Sonographic Findings of Morbidly Adherent Placenta in the First Trimester

Martha W. F. Rac, MD, Elysia Moschos, MD, C. Edward Wells, MD, Donald D. McIntire, PhD, Jodi S. Dashe, MD, Diane M. Twickler, MD

Objectives—The purpose of this study was to evaluate the association between first-trimester sonographic findings and morbidly adherent placenta at delivery.

Methods—We conducted a retrospective review of all first-trimester sonographic examinations from pregnancies that underwent third-trimester sonography for placenta previa or low-lying placenta between September 1997 and October 2011. Only women with a prior cesarean delivery were included. Transabdominal and transvaginal images from these first-trimester studies were reviewed for the following sonographic parameters: distance from the inferior border of the gestational sac to the external cervical os, location of the decidua basalis, presence of anechoic areas, uterine-bladder interface irregularity, and smallest anterior myometrial thickness. Morbidly adherent placentation was confirmed on histologic examination of hysterectomy specimens. Statistical methods included univariate and multivariate analyses.

Results—Thirty-nine patients met inclusion criteria, of whom 14 (36%) had confirmed placental invasion. The number of prior cesarean deliveries was significantly associated with placental invasion ($P < .0001$). The only first-trimester sonographic finding associated with invasion was the smallest anterior myometrial thickness measured in the sagittal plane ($P < .02$). Multivariate analysis based on these two variables yielded an area under the receiver operating characteristic curve of 0.94 (95% confidence interval, 0.87–1.00) and significantly improved the prediction of placental invasion compared to using the number of prior cesarean deliveries alone.

Conclusions—In women with persistent placenta previa or low-lying placenta and prior cesarean delivery, the smallest anterior myometrial thickness on first-trimester sonography significantly improved detection of morbidly adherent placenta.

Key Words—first trimester; morbidly adherent placenta; obstetric ultrasound; sonography

S ince its initial description in the 1880s,[1] abnormally or morbidly adherent placenta (accreta, increta, or percreta) has garnered increasing recognition. A direct result of the rising cesarean delivery rate, morbidly adherent placenta now occurs as frequently as 1 per every 533 deliveries.[2,3]

Given its substantial morbidity and mortality, there has been a surge of interest in the early prediction of morbidly adherent placenta by sonography in the first trimester. After a series of case reports published on torrential hemorrhage during early pregnancy evacuations proven to be placental invasion on histologic examination,[4–7]

in 2002, Chen et al[8] was the first to describe the sonographic findings of placenta accreta in the first trimester. Since then, others have continued to describe the natural history and improve on the early sonographic diagnosis of morbidly adherent placenta. Sonographic findings that have been described during the first trimester include implantation of the gestational sac into the lower uterine segment near or within the prior cesarean scar, presence of anechoic areas within the developing placental mass, thinning of the retroplacental myometrial zone, and an irregular placental-myometrial interface.[8–13] Most recently, emphasis has been placed on the sonographic and histologic similarities between cesarean scar pregnancies and morbidly adherent placentation.[11,14–16] As more evidence is being published on the first-trimester sonographic appearance of pregnancies found to have placental invasion at delivery, it is becoming clear that cesarean scar pregnancy and placenta accreta share a common pathogenesis.

We previously reviewed first-trimester sonographic examinations from patients with prior cesarean deliveries and cervicoisthmic implantations and found that the smallest myometrial thickness measured from the anterior trophoblastic border of the gestational sac to the uterine serosa was significantly smaller in abnormally adherent trophoblastic implantations, which included both cesarean scar pregnancies and those with placental invasion at delivery.[16] Interestingly, most of these pregnancies ended before fetal viability. As such, the aim of this study was to evaluate the association between first-trimester sonographic findings and morbidly adherent placenta at delivery.

Materials and Methods

We conducted a retrospective review of our obstetric ultrasound database for patients with a history of prior cesarean delivery who had placenta previa or low-lying placenta diagnosed on third-trimester sonography between September 1997 and October 2011. The study was approved by the Institutional Review Board at the University of Texas Southwestern Medical Center. Informed consent was waived given the retrospective nature of the study.

The diagnosis of placenta previa was based on the presence of placental tissue covering the internal cervical os. Low-lying placenta was diagnosed when the placenta was within 2 cm from the internal cervical os but did not cover it. From this group, only those women with a first-trimester sonographic examination during the same pregnancy and who delivered at our institution were included in the study. As routine first-trimester imaging was not standardly per-

formed at our institution during the study period, all sonographic examinations were performed for clinical indications. Images were obtained by certified registered diagnostic medical sonographers, and digitally stored first-trimester transvaginal images were reviewed by a single investigator (M.W.F.R.), who was blinded to both pregnancy outcomes and sonographic reports. If transvaginal imaging was not performed, transabdominal images were reviewed. Sonographic parameters assessed included distance from the inferior border of the gestational sac to the external cervical os, location of the decidua basalis, presence of anechoic areas, uterine-bladder interface irregularity, and smallest myometrial thickness, defined as the smallest distance from the anterior trophoblastic border of the gestational sac to the uterine serosa (Figure 1). Color Doppler parameters were not assessed because color Doppler sonography was not a standard part of first-trimester imaging during the study period.

Clinical records of patients identified by the ultrasound query as described above were then reviewed. Maternal demographics, gestational ages at first-trimester sonography, and delivery outcomes were collected. Pathologic reports were also reviewed. Placental invasion was established if placenta accreta, increta, or percreta was diagnosed after a standardized histologic examination of the cesarean or hysterectomy specimen by our pathology department. Patients were then divided into those with and without histologically confirmed placental invasion for comparison.

Figure 1. Schematic illustration of a sagittal transvaginal image of the biometric measurements for a first-trimester cervicoisthmic trophoblastic implantation.[16] Measurements correspond to the following labels: A, smallest distance from the anterior trophoblastic border to the uterine serosa; the measurement is taken from between, but not including, the two echogenic lines of the uterine serosal interface and the anterior decidual reaction of the gestational sac; and B, distance from the external cervical os to the inferior trophoblastic border of the gestational sac.
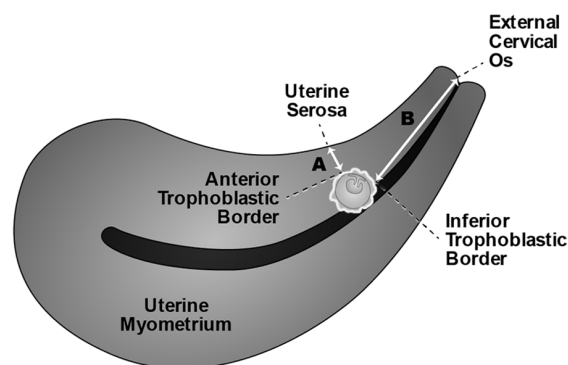
Our aim was to identify first-trimester sonographic parameters associated with histologically confirmed placental invasion at delivery. Independent variables considered for a predictive model were the demographic, clinical, and sonographic parameters described above. Considering these predictors, a final logistic regression model was selected to include only those variables whose multivariate combination was most predictive for the outcome variables. Model fit was assessed by using the area under the receiver operating characteristic curve. Group characteristics and demographics were compared by the Student t test for continuous variables or χ^2 test for categorical variables, where appropriate. Mantel-Haenszel and Jonckheere-Terpstra tests were used for trends. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated for each myometrial thickness, with 95% confidence intervals, by using standard methods for rates and proportions. All P values in the analysis presented were 2 sided and considered significant at $P < .05$. The data were analyzed with the SAS version 9.2 statistical package (SAS Inc, Cary, NC).

Results

There were 184 patients identified with a history of prior cesarean delivery and placenta previa or low-lying placenta diagnosed on third-trimester sonography during the 14-year study period. Of these, 39 (21%) had a first-trimester sonographic examination during the same pregnancy available for review. Characteristics of the entire cohort included an mean maternal age ± SD of 31 ± 5 years, with median gravidity of 4 (range, 2–8), median parity of 2 (range, 1–6), and a median number of 2 prior cesarean deliveries (range, 1–4). Thirty-six patients (92%) in our cohort were Hispanic, which is reflective of our general obstetric population. The mean gestational age at first-trimester sonography was 9.25 weeks (range, 5.5–13.6 weeks), and the most common indication for sonography was vaginal bleeding (51%). Patient characteristics were then analyzed by the presence or absence of placental invasion at delivery (Table 1). No difference was noted in maternal age, race, gestational age at first-trimester sonography, or indication for sonography. More women with proven invasion at delivery received a transvaginal sonographic examination in the first trimester (11 [79%]) versus 10 [40%]; $P = .02$). The number of prior cesarean deliveries was strongly associated with morbidly adherent placenta at delivery (2.36 versus 1.32; $P < .0001$).

Delivery outcomes are shown in Table 2. Twenty-two women had uncomplicated cesarean deliveries, and 17

underwent a cesarean hysterectomy for gross evidence of placental invasion at delivery. On histologic examination of the hysterectomy specimens, 14 (82%) had confirmed placental invasion. Of those with invasion, 12 (86%) had

Table 1. Characteristics of Patients With and Without Placental Invasion at Delivery

Characteristic	No Invasion (n = 25 [64%])	Invasion (n = 14 [36%])	P
Age, y	30.9 ± 4.8	31.4 ± 5.6	.77
Race			.40
Black	2 (8)	0	
White	1 (4)	0	
Hispanic	22 (88)	14 (100)	
Other	0	0	
Gravidity	3.8 (1.4)	4.3 (1.6)	.32
Parity	2.2 (1.3)	2.7 (1.1)	0.23
Cesareans	1.32 ± 0.48	2.36 ± 0.74	<.0001
1	17 (68)	1 (7)	<.0002
2	8 (32)	8 (57)	
≥3	0	5 (36)	
Prior dilation and curettage	5 (20)	2 (14)	.66
Gestational age at 1st-trimester sonography, wk	9.8 ± 2.7	8.3 ± 2.2	.10
Transvaginal sonography	10 (40)	11 (79)	.02
Indication for 1st-trimester sonography			.65
Bleeding	11 (44)	9 (64)	
Pain	4 (16)	1 (7)	
Gestational age assessment	7 (28)	3 (21)	
Other	3 (12)	1 (7)	
Gestational age at 3rd-trimester sonography, wk	36.7 ± 2.3	35.5 ± 2.3	.13

Data are presented as mean ± SD and number (percent).

Table 2. Delivery Outcomes

Outcome	No Invasion (n = 25 [64%])	Invasion (n = 14 [36%])	P
Gestational age at delivery, wk	36.7 ± 2.3	35.5 ± 2.3	.17
Indication for delivery[a]			.29
Scheduled delivery	11 (44)	7 (50)	
Labor	6 (24)	4 (29)	
Bleeding	9 (36)	3 (21)	
Other	3 (12)	2 (14)	
Estimated blood loss, mL	1500 (1000, 2000)	2750 (2000, 4625)	<.01
Anterior placentation	13 (52)	13 (93)	.01
Degree of Invasion	NA		
Accreta		12 (86)	
Increta		1 (7)	
Percreta		1 (7)	

Data are presented as mean ± SD, number (percent), and median (first quartile, third quartile). NA indicates not applicable.
[a]More than 1 indication was present in some cases.

placenta accreta; 1 (7%) had placenta increta; and 1 (7%) had placenta percreta. Thus, overall, 25 patients (64%) had normal placentation at delivery, and 14 (36%) had abnormally adherent placentation at delivery. No significant difference in gestational age at delivery or delivery indication was noted between those with and without placental invasion. Anterior placentation was more common in women with morbidly adherent placenta at delivery (13 [93%] versus 13 [52%]; $P < .01$). Estimated blood loss was greater in those patients with histologically confirmed invasion (2750 versus 1500 mL; $P < .01$).

Sonographic biometric measurements are shown in Table 3. Given the retrospective study design, ascertainment of certain biometrics was limited by available images, dropout signals, early gestational age, lack of bladder fullness, and suboptimal tissue penetration either from early ultrasound technology or transabdominal imaging. Uterine-bladder interface irregularity was able to be assessed in 32 women (82%), and the smallest anterior myometrial thickness was assessed in 37 (95%) and 28 (72%) in sagittal and transverse planes, respectively. When comparing pregnancy outcomes, the smallest anterior myometrial thickness measured in the sagittal plane (as shown in Figure 1) was significantly smaller in pregnancies with morbidly adherent placenta at delivery (4.1 versus 7.4 mm; $P = .01$; Figures 2 and 3). As the smallest myometrial thickness decreased, the incidence of morbidly adherent placentation at delivery increased ($P = .02$). Other biometric parameters evaluated, including distance from the inferior border of the gestational sac to the external cervical os, were not significantly different between abnormally and normally implanted pregnancies.

The sensitivity, specificity, positive predictive value, and negative predictive value at each myometrial thickness presented as integer values are shown in Table 4. The highest threshold myometrial thickness value of 8 mm yielded sensitivity of 85%. As myometrial thickness decreased, sensitivity also decreased but with improving specificity. Multiparametric analysis and logistic regression were performed using the smallest anterior myometrial thickness measured in the sagittal plane and number of prior cesarean deliveries. Figure 4 displays the differing areas under the receiver operating characteristic curve using only the number of prior cesarean deliveries and a combination of prior cesarean deliveries and the smallest myometrial thickness. When compared to the number of

Figure 2. First-trimester sonogram measuring the smallest anterior myometrial thickness in the sagittal plane with placental invasion at delivery. The pregnancy depicted had histologic evidence of morbidly adherent placenta at delivery.

Figure 3. First-trimester sonogram measuring the smallest anterior myometrial thickness in the sagittal plane without placental invasion at delivery.

Table 3. First-Trimester Sonographic Characteristics of Patients With and Without Morbidly Adherent Placenta at Delivery

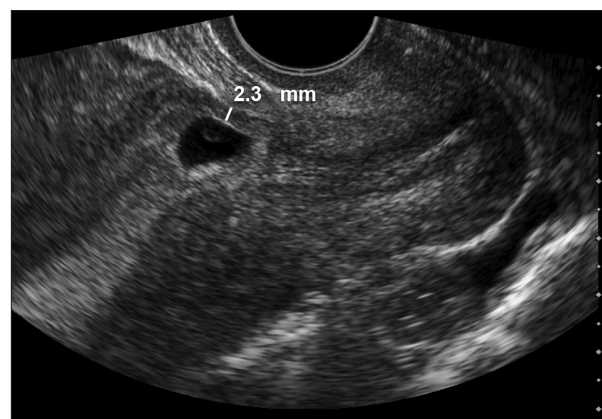| Characteristic	No Invasion (n = 25 [64%])	Invasion (n = 14 [36%])	P
Distance of gestational sac from external cervical os, mm	4.3 ± 1.0	3.8 ± 0.8	.12
Anterior decidua basalis	14 (56)	12 (86)	.06
Anechoic areas	8 (32)	4 (29)	.82
Irregular uterine-bladder interface	0	2 (17)	.05
Smallest sagittal myometrial thickness, mm[a]	7.4 (5.5, 16.3)	4.1 (2.5, 6.0)	.01
Smallest transverse myometrial thickness, mm	8.0 (5.2, 10.0)	4.5 (3.2, 7.8)	.05
Crown-rump length, cm	3.9 ± 2.7	2.2 ± 2.0	.05

Data are presented as mean ± SD, number (percent), and median (first quartile, third quartile).
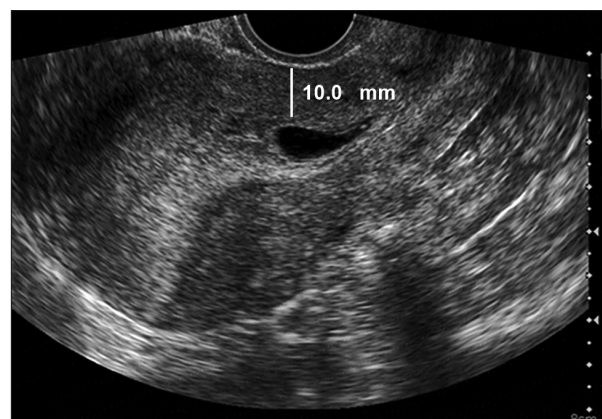[a]Thirty-seven patients had the smallest myometrial thickness measured in the sagittal plane (24 without invasion and 13 with invasion).

prior cesarean deliveries alone, the addition of the smallest anterior myometrial thickness in the sagittal plane significantly improved the prediction of placental invasion at delivery ($P = .04$).

Discussion

Our results provide data regarding sonographic findings during the first trimester of pregnancies with histologically proven placental invasion in the third trimester. In addition, the use of a comparison group with nonadherent placenta previa or low-lying placenta allowed us to distinguish between sonographic findings that are true harbingers of morbidly adherent placenta versus those that might simply be early but nonpathologic findings of pregnancies implanted into the lower uterine segment. Of the various parameters previously described during the first trimester, we found that only the biometric measurement of the smallest anterior myometrial thickness measured in the sagittal plane was predictive of morbidly adherent placenta at delivery. As the myometrial thickness decreased, the risk of invasion increased. Although no smallest myometrial thickness was 100% predictive of placental invasion in our cohort, measuring the smallest anterior myometrial thickness during first trimester sonography in women with prior cesarean deliveries significantly improved detection. The application of our findings to clinical practice would mean being able to provide our patients a risk gradation based on their myometrial thickness, allowing more informed decisions regarding pregnancy continuation.

Thinning of the anterior myometrium has previously been described as a sonographic finding in placental invasion.[17–19] Histologic evidence from cases of abnormally adherent placentation shows that the retroplacental myometrium is markedly thinned or absent.[20] Measuring the smallest myometrial thickness during first-trimester sonography in at-risk women correlates to what has been observed histologically. Quantification of the anterior myometrial thickness was first introduced by Twickler et al[17] in 2000, when they found that an anterior myometrium of less than 1 mm during third-trimester sonography detected all cases of placental invasion. Applying the same principle to first-trimester sonographic evaluations, in 2014, Moschos et al[16] found that an anterior myometrial thickness of less than 5 mm was equally predictive of abnormally adherent placentation. Although we did not achieve 100% sensitivity at similar values in our study, our data confirm an inverse relationship between anterior myometrial thickness and morbidly adherent placenta and lays the groundwork for a prospective study. The use of a con-

tinuous parameter, such as the smallest myometrial thickness, may be a more clinically relevant method of risk gradation compared to an absolute cutoff value for invasion versus no invasion.

Parameters found not to be significant in our study provide insight into the early sonographic appearance of pregnancies implanted in the lower third of the uterus. The anterior/posterior position of the decidua basalis during first-trimester sonography was not associated with morbidly adherent placenta at delivery. Thus, anterior myometrial thickness was predictive of placental invasion independent of early placental location. In contrast, anterior placentation at delivery was significantly associated

Table 4. Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value at the Smallest Anterior Myometrial Thicknesses Measured in the Sagittal Plane During First-Trimester Sonography

Threshold, mm	Sensitivity, %	Specificity, %	PPV, %	NPV, %
≤8	85 (55–98)	46 (26–67)	46 (26–67)	85 (55–98)
≤7	77 (46–95)	50 (29–71)	45 (24–68)	80 (52–96)
≤6	77 (46–95)	71 (49–87)	59 (33–82)	85 (62–97)
≤5	69 (39–91)	75 (53–90)	60 (32–84)	82 (60–95)
≤4	46 (19–75)	79 (58–93)	55 (23–83)	73 (52–88)
≤3	46 (19–75)	92 (73–99)	75 (35–97)	76 (56–90)

Values in parentheses are 95% confidence intervals. NPV indicates negative predictive value; and PPV, positive predictive value.

Figure 4. Receiver operating characteristic curve for prediction of placental invasion using the number of prior cesarean deliveries and a combination of the smallest anterior myometrial thickness and number of prior cesarean deliveries. The addition of the smallest myometrial thickness significantly improved the prediction of placental invasion ($P = .04$). AUC indicates area under the curve.
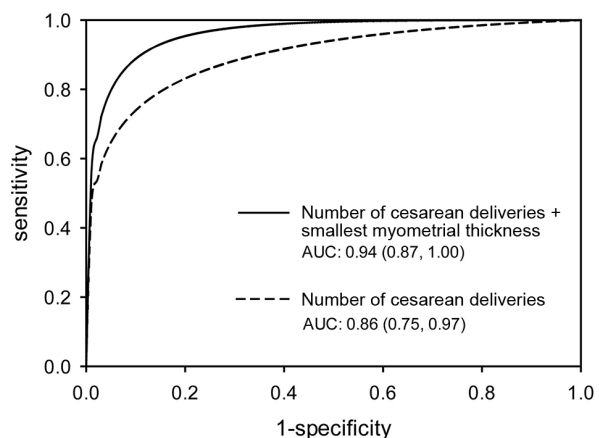
with morbidly adherent placenta, consistent with previously reported risk factors.[21–23] Several explanations may exist for this discrepancy. First, our cohort spanned 14 years, a time during which ultrasound technology was rapidly advancing. Second, not all patients underwent transvaginal imaging. In addition, we did not have information on body mass indices or patient comorbidities that could have theoretically affected image resolution. Although cohort characteristics and study methods could have influenced the sonographic identification of early trophoblast location, placental migration is another possible explanation for the discrepancy between placental location during the first and third trimesters, a phenomenon recognized as early as 1981.[24,25] Additionally, anechoic areas and the implantation level of the gestational sac were not found to be significant in our study, in contrast to previous studies.[8,12,16,26] Anechoic areas were infrequent sonographic findings, which were observed with similar frequencies in women with and without placental invasion at delivery and occurred in approximately one-third of patients in both groups. Moschos et al[16] quantified low implantation as less than 5 cm from the inferior trophoblastic border of the gestational sac to the external cervical os. Although our data support the definition of low implantation as less than 5 cm, we did not find it to be discriminating for morbidly adherent placenta. Since all women in our study had placenta previa or low-lying placenta at delivery, we hypothesize that implantation onto the lower segment of the uterus during the first trimester is more indicative of developing placenta previa or low-lying placenta rather than morbidly adherent placenta.

Because of its retrospective nature, limitations of our study should be noted. First, we were unable to control for image acquisition, including bladder fullness. An empty bladder could have influenced the exact location of the true bladder-serosal interface and measurement of the anterior myometrial thickness. Optimal first-trimester imaging of women at risk for morbidly adherent placenta includes a transvaginal approach with a full bladder and the use of color Doppler imaging. Second, Doppler sonography was not used, and vascularity was not assessed. Additionally, as all first-trimester studies were performed with the intention of locating the pregnancy and not for evaluation of morbidly adherent placenta, not all patients underwent transvaginal imaging, which may have affected acquisition of sonographic parameters. Last, our study did not evaluate all women with morbidly adherent placenta. It is possible that some women were referred to our institution beyond the first trimester. Furthermore, only women with a prior cesarean delivery and placenta previa

or low-lying placenta in the third trimester were included, and our results may not be applicable to a patient without these characteristics. Since we did not perform routine first-trimester sonography during the study period, patients who were not symptomatic during the first trimester were not captured.

Despite these limitations, we believe that our data make important contributions to the understanding of morbidly adherent placentation in terms of its early sonographic appearance and diagnosis. We have demonstrated that the smallest anterior myometrial thickness measured in the sagittal plane has the ability to identify those patients at highest risk for placental invasion, and when combined with the number of prior cesarean deliveries, the prediction of placental invasion is significantly improved. If confirmed in a prospective trial, the smallest anterior myometrial thickness measured in the sagittal plane during the first trimester may act as an early screening tool for patients with a low implantation in the setting of a prior cesarean delivery regarding the likelihood of placental invasion at delivery.

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