Gynecologic and
Obstetric Investigation

Clinical and Ultrasound Predictors of Placenta Accreta in Pregnant Women with Antepartum Diagnosis of Placenta Previa: A Multicenter Study

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Abstract

Background/Aims: Abnormally invasive placenta (AIP) includes placenta *accreta*, *increta*, and *percreta* and represents major complications of pregnancy. This study was designed to assess the role of ultrasonography in the identification of AIP among pregnant women with antepartum diagnosis of placenta *previa*. ***Methods:*** A cross-sectional study was performed between May 2015 and April 2016 in 11 centers, including 242 women with *antepartum* diagnosis of placenta *previa*. ***Results:*** Ninety-eight out of 242 (40.49%) women had a histological diagnosis of placenta *accreta*. A higher number of caesarean deliveries (*p* = 0.001) and curettages (*p* = 0.027) and older age of the woman at the delivery (*p* = 0.031) were identified as risk factors for placenta *accreta*. The presence of irregularly shaped placental lacunae (vascular spaces) within the placenta (*p* = 0.008), protrusion of the placenta into the bladder (*p* < 0.0001), and turbulent blood flow through the lacunae on Doppler ultrasonography (*p* = 0.008) were predictors of placenta *accreta*. ***Conclusions:*** Women with a prior delivery by caesarean section have a high incidence of placenta *accreta* among women with antepartum diagnosis of placenta *previa*.

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Introduction

Abnormally invasive placenta (AIP) defines a placenta that does not separate spontaneously at delivery and its removal causes abnormally high blood loss; AIP encompasses the histopathological diagnosis of placenta accreta, placenta increta (PI), and placenta percreta [1]. Placenta *accreta* is more common in women with a history of multiple caesarean sections and the presence of a placenta previa than women without these risk factors. Placenta *accreta* increases the risk of major complications, such as fetal loss [2], bleeding [3], and hysterectomy [4]. Due to an increasing proportion of caesarean deliveries [5], the risk of placenta *accreta* has increased in the last 2 decades [6].

Silver et al. [7] reported that placenta *accreta* was present in 15 (0.24%), 49 (0.31%), 36 (0.57%), 31 (2.13%), 6 (2.33%), and 6 (6.74%) women undergoing their first, second, third, fourth, fifth, and sixth or more cesarean deliveries respectively.

AIP should be investigated in women with previous uterine surgery [8, 9] and women with placenta previa [8]. Several ultrasound features have been suggested for diagnosis of placenta *accreta* such as irregularly shaped placental lacunae (vascular spaces), thinning of the myometrium overlying the placenta, loss of the retroplacental "clear space", protrusion of the placenta into the bladder, increased vascularity of the uterine serosa/bladder interface, and turbulent blood flow through the lacunae on Doppler ultrasonography [10].

Magnetic resonance imaging (MRI), even if used widely in cases of suspected AIP, is yet to be proven to improve pregnancy outcome. Furthermore, diagnostic accuracy depends on the training and level of experience of the physician, irrespective of the imaging technique [1]. Ultrasound is the primary tool to diagnose AIP in women at risk, such as those with placenta previa and a prior cesarean section (CS), whereas prenatal MRI is usually reserved for cases with inconclusive ultrasound assessment [11]. In fact, ultrasound had an overall good diagnostic accuracy in identifying the depth of placental invasion with sensitivities of 90.6, 93.0, 89.5, and 81.2% for placenta accreta, increta, accreta/increta, and percreta respectively [12].

Here we aimed to assess whether ultrasonography might help identify predictors of placenta *accreta* and hysterectomy in a large group of pregnant women in Italy with antepartum diagnosis of placenta *previa*.

Fig. 1. *Antepartum* diagnosis of placenta *previa* at ultrasound scan.

Methods

The study was approved by the Institutional Review Boards (IRB) of the hospitals in which it was performed. Furthermore, IRB of Sassari University approved the study.

Participants and Clinical Characteristics

A cross-sectional study was performed in 11 centers placed in Italy.

Caucasian women with an ultrasound diagnosis of placenta *previa* in pregnancy delivering at the participating centers were recruited between May 2015 and April 2016.

Placenta *previa* was classified based on the relationship between the placental margin and the internal os. Antepartum diagnosis of placenta previa should be only used when the placental edge overlaps or is within 2 cm of the internal cervical os (Fig. 1) [13].

All women underwent a transabdominal ultrasound scan followed by a transvaginal scan and placental evaluation performed from 25 + 0 weeks to 40 weeks of gestational age, investigating the following criteria [2]: (1) irregularly shaped placental lacunae (vascular spaces), (2) thinning of the myometrium overlying the placenta with a cut-off of 1 mm, (3) loss of the retroplacental "clear space", (4) protrusion of the placenta into the bladder, (5) increased vascularity of the uterine serosa/bladder interface, (6) and turbulent blood flow through the lacunae on Doppler ultrasonography (Fig. 2).

Placenta *accreta* was defined as trophoblastic attachment to the myometrium without intervening decidua. If the trophoblast invades the myometrium, it is termed PI, and if it invades through the myometrium beyond the serosa and into surrounding structures such as the bladder, it is termed a *percreta*. Often the term placenta *accreta* is used to refer to the entire spectrum of conditions including *accreta*, *increta*, and *percreta* as well as to cases of clinically apparent morbidly adherent placenta. In this study, the term placenta *accreta* refers to the entire spectrum unless specifically noted.
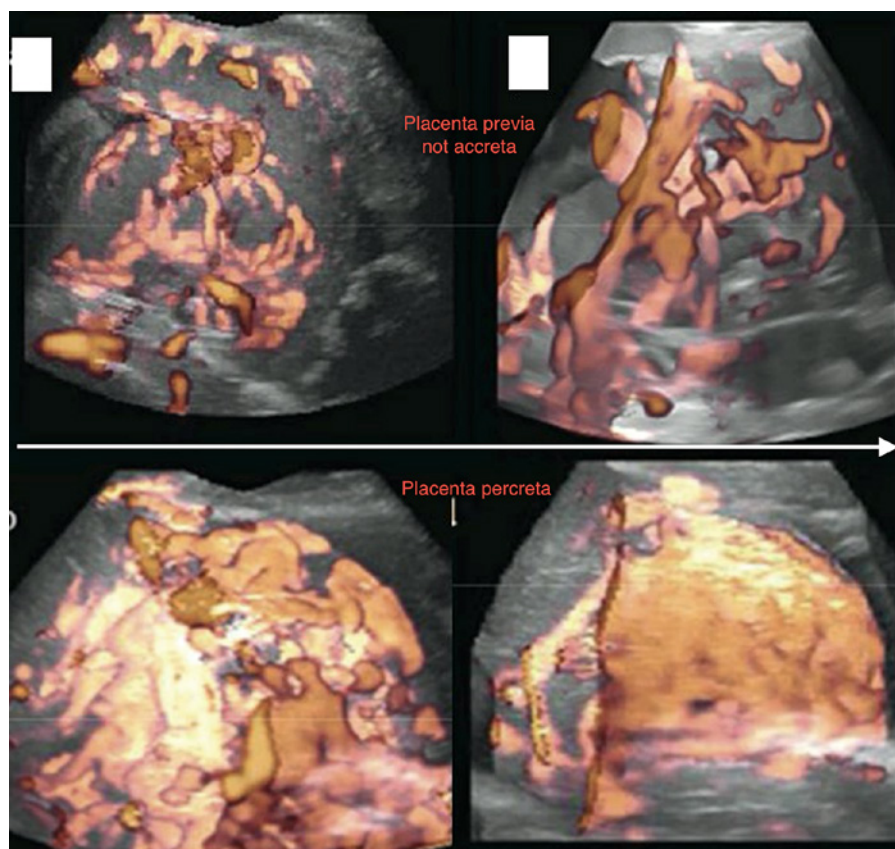
Fig. 2. Placenta *percreta*: 3D color ultrasound shows increased vascularity of the uterine sierosa/bladder interface.

AIP was established at *postpartum* histological evaluation. Placenta accreta was separated into 3 categories: placenta creta when the villi simply adhere to the myometrium, PI when the villi invade the myometrium, and placenta percreta when the villi invade the full thickness of the myometrium [14].

A detailed anamnesis was obtained including age, parity with number of vaginal deliveries and caesarean deliveries, previous myomectomies, curettages, and resectoscopies.

The respective Ethical Committees of all participating sites approved the study and all patients provided their written informed consent.

Endpoints: Placenta Accreta

The association between placenta *accreta* and general characteristics and ultrasound findings was the primary outcomes of the study.

Statistical Analysis

Continuous variables were expressed as mean ± SD and compared with t test, if normally distributed, and with the Mann-Whitney U test, if not normally distributed. Normality of variables was tested using the Kolmogorov-Smirnov test. Categorical variables are expressed as proportions and compared using a χ^2 test. To determine the risk factors associated with placenta accreta and hysterectomy, logistic regression analyses (backward conditional) were performed including all the demographic, clinical, and ultrasound features. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS 22.0) software (SPSS Inc., Chicago, IL, USA). $p < 0.05$ was considered statistically significant.

Results

Two hundred and forty-two women with antepartum diagnosis of placenta *previa* were included.

The mean age ± SD was 33.2 ± 4.9 years, mean number of vaginal deliveries ± SD was 2.2 ± 1.9, and mean number of caesarean deliveries ± SD was 1.0 ± 1.1.

Out of 242 women, 66 (27.27%) were nulliparous, 82 (33.89%) had 1 previous CS, 64 (26.45%) had 2 previous CS, 26 (10.74%) had 3 previous CS, and 4 (1.65%) had 4 previous CS.

From the anamnesis 22 out of 242 patients (9.09%) had a myomectomy, 100 out of 242 (41.32%) had a curettage, and 5 out of 242 (2.07%) had a resectoscopy.

Out of 242 patients, 98 (40.49%) had a histological diagnosis of placenta *accreta* after the delivery.

Out of these 98 patients, placenta *accreta* was reported in 12 (12.25%), 31 (31.63%), 36 (36.73%), and 19 (19.39%)

Table 1. Demographic, clinical, and sonographic characteristics of women with and without placenta accreta at delivery

	Placenta accreta (n = 98)	No placenta accreta (n = 129)
Age, years, mean ± SD	34.0±5.1*	32.7±4.7
Number of vaginal deliveries, mean ± SD	2.1±2.0	2.1±1.8
Number of caesarean deliveries, mean ± SD	1.2±1.3*	0.7±0.8
Myomectomies, n (%)	3/98 (3.06)*	15/129 (11.63)
Curettages, n (%)	40/98 (40.82)	48/129 (37.21)
Resectoscopies, n (%)	1/98 (1.02)	4/129 (3.10)
Ultrasound, n (%)		
Sign 1	41/98 (41.84)*	47/129 (36.43)
Sign 2	40/98 (40.82)*	43/129 (33.33)
Sign 3	36/98 (36.73)*	34/129 (26.36)
Sign 4	33/98 (33.67)*	7/129 (5.43)
Sign 5	26/98 (26.53)*	1/129 (0.78)
Sign 6	27/98 (27.55)*	1/129 (0.78)

* $p < 0.005$.
Sign 1: placental lacunae (vascular spaces); Sign 2: thinning of the myometrium overlying the placenta; Sign 3: loss of the retroplacental "clear space"; Sign 4: protrusion of the placenta into the bladder; Sign 5: increased vascularity of the uterine serosa/bladder interface; Sign 6: turbulent blood flow through the lacunae on Doppler ultrasonography.

Table 2. Risk factors associated with placenta accreta

	OR	95% CI for OR		p value
		lower	upper	
Age	1.116	1.010	1.233	0.031
Number of vaginal deliveries	0.462	0.265	0.804	0.006
Number of caesarean deliveries	7.002	2.119	23.135	0.001
Curettage	3.577	1.160	11.037	0.027
Placental lacunae (vascular spaces)	6.226	2.076	10.673	0.008
Protrusion of the placenta into the bladder	24.408	5.359	111.179	0.000
Turbulent blood flow inside the lacunae on Doppler ultrasonography	24.695	2.278	267.711	0.008

women undergoing their first, second, third, and fourth cesarean deliveries respectively.

Table 1 shows demographic, clinical, and ultrasound features of women who had versus those who did not have a placenta *accreta*.

Women with placenta *accreta* had a higher number of caesarean deliveries, older age compared to women with no abnormal placental adherence, and higher probability to have at least 1 ultrasound feature among signs numbers 1, 2, 3, 4, 5, and 6. A higher number of caesarean deliveries (OR 7.002, 95% CI 2.119–23.135; $p = 0.001$) and curettages (OR 3.577, 95% CI 1.160–11.037; $p = 0.027$), older

age of the woman at the delivery (OR 1.116, 95% CI 1.010–1.233; $p = 0.031$), and lower number of vaginal deliveries (OR 0.462, 95% CI 0.265–0.804; $p = 0.006$) were identified as risk factors for placenta *accreta*. At ultrasound, the presence of irregularly shaped placental lacunae (vascular spaces; OR 6.226, 95% CI 2.076–10.673; $p = 0.008$), protrusion of the placenta into the bladder (OR 24.408, 95% CI 5.359–111.179; $p < 0.0001$), and turbulent blood flow through the lacunae (OR 24.695, 95% CI 2.278–267.711; $p = 0.008$) were predictors for placenta *accreta* (Table 2). No other variables were significantly associated with the diagnosis of placenta *accreta*.

De Vita et al.

Out of 242 patients, 61 (25.21%) were diagnosed with placenta *accreta* had hysterectomy; 17 (6.9%) had hysterectomy without diagnosis of placenta *accreta*.

Discussion

In an Italian population of 242 women with *antepartum* diagnosis of placenta *previa*, 98 (40.49%) had a histological diagnosis of placenta *accreta*, 61 (25.21%) patients with diagnosis of placenta *accreta* had a hysterectomy at the time of the delivery and 17 (67.02%) had hysterectomy without diagnosis of placenta *accreta*.

A prior delivery by caesarean section was the main risk factor for placenta *accreta*. A history of previous myomectomy did not increase the risk.

With regard to ultrasound findings, we found 2 strong predictors of morbidly adherent placenta: protrusion of the placenta into the bladder and turbulent blood flow through the lacunae.

Our data confirm that an increasing incidence of placenta *accreta* is mainly due to the increased number of deliveries by caesarean section. In almost all cases, an abnormal placental invasion was at the site of the uterine scar [15]. We also found that older maternal age and curettages are important risk factors for placenta *accreta* as shown previously [16]. In fact, women at most increased risk of placenta *accreta* were those who had a history of curettages, no vaginal deliveries, and previous caesarean sections with a placenta *previa* overlying the uterine scar.

The *antepartum* identification of women at higher risk of placenta *accreta* is pivotal for the reduction of maternal/fetal morbidity and mortality by allowing clinicians to choose the best time and place of birth. Multidisciplinary surgical management, neonatal intensive care, uterine artery embolization, and an adequate number of blood products available in the operating room can only be achieved effectively through the early detection of the placental pathology [10].

Ultrasonography may be used for diagnosis of abnormal placental adherence, but diagnostic criteria and accuracy are still under debate [17–19].

Here, we found that having protrusion of the placenta into the bladder and turbulent blood flow through the lacunae would help to identify the vast majority of women who had a histological diagnosis of placenta *accreta* at the time of delivery.

Ultrasound is the primary tool to diagnose AIP in women at risk, such as those with placenta previa and a prior CS, whereas prenatal MRI is usually reserved for cases with inconclusive ultrasound assessment [11].

On the other hand, having turbulent blood flow through the lacunae on Doppler ultrasonography was already found in prior studies [17–20].

Recently, a systematic review and meta-analysis of D'Antonio et al. [21] summarized several papers showing that ultrasound signs of AIP are already present during the first trimester of pregnancy, especially before 11 weeks of gestation. Low anterior implantation of the placenta/sac close to or within the scar was the most common early US signs suggestive of AIP, although its individual predictive accuracy was not high.

Rac et al. [22] constructed a receiver operating characteristic curve with the combination of smallest sagittal myometrial thickness, lacunae, and bridging vessels, in addition to a number of cesarean deliveries and placental location, yielding an area under the curve of 0.87 (95% CI 0.80–0.95). Using logistic regression, a predictive equation was generated, termed the "Placenta Accreta Index." Each parameter was weighted to create a 9-point scale in which a score of 0–9 provided a probability of invasion that ranged from 2–96%; they concluded that this Index may be helpful in predicting individual patient risk of morbidity adherent placenta.

The main limitation of this study may be that the *antepartum* diagnosis was based only on ultrasound and no MRI evaluations have been performed. MRI may be helpful when the placenta is difficult to visualize on ultrasound due to patients' habitus or to a posterior location of the placenta [23–26]. However, no statistical difference in sensitivity or specificity between ultrasound and MRI has been reported [27–28].

Planning individual management for delivery is possible only with accurate evaluation of prenatal risk of *accreta* placentation in women presenting with a low-lying placenta/previa and a history of prior cesarean delivery. Ultrasound is highly sensitive and specific in the prenatal diagnosis of accreta placentation when performed by skilled operators [29].

In conclusion, women with a prior delivery by caesarean section have a high incidence of placenta *accreta* among women with antepartum diagnosis of placenta *previa*.

Disclosure Statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Research Involving Human Participants and Animals

All procedures performed in studies involving human participants were in accordance with the ethical standards the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

IRB Approval

The study was approved by the IRBs of the hospitals in which it was performed. Furthermore, IRB of Sassari University approved the study.

Informed Consent

Our study involved collection of data and formal consent was obtained from the participants of the study.

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