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Evaluation of the relationship between quantitative ultrasound findings and morbidly adherent placenta

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Abstract

Aim: The accuracy of ultrasound findings in predicting the incidence of morbidly adherent placenta has been evaluated previously. In this study, we assessed the sensitivity and specificity of different quantitative findings of color Doppler and grayscale ultrasonography in predicting morbidly adherent placenta. **Material and methods:** In this prospective cohort study, all pregnant women over 20 weeks of gestational age with anterior placenta and a history of previous cesarean section were evaluated for inclusion. Various ultrasound findings were measured. The non-parametric receiver operating characteristic curves, the area under the curve, and the cut-off values were assessed. **Results:** A total of 120 patients were ultimately included for analysis, of whom 15 had morbidly adherent placenta. The two groups were significantly different regarding the number of vessels. Based on color Doppler ultrasonography, in predicting the morbidly adherent placenta, more than two intraplecental echolucent zones with color flow had 93% and 98% sensitivity and specificity, respectively. According to grayscale ultrasonography, more than thirteen intraplacental echolucent zones had the sensitivity and specificity of 86% and 80% in predicting morbidly adherent placenta, respectively. Echolucent zone >11 mm at non-fetal surface had a sensitivity of 93% and a specificity of 66% in detecting morbidly adherent placenta. **Conclusions:** According to the results, the quantitative findings of color Doppler ultrasound have considerable sensitivity and specificity in detecting morbidly adherent placenta. More than two echolucent zones with color flow are recommended as the main diagnostic parameter indicating the presence of morbidly adherent placenta with a sensitivity of 93% and a specificity of 98%.

Introduction

Morbidly adherent placenta (MAP) is characterized by abnormal placental implantation and invasion of chorionic villi into the uterine myometrium leading to incomplete separation or non-separation of placenta from the uterine wall during labor. It is one of the most serious pregnancy complications that may lead to post-partum hemorrhage, uterine perforation, and infection[1].

MAP remains undiagnosed before delivery in one-half to two-thirds of all cases. The prenatal diagnosis of MAP is vital to prevent the associated maternal and neonatal morbidity and mortality, and to perform appropriate risk assessment and adequately plan for delivery[2]. The incidence of MAP is rapidly increasing along with the upward trend in cesarean delivery, which is proposed as a major risk factor for MAP in subsequent deliveries[3,4].

The first-line imaging modality for screening and diagnosing MAP is ultrasound evaluation, which is used routinely because of its low cost and wide availability; however, its diagnostic criteria and accuracy are still under investigation[5,6]. Magnetic resonance imaging (MRI) has also shown high sensitivity and specificity in predicting

MAP and can be used as an additional effective modality for cases with inconclusive ultrasound findings[6].

According to a meta-analysis, ultrasound criteria, including the loss of subendometrial echolucent zone or the presence of abnormal placental lacunae, were highly sensitive and specific when performed by skilled operators[7]. The predictive value of ultrasound criteria has been assessed in several studies[5,6,8]; however, there is not enough evidence for the sensitivity and specificity of quantitative ultrasound findings in detecting MAP.

Placental lacunae are defined as vascular structures with different sizes and shapes in placental parenchyma, and have been proposed as one of the primary indicators of MAP on ultrasonography[8]. Although the presence of vascular lakes is not significantly related with MAP, these structures are detected as intrauterine echolucent areas similar to lacunae. Color Doppler turbulent flow of the lacunae has also shown diagnostic value but there is no clear quantitative definition in this regard[9,10].

Despite advances in imaging modalities, there is no single diagnostic technique with 100% accuracy for predicting MAP because of variability across the studies. In this study, we quantitatively defined ultrasound findings and evaluated their accuracy in predicting MAP.

Materials and methods

In this prospective cohort study, all the consecutive patients with anterior placenta and a history of at least one previous cesarean section who were referred to the Ghaem hospital, Mashhad, Iran, for routine prenatal screening by ultrasound between 2020 and 2021 were evaluated. All the enrolled patients signed written informed consent forms. The exclusion criteria were patients who did not observe their follow-up appointment sessions and those who gave birth in other hospitals. The study was approved by Ethics Committee of Mashhad University of Medical Sciences (approval number 971407).

Ultrasound evaluations were performed using a Medison V20 unit and a 5 MHz probe to assess the presence and extent of echolucent zones within the placenta. To examine the diagnostic value of the echolucent area, the number and maximum size of echolucent zones at different sites of the placenta were measured and recorded in each case using grayscale and color Doppler ultrasound. The echolucent zone was defined as any echolucent area >5×5 mm, including the venous lake or lacuna. The vessels were defined as blood vessels traversing more than 50% of the placental thickness. The number of detected echolucent zones was measured at various placental sites including the intraplacental (enclosed in the placenta), non-fetal surface (between uterus and placenta), fetal surface, fetal to non-fetal extended, and total (sum of all the detected echolucent zones in any part of the placenta) in each patient.

We also examined all the patients by color Doppler ultrasound. To adjust the color box (region of interest), the color gain was set at the highest level without any aliasing artifact, and the pulse repetition frequency (PRF) was also set at 11–14 cm/s. After adjusting the color box and color gain, the number of echolucent zones with blood flow, vessels, and vascularity of the posterior placenta was measured (Fig. 1).

All the patients were referred to a gynecologist and delivered at the Ghaem hospital. The presence or absence of adhesions during delivery was recorded by a surgeon. In cases with cesarean section or hysterectomy, data regarding the type of adhesion (accreta, increta or percreta) were recorded according to pathology. Ghaem Hospital Information System (HIS) was used to retrieve relevant information on patients' maternity.

The independent t-test was used to compare the quantitative variables with normal distribution, and the Mann-Whitney test was employed to compare the non-normally distributed quantitative variables. The chi-square or Fisher's test was used to compare the qualitative variables. A p value <0.05 was considered significant. Then, the appropriate cut-off point for the variables was determined using SPSS 26 software and ROC curve diagram. The sensitivity and specificity of the primary ultrasonography parameters were also obtained. The census method was used for sample size, and data were analyzed using SPSS 26 software. The non-parametric receiver operating characteristic (ROC) curves and the area under the curve (AUC) were evaluated using the method proposed by Delong *et al.*[11] to assess the diagnostic accuracy of the measured ultrasound parameters.

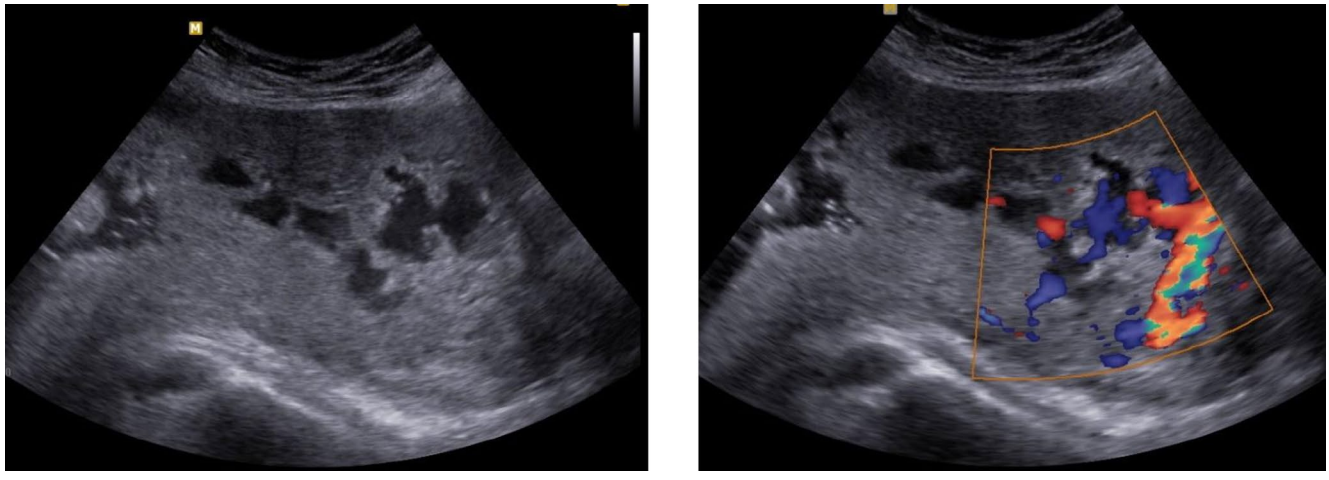

Fig. 1. *Echolucent areas with color flow*

Results

A total of 120 pregnant women gave birth at the Ghaem hospital during the study period. MAP was detected in 15 out of 120 cases. Patients had a mean age of 33.47 ± 4.7 years (range: 23–43). The median of the numbers of previous cesarean sections and abortions were 2 and 0, respectively.

Based on the pathology report, cases with MAP included four subjects with placenta accreta (26.6%), seven subjects with placenta increta (46.6%), and four subjects with placenta percreta (26.6%). Twelve cases with MAP had a cesarean section with hysterectomy (80%), and three patients had cesarean section without hysterectomy (20%). The placenta was attached to the uterus in 11 cases (73.3%), and to the bladder in four cases (26.6%).

There was a significant difference between two groups (i.e. cases with MAP compared to cases without MAP) regarding the number of vessels in the placenta, size and number of echolucent zones with/without color flow at various sites, including the fetal surface (p value = 0.002), non-fetal surface (p value <0.001), fetal to non-fetal extended surface (p value = 0.004), and enclosed in placenta surfaces (p value <0.001). The difference in total numbers of echolucent zones was also significant (p value <0.001). Subjects with MAP had an average of 5.53 ± 1.68 intraplacental vessels traversing more than 50% of placental thickness, compared to normal subjects with an average of 2.39 ± 2 (p value <0.001) (Tab. 1).

The diagnostic accuracy of the number of echolucent zones at the intraplacental, fetal, non-fetal, fetal to non-fetal extended surfaces and sum of all the detected echolucent zones in any part of the placenta in predicting MAP was measured using ROC curve analysis. The total number of echolucent zones had the largest ROC AUC (AUC = 0.85).

ROC curve diagram and AUC related to the diagnostic accuracy of the largest size of echolucent zones at different sites in predicting MAP was also measured. The size of the largest echolucent zone at non-fetal site had the highest AUC (AUC = 0.80).

The ROC curve regarding the accuracy of the number of echolucent zones with color flow at different evaluated sites was measured as well. The number of echolucent zones with color flow at the fetal and non-fetal surfaces had an AUC >0.80. However, the total number of echolucent zones with flow (sum of the number of echolucent zones at all the evaluated surfaces) had an AUC = 0.99.

Table 2 summarizes the cut-off values of the ultrasound criteria with the highest AUC as well as estimated sensitivity and specificity. Figure 2 shows the ROC curve of ultrasound criteria with the highest diagnostic accuracy for predicting MAP. The total number of echolucent zones with color flow had the highest AUC.

Discussion

Early antenatal detection of MAP is vital for guiding maternal counseling, managing the delivery plans, and reducing the associated risk of maternal and fetal morbidity and mortality. In this study, the predictive accuracy of ultrasonographic criteria in detecting MAP was evaluated. In some previous studies, vascular lacunae, loss of the normal hypoechoic retroplacental zone, abnormal vessels at the bladder-myometrium interface, and bladder invasion were the examined ultrasonographic criteria for predicting the incidence of

Tab. 1. Comparison of the two study groups regarding the number of vessels in the placenta, size and number of echolucent zones with/without color flow at different sites

Variables	Patients with morbidly adherent placenta (mean ± SD)	Patients without morbidly adherent placenta (mean ± SD)	*P* value
Size of the largest echolucent areas at the fetal surface (mm)	21.3 ± 8.1	15.42 ± 11.68	0.001
Size of the largest echolucent areas at the non-fetal surface (mm)	19.4 ± 7.04	9.21 ± 10.64	<0.001
Size of the largest echolucent areas extended to both surfaces (mm)	21 ± 15.3	7.77 ± 14.41	<0.001
Size of the largest echolucent areas enclosed in placenta (mm)	16.93 ± 7.34	11.63 ± 7.60	0.01
Size of the largest echolucent area at any site (mm)	29.4 ± 8.4	21.66 ± 12.83	0.004
Number of echolucent areas at the fetal surface	4.86 ± 2.89	2.49 ± 2.08	<0.001
Number of echolucent areas at the non-fetal surface	3.53 ± 3.39	1.11 ± 1.29	<0.001
Number of echolucent areas extended to both surfaces	1.0 ± 0.84	0.40 ± 0.87	0.001
Number of echolucent areas enclosed in placenta	9.06 ± 2.40	5.10 ± 4.26	<0.001
Total number of intraplacental echolucent areas*	18.40 ± 6.78	9.12 ± 6.45	<0.001
Number of echolucent areas with flow at the fetal level	1.86 ± 1.55	0.06 ± 0.28	<0.001
Number of echolucent areas with flow at the non-fetal level	1.4 ± 1.24	0.08 ± 0.39	0.01
Number of echolucent areas with flow extended to both surfaces	0.73 ± 0.70	0.04 ± 0.25	<0.001
Number of echolucent areas with flow enclosed in placenta	4.33 ± 5.12	0.06 ± 0.31	<0.001
Total number of intraplacental echolucent areas with flow*	7 ± 3.6	0.24 ± 0.76	<0.001
Number of vessels in placenta	5.53 ± 1.68	2.39 ± 2	<0.001
* Sum of all the detected echolucent zones in any part of the uterine			

Tab. 2. Sensitivity and specificity of echolucent areas in predicting morbidly adherent placenta

Variables	Amount	Sensitivity	Specificity
Total number of intraplacental echolucent areas with flow	>2	0.93	0.98
Total number of intraplacental echolucent areas	>13	0.86	0.80
Size of the largest echolucent area in non-fetal part	>11	0.93	0.66

MAP[8,12]. However, in the present study, we evaluated these ultrasound criteria quantitatively. The diagnostic criteria included the number and size of echolucent areas at different locations as well as the number of detected vessels. The predictive value of these diagnostic criteria was assessed quantitatively, and the cut-off value was also measured for these factors.

Results of the current study showed that more than two echolucent zones with flow (by color Doppler ultrasound) in the placenta had the highest sensitivity and specificity (93% and 98%, respectively) in diagnosing MAP. Similarly, more than 13 echolucent zones in the placenta has gained the highest sensitivity and specificity in predicting MAP based on grayscale ultrasound (86% and 80%, respectively). Gao *et al.* designed a scoring system based on patients' characteristics and ultrasonography for predicting placenta accreta spectrum. In this study, subplacental hypervascularity, number of abnormal lacunae ≥3, extreme subplacental hypervascularity, and lacuna maximum dimension ≥2 cm received 1, 2, 3, and 5 points, respectively[13]. Our results indicated that the number of echolucent areas with/without flow was the main predictive ultrasound criterion of MAP; however, the site of echolucent areas in the placenta did not have a significant diagnostic value. Moreover, the number of vessels traversing more than 50% of the thickness of placenta was significantly higher in patients with MAP, compared to normal subjects.

The relationship between echolucent areas and the incidence of MAP was assessed quantitatively in a similar study that showed all the patients with placenta percreta to have more than six lacunae with turbulent flow[9]. Some other research groups also reported a strong association between the number of intraplacental echolucent areas and the incidence of MAP. The frequency of diffuse lacunar flow pattern was reported to be linked to the prediction of adherent placenta. Based on these studies, the presence of numerous intraparenchymal lacunar vascular spaces within the placenta is a separate risk criterion for placenta accreta and these findings are consistent with our results[14–19].

Our results were also consistent with the study by Tovbin *et al.* who also used a scoring system and proposed Doppler flow as a highly efficient predictor of MAP. They also recommended the combination of the number of placental lacunae and obliteration of hypoechoic uteroplacental demarcation as the most effective ultrasound criterion directly correlated with MAP[20]. In a meta-analysis, the accuracy of color Doppler in diagnosing invasive placentation was evaluated[21]. In this study, color Doppler abnormalities were reported to have the best predictive accuracy among different ultrasound signs, which was in line with our results. In another meta-analysis, ultrasound evaluation revealed a considerable diagnostic accuracy in

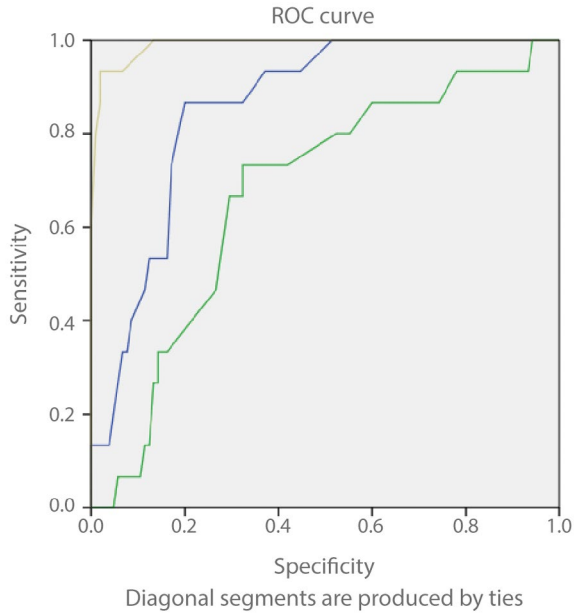

Fig. 2. *Diagnostic accuracy of the total number of echolucent zones (blue), total number of echolucent zones with color flow (yellow), and the largest size of echolucent zones (green) in predicting morbidly adherent placenta using ROC curve analysis*

predicting abnormally invasive placentation but its diagnostic value in determining the severity of invasion needs to be further studied. According to the five related studies pooled in this meta-analysis, the presence of lacunar flow was significantly associated with the occurrence of placenta accreta, increta, and percreta, and had high sensitivity and specificity for identifying placenta accreta and increta[17].

Based on the findings, the size of the largest echolucent zone at non-fetal surface was a significant predictor of MAP. At the non-fetal surface, the size of the largest echolucent zone >11 mm had 93% sensitivity in predicting the incidence of MAP with 66% specificity, which was considerably low compared to the number of echolucent zones.

In the study by Calì *et al.*, identifying extensive hypervascular appearance (a group of discretely distributed vessels) at uterine serosa-bladder interface using 3D power Doppler was also reported in the cases of MAP[9]. The number of coherent vessels visualized on 3D power Doppler was proposed as the main diagnostic criterion of placenta accreta with high sensitivity and specificity. This was similar to our result regarding the significant difference in intraplacental vascularity between groups with and without MAP[9,22]. The diagnostic accuracy and predictive value of subplacental and uterovesical hypervascularity have also been reviewed in some other previous studies[13,23].

Previous investigations have evaluated the diagnostic value of grayscale ultrasound in predicting MAP. The presence of placental lacunae has been suggested as one of the most significant criterion in grayscale ultrasound for predicting MAP; however, the highest reported sensitivity was 82.72%[22,24,25]. In our study, more than 13 echolucent areas at the intrauterine level based on grayscale ultrasound were representative of MAP with the sensitivity and specificity of 86% and 80%, respectively.

The use of accurate and reproducible definitions for echolucent areas in the placenta with/without flow is one of the strengths of this study. Another strength is that we evaluated the accuracy of the size of echolucent zones and their number as well as their color flow at different sites of placenta in predicting MAP. However, our research also had certain limitations. The number of patients with confirmed MAP was low, so further studies with larger sample sizes and longer periods of study time are recommended.

Conclusion

According to the results obtained in the study, quantitative ultrasonographic criteria, including the number of echolucent zones with/without flow and the size of the largest echolucent zone, showed significant sensitivity and specificity in diagnosing MAP.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Author contributions

Original concept of study: FSA, FT, AMA, NS, FST, FK, ME, SM, BA. Writing of manuscript: FSA, AMA. Analysis and interpretation of data: ME. Final approval of manuscript: FSA, FT, AMA, NS, FST, FK, ME, SM, BA. Collection, recording and/or compilation of data: FK, SM, BA. Critical review of manuscript: FT, NS, FST, BA.

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