea. La precisión diagnóstica de EIC, en combinación con los indicios ecográficos típicos de los trastornos del EPA, se evaluó calculando estimaciones estadísticas descriptivas de la sensibilidad, la especificidad, los valores predictivos positivos y negativos, los cocientes de verosimilitud positivos y negativos y las razones de momios del diagnóstico (RMD).

Resultados En el análisis se incluyó un total de 332 mujeres con placenta previa o placenta baja, con una mediana de la edad materna de 33,0 años (rango intercuartil, 29,0–37,0). Se observaron EIC en el 15,1% de las pacientes. En el análisis de regresión logística, la presencia de EIC se asoció de forma independiente con la hemorragia puerperal grave (razón de momios (RM), 3,3 (IC 95%, 1,6–6,5); $P < 0,001$), la histerectomía por cesárea (RM, 7,0 (IC 95%, 2,1–23,9); $P < 0,001$) y la placenta percreta (RM, 2,8 (IC 95%, 1,3–5,8); $P \leq 0,01$), pero no con la presencia de ningún trastorno del EPA (RM, 1,6 (IC 95%, 0,7–3,5); $P = 0,2$). En comparación con el grupo de pacientes sin indicios de ultrasonido de algún trastorno del EPA, la presencia de al menos un indicio ecográfico típico de trastorno del EPA en combinación con EIC tuvo una RMD de 217,2 (IC 95%, 27,7–1703,4; $P < 0,001$) para la placenta percreta y de 687,4 (IC 95%, 121,4–3893,0; $P < 0,001$) para la histerectomía por cesárea.

Conclusión Los EIC pueden representar un marcador de invasión profunda de las vellosidades en mujeres con sospecha de algún trastorno del EPA basado en la ecografía prenatal y anticipar la presencia de una morbilidad materna grave.

作为胎盘增生频谱紊乱超声征象的前置胎盘或低位胎盘患者宫颈内血池

摘要

目标：评估一种新型超声征象宫颈内血池（ICL）在预测前置胎盘或低位胎盘患者胎盘增生频谱（PAS）紊乱和分娩结果中的诊断准确性。

方法：这是一项针对2015年1月至2018年9月间，转诊至意大利三家三级医院的妊娠满26周前置胎盘或低位胎盘女性患者的回顾性多中心研究。评估转诊时获得的超声图像确定是否存在ICL，即彩色多普勒超声检测显示宫颈内出现血管增生的迂曲无回声间隙。首要目的是研究ICL在检测PAS紊乱及其深度时的诊断准确性。次要目的是研究该征象在估计剖宫产预计总失血量、产前出血、产后大出血，以及是否需要剖宫产子宫切除术时的准确性。计算敏感性、特异性、阳性和阴性预测值、阳性和阴性似然比和诊断比值比（DOR）汇总估算，以此评估ICL结合典型PAS紊乱超声征象的诊断准确性。

结果：总共分析了332名前置胎盘或低位胎盘女性患者，孕产妇年龄中位数为33.0岁（四分位间距29.0–37.0）。发现15.1%的病患出现ICL。逻辑回归分析表明ICL与产后大出血（比值比OR 3.3 (95% CI, 1.6–6.5); $P < 0.001$)、剖宫产子宫切除术(OR, 7.0 (95% CI, 2.1–23.9); $P < 0.001$)以及植入胎盘(OR, 2.8 (95% CI, 1.3–5.8); $P \leq 0.01$)独立相关，但与任何PAS紊乱无关(OR, 1.6 (95% CI, 0.7–3.5); $P = 0.2$)。对照未出现PAS紊乱超声征象的病患组，(植入胎盘中)至少一种典型的PAS紊乱超声征象结合ICL的DOR为217.2 (95% CI, 27.7–1703.4; $P < 0.001$)，剖宫产子宫切除术为687.4 (95% CI, 121.4–3893.0; $P < 0.001$)。

结论：ICL可能是一种产前超声检测中显示疑似PAS紊乱的孕产妇深绒毛浸润标志物，可以预测重度孕产妇疾病发病率。