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Accuracy of ultrasound in antenatal diagnosis of placental attachment disorders

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KEYWORDS: placenta accreta; placental attachment disorders; placenta previa; ultrasound

ABSTRACT

Objectives *To evaluate the accuracy of ultrasound in the diagnosis of placenta accreta and its variants, and to assess the impact of prenatal diagnosis in our population.*

Methods *A total of 314 women with placenta previa were enrolled prospectively and underwent transabdominal and transvaginal ultrasound examinations. An ultrasound diagnosis (grayscale and color/power Doppler) of placental attachment disorder (PAD) was based on the detection of at least two of the following ('two-criteria system'): loss/irregularity of the retroplacental clear zone, thinning/interruption of the uterine serosa–bladder wall interface, turbulent placental lacunae with high velocity flow, myometrial thickness < 1 mm, increased vascularity of the uterine serosa–bladder wall interface, loss of vascular arch parallel to the basal plate and/or irregular intraplacental vascularization. Definitive diagnosis was made at delivery by Cesarean section. Maternal outcome in cases diagnosed antenatally was compared with that in cases diagnosed at delivery.*

Results *There were 37/314 cases of PAD (29 anterior and eight posterior). The two-criteria system identified 30 cases of placenta accreta, providing a sensitivity of 81.1% and specificity of 98.9%. When anterior and posterior placentae were considered separately, the detection rates of PAD were 89.7 and 50.0%, respectively. Maternal outcome was better in women with prenatal diagnosis of PAD, as seen by less blood loss and shorter hospitalization.*

Conclusions *Our data confirmed that grayscale and color Doppler ultrasound have good performance in the diagnosis of PAD and that prenatal diagnosis improves maternal outcome. Copyright © 2015 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Placental attachment disorder (PAD) encompasses a spectrum of conditions characterized by abnormal adherence of the placenta to the implantation site, with three variants classified according to their degree of trophoblastic invasion through the myometrium and the uterine serosa: placenta accreta, increta and percreta. Placenta accreta, the most common variant, is defined as a placenta that is adhered abnormally to the uterus, wherein the chorionic villi have embedded directly into the myometrium in the absence of decidua[1]. All varieties are associated with a significant increase in maternal morbidity and mortality, mainly due to blood loss, local organ damage, urgent hysterectomy (33–50%) and postoperative complications[2–6]. PAD is a life threatening disease; Comstock *et al.* reported a mortality rate of 7%[7].

Placenta previa and previous uterine surgery are the major risk factors for invasive placentation[8,9]. Placenta previa is defined as a placenta that either lies in close proximity to the internal cervical os or partially or completely covers it[1], and is associated with a high rate of maternal and fetal morbidity and mortality[10]. Placenta previa and accreta and their complications are increasing due to a higher number of Cesarean sections being performed and advanced maternal age[1,10].

Although placenta previa is *per se* a risk factor, the most common is a uterine scar. The risk increases from 0.3% after one prior Cesarean section to 0.6, 2.1, 2.3 and 6.7% after two, three, four and more than four Cesarean sections, respectively[11].

Although ultrasound is routinely used to diagnose PAD, diagnostic criteria and accuracy are still under debate. Most studies have included small cohorts[12–17] and some larger studies[18,19] used different techniques and different diagnostic criteria. As there are reports in the

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literature that maternal complications, such as peripartum blood loss, need for blood transfusion and peripartum hysterectomy, are reduced when affected pregnancies are referred to a tertiary medical center, an accurate antenatal diagnosis of invasive placentation is important[7,20–22]. This study aimed to evaluate the accuracy of grayscale and color Doppler ultrasound in the diagnosis of PAD, and subsequent assessment of the impact of prenatal diagnosis on our study population.

SUBJECTS AND METHODS

Between January 2011 and January 2014, 314 consecutive pregnant women with persistent placenta previa (after 26 weeks' gestation), who delivered subsequently at Sant' Anna Hospital in Turin, were enrolled prospectively into this study. The majority of patients with a suspected diagnosis of placenta previa in the Piedmont region are referred to our center (approximately 7500 deliveries/year) for definitive diagnosis and delivery. The number of deliveries in the region during the 3-year study period was 108 000.

Placenta previa was defined as central when it covered the internal os and as marginal when the placental edge was < 20 mm from the internal os[22]. The patient history was obtained with details of any previous uterine surgery, such as Cesarean section or uterine curettage. Transabdominal and transvaginal ultrasound examinations were performed in each woman by at least two different operators between 26 and 36 weeks' gestation, using two-dimensional (2D) grayscale and color/power Doppler imaging. Examinations were performed using an ultrasound system equipped with a 4–8-MHz transabdominal transducer and a 5–9-MHz transvaginal transducer (Voluson 730, GE Medical Systems, Zipf, Austria, and HD 11, Philips, Amsterdam, The Netherlands).

The following characteristics were evaluated: (1) loss or irregularity of the hypoechoic area between the uterus and placenta, the 'retroplacental clear zone' (Figure 1a); (2) thinning or interruption of the uterine serosa–bladder wall interface (Figure 1b); (3) myometrial thickness < 1 mm (Figure 1c and d); (4) turbulent placental lacunae with high velocity flow (> 15 cm/s) (Figure 1e and f); (5) increased vascularity of the uterine serosa–bladder wall interface (Figure 1g); and (6) loss of vascular arch parallel to the basal plate and irregular intraplacental vascularization (Figure 1h)[7,17–19,23–25]. The presence of at least two of the aforementioned characteristics ('two-criteria system') were considered diagnostic for placenta accreta, increta and percreta.

All pregnancies enrolled in this study were delivered by Cesarean section in our division (tertiary center). A definitive diagnosis of PAD was made at delivery when it was not possible to remove the placenta or by the pathological examination of the uterus after hysterectomy. The pathologist was blinded to the ultrasound diagnosis.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the two-criteria system and each of the six features involved were calculated separately and were also calculated for anterior and posterior placentae independently.

The following procedures were adopted at Cesarean section if there was an antenatal diagnosis of placenta accreta: the uterine incision was made above the upper margin of the placenta to avoid excessive bleeding; following delivery of the fetus and clamping of the cord, the placenta was removed by the administration of oxytocin and application of controlled cord traction. No attempt was made to remove the placenta manually if it was evident that the placenta had reached the uterine serosa (Figure 2); in the absence of heavy bleeding, the whole placenta, or part of it, was left *in situ*. In the event of failed placental detachment and in the presence of heavy bleeding, a peripartum hysterectomy was performed, preserving the adnexa. In some cases, hysterectomy was planned before delivery; the uterine incision was made towards the fundus, followed by delivery of the fetus, suture of the uterus and hysterectomy[21,22,26]. Lastly, we compared maternal outcome in diagnosed *vs* undiagnosed PAD, taking into consideration the hysterectomy rate, blood loss, the need for blood transfusion, days in the intensive care unit (ICU), infection rate and the 5-min Apgar score.

Statistical analysis

Analyses were based on a series of patients recruited prospectively from a single center. With respect to aims of this study, a formal evaluation of required sample size was not performed due to difficulty in assessing both the actual rate during the study period and a reliable estimate of the prevalence of placental disorders following Cesarean section. Logically, given our aim was to evaluate the accuracy of a test that includes several measurements, we hoped to be able to include a large series of patients. However, after nearly 3 years of work for recruitment and measurements in patients, we decided to proceed with the analysis to assess whether a test based on clinical and ultrasound parameters could be promising for the purpose of an accurate diagnosis.

RESULTS

During the 3-year study period, a total of 314 women were enrolled; 160 had an antenatal diagnosis of central previa and 154 a diagnosis of marginal previa. The average age at diagnosis was 36 ± 1.7 years and 161 (51%) women had a history of uterine hysterotomy (at least one Cesarean section or myomectomy). Placenta accreta and its variants (including increta and percreta) were present in 37/314 (11.8%) subjects at the time of Cesarean delivery; 29 (78.4%) were anterior and eight (21.6%) were posterior. Of the 277 patients without placenta accreta, 206 (74.4%) had anterior or anterolateral and 71 (25.6%) had posterior placenta. There was a higher rate of PAD in women who reported having had a previous hysterotomy (25/161; 15.5%) than in those with no

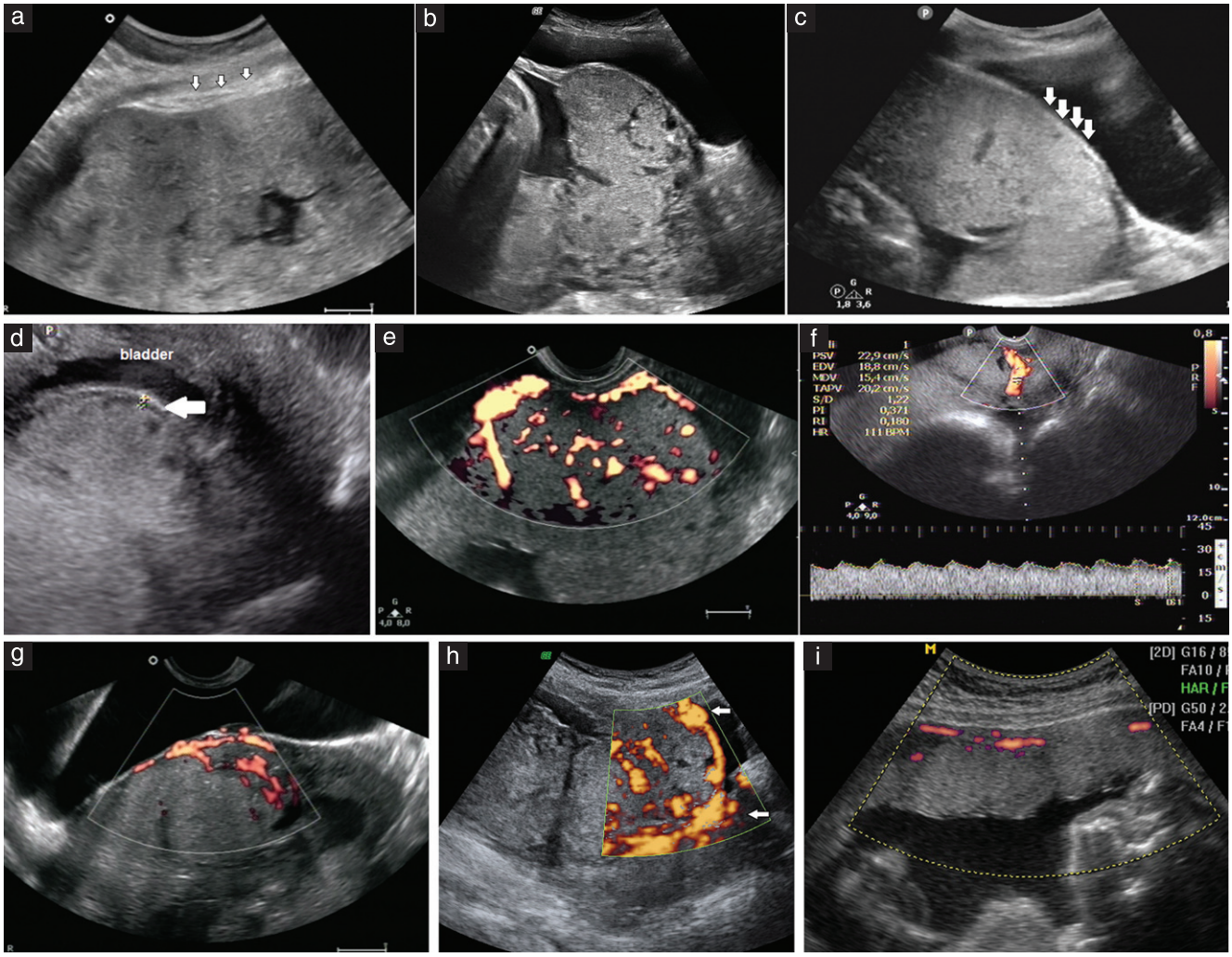

Figure 1 Grayscale (a–d) and power Doppler (e–i) ultrasound images, showing the ultrasound criteria used for diagnosing placental attachment disorder. (a) Loss/irregularity of retroplacental clear zone (arrows); peripartum hysterectomy was performed at Cesarean section for heavy bleeding, and pathological examination identified placenta accreta and increta. (b) Thinning/interruption of the uterine serosa–bladder interface; at Cesarean section, uterine incision was made towards the fundus, no attempt was made to remove the placenta, and hysterectomy was performed. Pathological examination identified placenta percreta. (c) Myometrial thickness <1 mm (absent myometrial tissue, arrows); at Cesarean section a uterine incision was made towards the fundus, no attempt was made to remove the placenta, and hysterectomy was performed. Pathological examination identified placenta percreta and increta. (d) Myometrial thickness < 1 mm (arrow and calipers); hysterectomy was performed at Cesarean section for heavy bleeding and uterine atony and pathological examination identified placenta accreta and increta. (e) Turbulent placental lacunae; placenta was partly accreta with incomplete detachment at Cesarean section resulting in hemostatic sutures and 20% of placenta left *in situ*. (f) Placental lacunae with high velocity flow (22.9 cm/s); hysterectomy was performed at Cesarean section for heavy bleeding, and pathological examination identified placenta accreta. (g) Increased vascularity of uterine serosa–bladder wall interface; placenta was partly accreta with incomplete detachment at Cesarean section resulting in hemostatic sutures and 40% of placenta left *in situ*. (h) Loss of vascular arch parallel to basal plate (arrows) and irregular intraplacental vascularization; at Cesarean section a uterine incision was made towards the fundus, no attempt was made to remove the placenta, and hysterectomy was performed with small resection of bladder. Pathological examination identified placenta percreta. (i) Normal homogeneous placenta with vascular arch parallel to basal plate; at Cesarean section a uterine incision was made above the upper margin of the placenta and the placenta detached completely.

previous uterine surgery (12/153, 7.8%), although the difference did not reach statistical significance.

The two-criteria system diagnosed 30/37 women with confirmed PAD, providing a sensitivity of 81.1%, a specificity of 98.9% (274/277) and PPV and NPV of 90.9% and 97.5%, respectively (Table 1).

Evaluation of accuracy for individual sonographic signs demonstrated that loss/irregularity of the retroplacental clear zone had the same sensitivity and NPV as did the two-criteria system, but a lower specificity and PPV (Table 1). All other features had a considerably lower sensitivity than did the two-criteria system.

There were three false-positive cases (one showed three and two showed one of the ultrasound characteristics) and seven false-negative cases of PAD (six showed just one ultrasound criterion, which was loss/irregularity of retroplacental clear zone in three, and one showed no characteristic ultrasound criteria). The majority of the true-positive cases had two or three ultrasound criteria, whilst no case with four or more characteristics was a

Table 1 Accuracy of two-criteria system and individual ultrasound characteristics for diagnosing placental attachment disorder in 314 pregnant women with placenta previa

Diagnostic criteria	*TP* (n)	*TN* (n)	*FP* (n)	*FN* (n)	*Sensitivity* (95% CI) (%)	*Specificity* (95% CI) (%)	*PPV* (95% CI) (%)	*NPV* (95% CI) (%)
Two-criteria system	30	274	3	7	81.1 (69–94)	98.9 (98–100)	90.9 (82–100)	97.5 (96–99)
Thinning/interruption of uterine serosa–bladder interface	15	271	6	22	40.5 (27.9–53.1)	97.8 (96.7–98.9)	71.4 (62.3–80.5)	92.5 (90.7–94.3)
Myometrial thickness < 1 mm	7	275	2	30	18.9 (6.3–31.5)	99.3 (98.0–100)	77.8 (69.0–87.0)	90.2 (88.0–92.0)
Turbulent placental lacunae	18	262	15	19	48.6 (36.0–61.0)	94.6 (93.5–95.7)	54.5 (45.4–63.6)	93.2 (91.4–95.0)
Increased vascularity of uterine serosa–bladder wall interface	4	277	0	33	10.8 (0.0–23.0)	100 (98.0–100)	100 (91.0–100)	89.4 (87.5–91.0)
Loss of vascular arch parallel to basal plate and irregular intraplacental vascularization	25	254	13	12	67.6 (55.0–80.0)	91.7 (90.6–93.0)	65.8 (56.7–75.0)	95.7 (93.8–97.5)
Loss/irregularity of retroplacental clear zone	30	271	6	7	81.1 (68.5–93.7)	97.8 (96.1–99.5)	83.7 (71.2–95.5)	97.5 (95.6– 99.3)

FN, false negative; FP, false positive; NPV, negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive.

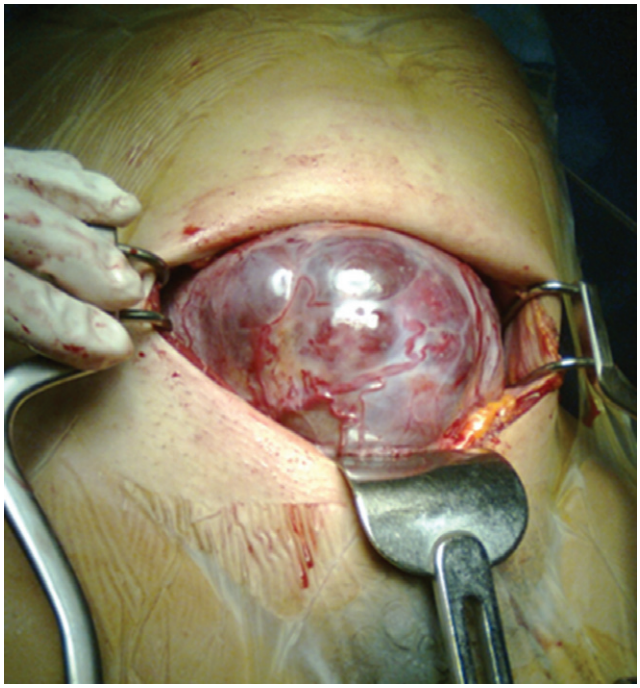

Figure 2 Intraoperative image in a case of placenta percreta diagnosed by ultrasound (as shown in Figure 1b).

false positive (Table 2). Four of the six cases with placenta percreta (Figure 1b) that were identified by the pathologist after hysterectomy had four or more diagnostic ultrasound characteristics. Four of the false negatives had posterior placenta and three had anterior placenta.

When anterior and posterior placentae were considered separately, the two-criteria system provided a higher accuracy for diagnosis of PAD in pregnancies with anterior placenta than in those with posterior placenta (Table 3).

As for maternal outcomes, the true positives had significantly less blood loss and required a shorter period in the ICU than did women with PAD who were

Table 2 Numbers of pregnancies diagnosed with placental attachment disorder (PAD) according to number of ultrasound criteria used for a positive diagnosis in 314 pregnant women with placenta previa

Number of criteria	*PAD diagnosed* (n)	*No PAD diagnosed* (n)
0	1	239
1	6	35
2	11	2
3	10	1
4	5	0
5	3	0
6	1	0

undiagnosed during pregnancy (Table 4). They also had a lower rate of infection; however, this did not reach statistical significance. A preventive hysterectomy was planned in 6/13 subjects in the true-positive group and no attempt was made to remove the placenta. Pathological examination of the uterus after hysterectomy confirmed the diagnosis of PAD in each of the 17 cases in which it was performed (seven placenta accreta, four placenta increta and six placenta percreta).

DISCUSSION

PADs are an increasingly frequent complication and the most recent guidelines report that delivery in a tertiary referral center improves maternal and fetal outcomes[6,21,22,26]. Scientific interest has led to a number of recent publications on the diagnosis of PAD. However, they have been carried out using different methods and often on small cohorts. Some authors have used only grayscale ultrasound, others have used color Doppler and/or three-dimensional (3D) ultrasound or all three, and most studies included only the anterior placenta[2,13,15,16,19,21]. An antenatal diagnosis of PAD was based on the presence of at least two ultrasound

Table 3 Accuracy of two-criteria system for diagnosing placental attachment disorder in 314 pregnant women with placenta previa, according to placental location

Placental location	*TP* (n)	*TN* (n)	*FP* (n)	*FN* (n)	*Sensitivity* (95% CI) (%)	*Specificity* (95% CI) (%)	*PPV* (95% CI) (%)	*NPV* (95% CI) (%)
Anterior ($n = 235$)	26	204	2	3	89.7 (78.6–100)	99.0 (97.7–100)	92.9 (83–100)	98.6 (97–100)
Posterior ($n = 79$)	4	70	1	4	50.0 (15–84.6)	98.6 (96–100)	80.0 (45–100)	94.6 (89–99.7)

FN, false negative; FP, false positive; NPV, negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive.

Table 4 Maternal outcome in 37 pregnancies with placental attachment disorder according to whether they were diagnosed prenatally by ultrasound (US)

Outcome	*US diagnosis* (n = *30*)	*No US diagnosis* (n = *7*)	P*
Hysterectomy	13 (43)	4 (57)	NS
Blood loss (mL)	1300 (300–5200)	3000 (700–8000)	0.049
Blood transfusion	17 (57)	6 (86)	NS
Days in intensive care unit	2 (0–5)	4 (0–9)	0.032
Infection	4 (13)	3 (43)	NS
Emergency Cesarean section	11 (37)	3 (43)	NS
5-min Apgar score	8 (4–9)	9 (6–9)	NS

Data are given as *n* (%) or median (range). *Mann–Whitney *U*-test was used to compare continuous variables and Fisher's exact test was used for categorical variables. NS, non-significant.

criteria in some studies; others used only one criterion, thus obtaining an increased sensitivity but a reduced specificity[17]. We obtained a sensitivity of 81.1%, a specificity of 98.9%, a PPV of 90.9% and a NPV of 97.5%, using the presence of at least two of six criteria for a diagnosis. The single criterion with the greatest sensitivity was the loss/irregularity of retroplacental clear zone (81%). Indeed, this alone had a sensitivity equal to that of ultrasound examination based on the two-criteria system, but a lower PPV (83.7% *vs* 90.9%) and specificity (97.8% *vs* 98.9%), with six false-positive cases compared to three.

When the other criteria were considered individually, all had a lower sensitivity; in particular, placental lacunae had the lowest PPV, in contrast to the findings of Yang *et al.*[31] who reported high accuracy using a four-grade classification for placental lacunae. This may be due to the fact that we did not consider the number of lacunae but only the presence/absence of them.

When only anterior placentae were considered, a higher accuracy rate was observed (Table 3). The two studies with the largest cohorts in the international literature were by Shih *et al.*[18], comprising 39 cases, and Cali *et al.*[19], comprising 41 cases, and they only considered anterior placenta. Both studies used 2D and color Doppler, but also 3D with power Doppler and both calculated the accuracy of a variety of criteria separately. The authors concluded that 3D had diagnostic advantages mainly in the presence of hypervascularity of the uterine serosa–bladder wall interface in cases of placenta percreta. Our overall performance results were not as good as theirs; however, when only cases of anterior placenta were taken into consideration, our accuracy was comparable. The higher specificity of 3D hypervascularity of uterine serosa–bladder wall interface reported by Cali *et al.*[19] may also be attributed to the higher prevalence of placenta percreta (41%) in their study compared to ours (16%). Indeed there were no false-positive percreta cases in our study group.

On the basis of the results obtained using the two-criteria system, the use of 3D, a time-consuming and expensive procedure, does not always seem to be indicated.

The sensitivity of the examination is very important, as a correct early diagnosis of PAD before Cesarean delivery may well reduce maternal and fetal morbidity if delivery is carried out in tertiary hospitals[2,20–22,26,27]. In addition, specificity and PPV should not be underestimated as patients with a diagnosis of placenta accreta may require invasive procedures, such as artery embolization or ureteral stents[28–30] or even a preventive hysterectomy[22,26]. Indeed, the fact that both specificity and PPV should be taken into consideration prompted us to base the antenatal diagnosis of PAD on at least two criteria; if we had used at least one criterion we would have seen 38 false positives instead of three (Table 2), risking overtreatment.

The use of a two-criteria system allowed for a good compromise between sensitivity and specificity, with high PPV and NPV. However, as our detection rate in cases of posterior placenta was only 50%, caution should be exercised when interpreting sensitivity in the absence of anterior placenta.

The impact of an antenatal diagnosis was assessed by comparing the outcomes in true-positive cases and false-negative ones (Table 4) and our conclusions were in agreement with those of Tikkanen *et al.*[20], who demonstrated that antenatal diagnosis of placenta accreta is associated with a reduction in blood loss. There was a statistically significant difference between deliveries of prenatally diagnosed placenta accreta compared to false-negative

cases, with less peripartum blood loss (1300 *vs* 3000 mL) and shorter hospitalization in the ICU (2 *vs* 4 days).

These favorable results for maternal morbidity may be attributed to the fact that a preventive hysterectomy was performed in 6/13 (46%) antenatally diagnosed cases, in which the fetus was delivered by incision on the fundus, without any attempt being made to either remove the placenta or pass through it, as reported by the most recent guidelines[22,26]. In all these cases, pathological examination confirmed the presence of placenta accreta, increta and percreta, confirming ultrasound findings.

A total of 46% of our study group had peripartum hysterectomy for PAD, in agreement with the rates reported in literature (30–55%)[7], and all cases were confirmed by a pathologist. There was a higher hysterectomy percentage in false-negative cases (57 *vs* 43%), even if the difference did not reach statistical significance.

Our data demonstrated that there is a net improvement in maternal outcome with an antenatal diagnosis of PAD. Although ultrasound sensitivity is high, in particular in the presence of anterior placenta, there is still room for improvement to avoid the serious complications of this pathology.

There are also some authors who do not agree with our conclusions: a recent study[32] with clinically blinded evaluation reported lower accuracy of ultrasound in the diagnosis of PAD and significant interobserver variability. A paradox bias due to the knowledge of the ultrasound findings by the surgeons could have affected our results, underestimating both the false-positive and the false-negative rates for placenta accreta. However, it is unlikely that it could affect the estimated accuracy for placenta percreta.

In conclusion, we have shown that grayscale and color Doppler ultrasound have good performance in the diagnosis of PAD and that prenatal diagnosis improves maternal outcome. Multicenter studies in referral centers using specific and homogeneous procedures for the management of PAD should be carried out on larger study groups to confirm the data obtained in our study.

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