AVOIDING OBSTETRIC EMERGENCIES

Diagnosing placenta accreta spectrum with prenatal ultrasound

Up to half of all placenta accreta spectrum cases escape prenatal detection. Consensus is that ultrasonography (US) should be the primary imaging modality. In this expert guide on identification, the authors describe the use of diagnostic US markers at their institution and address standardization, sensitivity, and specificity.

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IN THIS ARTICLE

Placenta accreta spectrum (PAS) describes abnormal invasion of placental tissue into or through the myometrium, comprising 3 distinct conditions: *placenta accreta*, *placenta increta*, and *placenta percreta*. This complication is relatively new to obstetrics, first described in 1937.[1]

The overall incidence of PAS has been increasing over several decades, in parallel to an increasing rate of cesarean delivery (CD), with an incidence from 1982 through 2002 of 1 in 533 pregnancies, representing a 5-fold increase since the 1980s.[2] PAS is associated with significant morbidity and mortality, including fetal growth restriction, preterm delivery, placental abruption antenatally, and hemorrhage during delivery or postpartum.

Prenatal diagnosis of PAS and planned delivery at an experienced center are associated with significant reduction in maternal and fetal morbidity.[3] In an era of advanced imaging modalities, prenatal detection of PAS regrettably remains variable and largely subjective: As many as 20% to 50% of cases of PAS escape prenatal diagnosis.[3,4]

In this article, we review the sonographic markers of PAS, including diagnostic accuracy, and propose a standardized approach to prenatal diagnosis. Throughout our discussion, we describe protocols for detection of PAS practiced at our Maternal-Fetal Medicine Program in the Department of Obstetrics and Gynecology, Eastern Virginia Medical School (also see "US evaluation of PAS risk: The authors' recommended approach," page 42).

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Numerous risk factors

There are many risk factors for PAS, including prior uterine surgery or instrumentation, such as CD, uterine curettage, myomectomy, pelvic radiation, and endometrial ablation. Other risk factors include smoking, in vitro fertilization, advanced maternal age, multi-

parity, and a brief interval between prior CD and subsequent pregnancy.[5] Of major significance is the increased risk of PAS in the presence of placenta previa with prior CD.[6] Knowledge of clinical risk factors by the interpreting physician appears to be associated with improved detection of PAS on ultrasonography (US).[4]

Ultrasonographic markers of PAS

First-trimester markers

Sonographic markers of PAS in the first trimester include:

- a gestational sac implanted in the lower uterine segment or in a CD scar
- multiple hypoechoic spaces within the placenta (lacunae).[7]

Lower uterine-segment implantation has been defined by Ballas and colleagues as 1) a gestational sac implanted in the lower one-third of the uterus between 8 and 10 weeks' gestation or 2) a gestational sac occupying primarily the lower uterine segment from 10 weeks' gestation onward (**FIGURE 1**, page 36).[8] Our experience is that it is difficult to accurately assess lower uterine-segment implantation beyond 13 weeks of gestation because the sac typically expands to fill the upper uterine cavity.

Color Doppler US can help differentiate lower uterine-segment implantation from a gestational sac of a failed pregnancy in the process of expulsion by demonstrating loss of circumferential blood flow in the failed pregnancy. Furthermore, applying pressure to the anterior surface of the uterus will result in downward movement of the gestational sac of a failed pregnancy.[9]

Not all gestational sacs that implant in the lower uterine segment lead to PAS: Subsequent normal pregnancies have been reported in this circumstance. In such cases, a normal thick myometrium is noted anterior to the gestational sac.[7] A patient with lower uterine-segment implantation without evidence of anterior myometrial thinning remains at risk for third-trimester placenta previa.[7]

Cesarean scar pregnancy carries significant risk of PAS. In these cases, the gestational sac is typically implanted within the scar, resulting in a thin anterior myometrium and significantly increased vascularity of the placental–myometrial and bladder–uterine wall interfaces (**FIGURE 2,** page 36).[9] Differentiating cesarean scar pregnancy from a lower uterine-segment implantation is easier to perform before the eighth week of gestation but becomes more difficult as pregnancy advances. Although it might be useful to distinguish between true cesarean scar pregnancy and lower uterine-segment implantation adjacent to or involving the scar, both carry considerable risk of PAS and excessive hemorrhage, and the approach to treating both conditions is quite similar.

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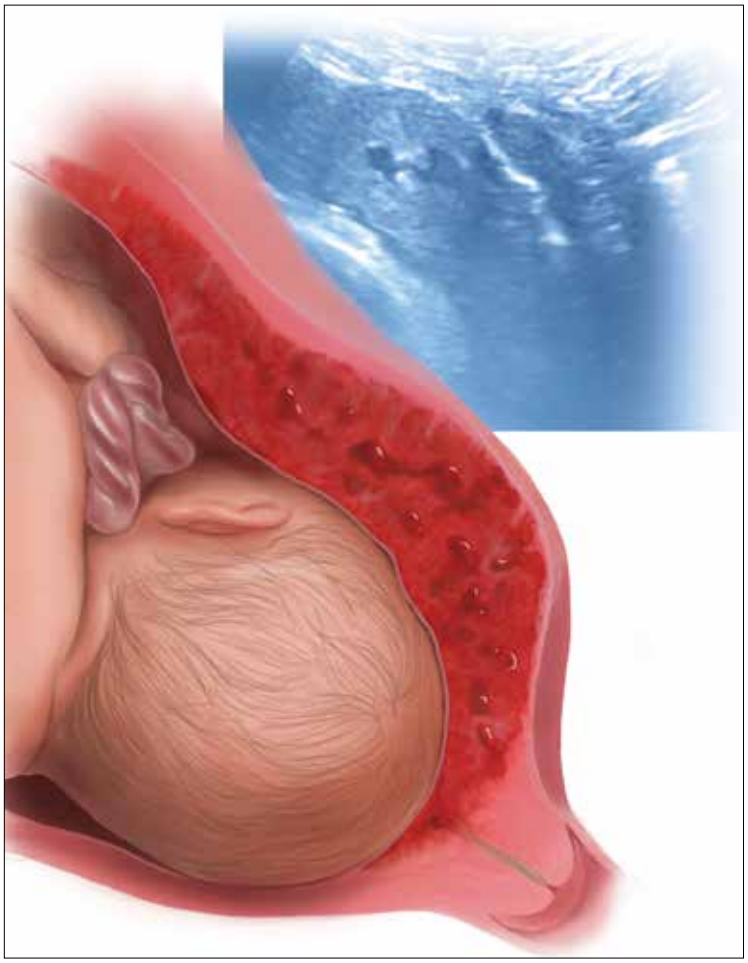

Anterior placental location, loss of "the clear space between the placenta and uterus," and the presence of multiple lacunae within the placenta are ultrasound markers of placenta accreta spectrum.

ILLUSTRATION: KIMBERLY MARTENS FOR OBG MANAGEMENT

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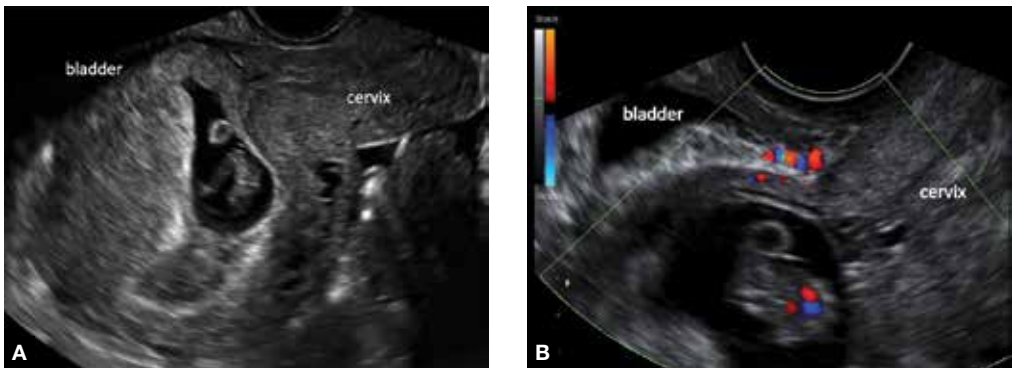
FIGURE 1 Two fetuses: Transvaginal US, mid-sagittal plane



Scans at 8 weeks' (A) and 9 weeks' gestation (B) demonstrate gestational sac implantation in the lower one-third of the uterus. Both sacs can be seen at the level of the internal os, directly posterior to the bladder wall. Thickening of the bladder wall is evident in B, with increased flow on color Doppler evaluation.

FAST TRACK

US evaluation in the 2nd trimester should be for placental location and for the finding of multiple hyperechoic vascular spaces within the placenta parenchyma

Lacunae, with or without documented blood flow on color Doppler US, are the third marker of PAS in the first trimester.[8] Although some retrospective series and case reports describe the finding of lacunae in the first trimester of patients with diagnosed PAS, more recent literature suggests that these spaces are seen infrequently and at a similar frequency in women with and without PAS at delivery.[7]

Second- and third-trimester markers

Multiple diagnostic sonographic markers of PAS have been described in the second and third trimesters.

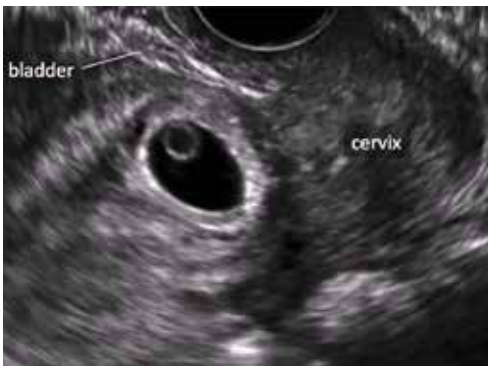
Placental location is a significant risk factor for PAS. Placenta previa in the setting of prior CD carries the highest risk of PAS—as high as 61% in women with both placenta previa and a history of 3 CDs.[10] An anterior placenta appears to be a stronger risk factor for PAS than a posterior placenta in women with prior CD; the location of the placenta should therefore be evaluated in all women in the second trimester.

Lacunae. The finding of multiple hypoechoic vascular spaces within the placental parenchyma has been associated with PAS (**FIGURES 3 AND 4,** page 38). The pathogenesis of this finding is probably related to alterations

AT OUR INSTITUTION…

…we define a first-trimester lower uterine-segment implantation as a gestational sac located just posterior to an empty bladder on transvaginal US examination. Special attention is then given to an anterior location of the placenta, and color Doppler US is applied to assess for surrounding vascularity. A cesarean scar implantation is diagnosed when the gestational sac is seen embedded into the cesarean scar, typically with a fusiform shape.

FIGURE 2 Cesarean scar pregnancy: Sonographic mid-sagittal plane



On a scan at 8 weeks' gestation, the gestational sac is anchored at the level of the cesarean section scar and has a fusiform shape. The bladder is empty but visible as a hyperechoic structure anterior to the sac.

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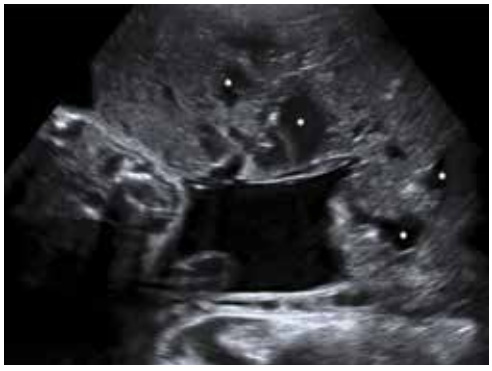
FIGURE 3 Anterior placenta accreta: Sonographic mid-sagittal plane



A scan at 32 weeks' gestation reveals multiple lacunae (asterisks).

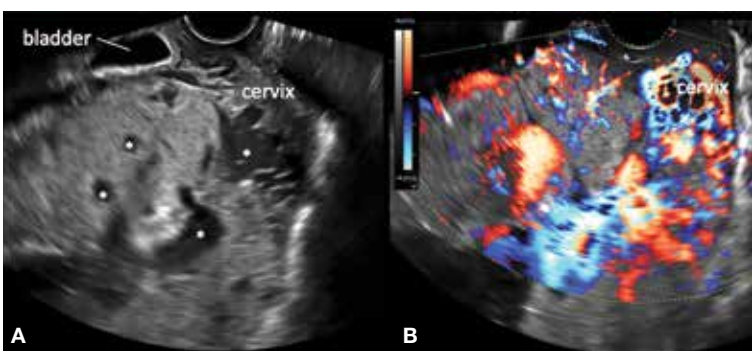
in placental tissue resulting from long-term exposure to pulsatile blood flow.[11]

Finberg and colleagues introduced a grading system for placental lacunae in 1992 that is still used:

- *Grade 0:* no lacunae seen
- *Grade 1:* 1 to 3 lacunae seen
- *Grade 2:* 4 to 6 lacunae seen
- *Grade 3:* multiple lacunae seen throughout the placenta.[12]

The sensitivity and specificity of lacunae as an independent marker for PAS have been reported to be 77% and 95%, respectively.[13] Despite these findings, several studies report a range of sensitivity (73% to 100%) and negative predictive value (88% to 100%).[14] Even in Finberg's original work, 27% of cases of confirmed PAS had Grade 0 or Grade 1 placental lacunae and 11% of cases of placenta previa, *without* PAS, demonstrated Grade 2 lacunae.[12] There is agreement, however, that, the more lacunae, the higher the risk of PAS.

FIGURE 4 Cervix and anterior placenta accreta: Sonographic mid-sagittal plane



Views in gray-scale (A) and color Doppler (B) US at 35 weeks' gestation reveal multiple lacunae in A and vascular invasion of the cervix in B.

AT OUR INSTITUTION…

…we define placental lacunae as anechoic spaces within the placenta, surrounded by placental tissue on all sides and measuring ≥5 mm at their greatest diameter. We utilize color Doppler US to evaluate the presence or absence of blood flow within the lacunae. To optimize visualization of low-velocity blood flow within lacunae, we use bidirectional (high-definition) color Doppler US at ≤5–10 cm/sec, with color filters set at the lowest level and color gain maximized.

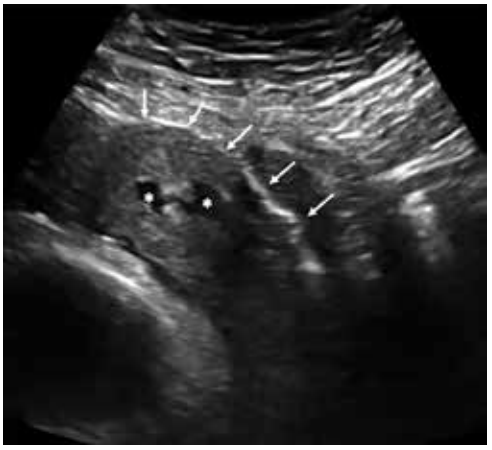
Other US markers of PAS

Retroplacental–myometrial interface

Loss of the normal hypoechoic (clear) retroplacental zone, also referred to as loss of the clear space between placenta and uterus, is another marker of PAS (**FIGURE 5**). This finding corresponds to pathologic loss of the decidua basalis as trophoblastic tissue invades directly through the myometrium.[15] This sonographic finding has been reported to have a detection rate of approximately 93%, with sensitivity of 52% and specificity of 57%, for PAS; the false-positive rate, however, has been in the range of 21% or higher. This marker should *not* be used alone because it is angle-dependent and can be found (as an absent clear zone) in normal anterior placentas.[16]

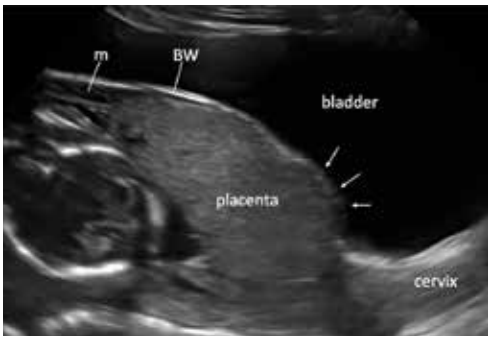
The strength of this US marker is in its negative predictive value, which ranges from 96% to 100%. The presence of a hypoechoic retroplacental clear space that extends the length of the placenta makes PAS unlikely.[17] Of note, the clear zone may appear falsely absent as a result of increased pressure from the US probe.

FIGURE 5 Anterior placenta accreta: Transabdominal US, mid-sagittal plane



A scan at 36 weeks' gestation demonstrates loss of the retroplacental clear zone and placental bulge (arrows), resulting in no measureable retroplacental myometrium. Multiple lacunae are present within the placenta (asterisks).

FIGURE 6 Anterior placenta accreta with distended bladder: Transabdominal US, mid-sagittal plane



On a scan at 18 weeks' gestation, the bladder wall (BW) is hyperechoic and disrupted by a placental bulge (arrows) into the bladder. The retroplacental myometrium (m) is thinned at the level of the placental bulge.

Retroplacental myometrial thickness

Another US finding characteristic of PAS is a retroplacental myometrial thickness of <1 mm (**FIGURE 6**).[15] This finding can result from trophoblastic invasion with minimal intervening myometrium. A thin myometrium also may be due to partial dehiscence (the so-called uterine window) of the uterine wall.[18]

Retroplacental myometrial thickness is difficult to assess because the lower uterine-segment myometrium thins in normal pregnancy as term approaches. This measurement also can be influenced by direct pressure of the US probe and fullness of the maternal bladder.[18] In patients who have had a CD but who do not have PAS, the median myometrial thickness of the lower uterine segment in the third trimester is 2.4 mm.[19]

Thinning of the myometrium in the upper uterine segment always should be of concern. Studies of this marker have reported sensitivity of US ranging from 22% to 100% and specificity from 72% to 100%.[9,20] Given such variability, it is important to standardize the gestational age and sonographic approach for this marker.

Uterovesical interface

Studies also have reported that abnormalities of the uterovesical interface are predictive of PAS. The uterovesical interface is best

FAST TRACK

Retroplacental myometrial thickness is difficult to assess: The lower uterine-segment myometrium thins in normal pregnancy as term approaches

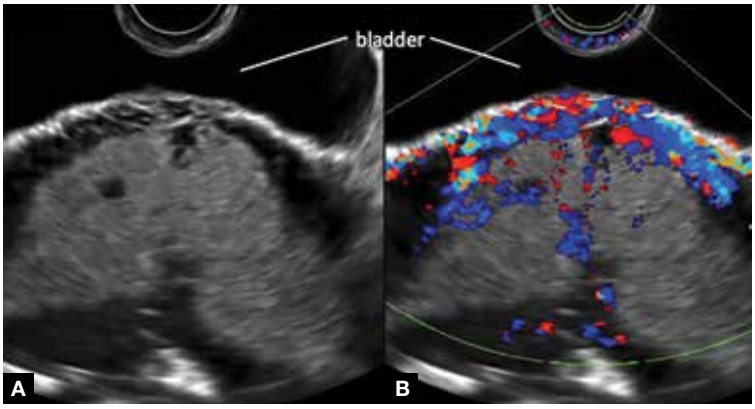
ON OUR US UNIT…

…we optimize transabdominal US imaging of the retroplacental–myometrial interface by applying minimal transducer pressure on the abdomen, minimizing image depth, and magnifying image display. We use linear sweeps to image the entire placenta.

AT OUR INSTITUTION…

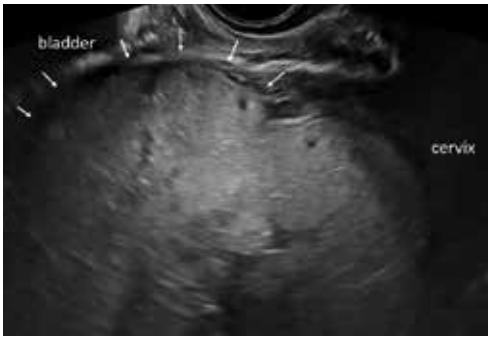
…we typically approach retroplacental myometrial thickness transabdominally by applying minimal transducer pressure on the abdomen, minimizing image depth, and magnifying image display. We measure the myometrium at its thinnest point, taking the measurement perpendicular to the long axis of the wall of the uterus. In the presence of placenta previa or low-lying placenta, we take a transvaginal approach.

FIGURE 7 Placenta accreta: Transvaginal US, transverse view



Views in gray-scale (A) and color Doppler (B) US at 20 weeks' gestation demonstrate increased vascularity of the uterovesical interface.

FIGURE 8 Anterior placenta accreta: Transvaginal US, mid-sagittal plane



A scan at 32 weeks' gestation demonstrates anterior placental bulge with loss of visualization of the retroplacental myometrium (arrows).

evaluated in a sagittal plane containing the lower uterine segment and a partially full bladder in gray-scale and color Doppler US.[15] The normal uterovesical interface appears as a smooth line, without irregularities or increased vascularity on sagittal imaging.

Abnormalities include focal interruption of the hyperechoic bladder wall, bulging of the bladder wall, and increased vascularity, such as varicosities (**FIGURES 5, 6, AND 7**).[15] These findings may be seen as early as the first trimester but are more commonly noted in the second and third trimesters.[7] The authors of a recent meta-analysis concluded that irregularity of the uterovesical interface is the most specific marker for invasive placentation (99.75% confidence interval; range, 99.5% to 99.9%).[13]

AT OUR INSTITUTION…

…we evaluate the uterovesical interface on transvaginal gray-scale and color Doppler US in a midline sagittal view, in which the bladder wall is seen as a hyperechoic band between the uterine serosa and bladder lumen. We subjectively define irregularity of the posterior bladder wall as disruption of the normally smooth bladder wall. We measure the thinnest portion of the myometrium at the uterovesical interface, perpendicular to the long axis of the wall of the uterus with an empty maternal bladder.

Other US markers and modalities

Other proposed US markers of PAS include placental bulge or focal exophytic mass (**FIGURE 8**). More concerning is disruption of the uterine serosa with placental extension, suggesting an exophytic mass, most commonly into the bladder.[21]

Three-dimensional US. Studies have evaluated the role of 3-dimensional (3D) US for predicting PAS. Application of 3D US in vascular mode has shown promise because it allows for semiquantitative assessment of placental vasculature.[22] Using 3D US to screen for PAS presents drawbacks, however: The technology is not well-standardized and requires significant operator expertise for volume acquisition and manipulation. Prospective studies are needed before 3D US can be applied routinely to screen for and diagnose PAS.

Color Doppler US. As an adjunct to gray-scale US, color Doppler US can be used for making a diagnosis of PAS. Color Doppler US helps differentiate a normal subplacental venous complex with nonpulsatile, low-velocity venous blood flow waveforms from markedly dilated peripheral subplacental vascular channels with pulsatile venous-type flow, which suggests PAS. These vascular channels are often located directly over the cervix. In addition, the observation of bridging vessels

ON OUR US UNIT…

…we apply color Doppler US to the retroplacental–myometrial interface and the uterovesical interface to evaluate for abnormal subplacental and uterovesical hypervascularity, defined subjectively by the presence of striking amount of color Doppler US signals in the placental bed, with numerous, closely packed, tortuous vessels demonstrating multidirectional flow and aliasing artifact.[23]

linking the placenta and bladder with high diastolic arterial blood flow also suggests invasion.[21] In a meta-analysis, overall sensitivity of color Doppler US for the diagnosis of PAS was 91%, with specificity of 87%.[13]

The value of utilizing multiple markers

The accuracy of US diagnosis of PAS is likely improved by using more than 1 sonographic marker. Pilloni and colleagues,[20] in a prospective analysis, found that 81% of cases of confirmed PAS had ≥2 markers and 51% of cases had ≥3 markers.

Several scoring systems have been proposed for making the diagnosis of PAS using combinations of sonographic markers, placental location, and clinical history.[19,24,25] In 2016, Tovbin and colleagues,[25] in a prospective study, evaluated a scoring system that included:

- number of previous CDs
- number of, maximum dimension of, and presence of blood flow in lacunae
- loss of uteroplacental clear zone
- placental location
- hypervascularity of the uterovesical or uteroplacental interface.

Tovbin assigned 1 or 2 points to each criterion. Each sonographic marker was found to be significantly associated with PAS when compared to a high-risk control group. A score of ≥8 was considered "at high risk" and predicted 69% of PAS cases.

Regrettably, no combination of US markers reliably predicts the depth of invasion of the placenta.[26]

TABLE How to report US markers for suspected PAS[23]

Always evaluate and report
• Abnormal placental lacunae
• Bladder-wall interruption
• Focal exophytic mass of placenta extending beyond the serosa
• Gray-scale evaluation of loss of the hypoechoic layer between myometrium and placenta
• Myometrial thinning to <1 mm
• Placental bulge distorting extrauterine organs
Also report when color Doppler US is utilized
• Placental lacunae feeder vessels causing turbulent flow
• Presence of bridging vessels from the placenta crossing the myometrium into adjacent structures
• Subplacental hypervascularity
• Uterovesical hypervascularity
Also document
• Suspicion of parametrial involvement

A standardized approach is needed

To decrease variability and improve the US diagnosis of PAS, it is important to define and standardize the diagnosis of each sonographic marker for PAS.[4] In 2016, the European Working Group on Abnormally Invasive Placenta (EW-AIP) proposed a set of US markers that always should be reported when performing an US examination for suspected abnormal placentation (**TABLE**).[23] Despite this effort by the EW-AIP, ambiguity remains over sonographic definitions of several PAS markers. For example, what determines a placental lacuna on US? And what constitutes an abnormal uterovesical interface? There is a need for a more objective definition of US markers of PAS and a standardized approach to the US examination in at-risk pregnancies.

The Society for Maternal-Fetal Medicine is coordinating a multi-society task force to address the need to define and standardize the US diagnosis of PAS.

Observations on other PAS diagnostic modalities

Magnetic resonance imaging

Adjunctive role. Magnetic resonance imaging (MRI) is often used as an adjunctive

US evaluation of the risk of placenta accreta spectrum: The authors' recommended approach

- Assess a priori risk for the patient before initiating the US exam
- In the presence of a placenta previa, or low-lying placenta, we strongly recommend a transvaginal, in addition to transabdominal, US to further assess for the presence of placenta accreta spectrum (PAS) markers
- Until prospective studies clearly define the diagnostic accuracy of PAS sonographic markers and their performance in high-risk and low-risk pregnancies, we recommend that US findings be reported as a risk profile—that is, high, moderate, and low risk of PAS
- Be especially cautious with patients who are at substantially increased risk for PAS, such as those with placenta previa and prior multiple CDs. In this setting, a low-risk report for PAS only should be provided when *none* of the PAS markers are seen on transabdominal and transvaginal US examinations
- While awaiting national guidelines that 1) standardize the approach to the US examination and 2) define PAS US markers, we encourage US laboratories to develop local protocols to standardize the sonographic evaluation of the placenta and ensure uniform and complete placental assessment

FAST TRACK

Until PAS sonographic markers are clearly defined, report US findings as a risk profile—high, moderate, and low risk of PAS

What is the diagnostic accuracy of US for PAS?

Overall, based on current literature, gray-scale US appears to be an excellent tool for prenatal diagnosis of PAS in women at risk: Sensitivity has been reported in the range of 80% to 90%; specificity, 91% to 98%; positive predictive value, 65% to 93%; and negative predictive value, 98%.[5,6]

However, these values might overestimate the true ability of prenatal US to predict PAS. Why? Early studies that assessed the accuracy of US prediction of PAS might have been biased by inclusion of single-expert observations, high suspicion of placenta accreta, and prior knowledge of patients' risk factors. In addition, small sample size, retrospective design, and wide variability in the definition of PAS and inclusion criteria led to inconsistency in performance and skewed sensitivity.[7]

In fact, when experienced providers, reviewing the same US images, were blinded to patients' clinical history, the accuracy of US diagnosis of PAS decreased in regard to sensitivity (to 54%), specificity (88%), positive (82%) and negative (65%) predictive value, and accuracy (65%).[4] Investigators also found wide inter-observer variability in the interpretation of markers of PAS.[4] Furthermore, there is evidence that several PAS US markers are commonly seen in low-risk normal pregnancy.

Although studies have yielded variable findings of the precise sensitivity and positive predictive value of US in the diagnosis of PAS, there is a general agreement that US should be the primary imaging modality for this purpose, and can be used exclusively in most cases.

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diagnostic modality in cases of suspected PAS. Several markers for PAS have been described on MRI, including[15]:

- intraplacental T2-weighted dark bands
- abnormal intraplacental vascularity
- heterogeneous intraplacental signal intensity
- focal interruption of the myometrium by the placenta
- uterine bulging.

Based on a recent meta-analysis, overall sensitivity of MRI for detecting PAS is 86% to 95%, with specificity of 80% to 95%. Although this is comparable to the sensitivity and specificity of US,[27] studies of MRI in PAS are smaller and more prone to bias than in studies of US, because MRI typically is used only in patients at highest risk for PAS. Few studies comparing US to MRI for PAS have been performed; all are small and lack statistical power.

Complementary role. MRI can be complementary to US in cases in which the placenta is posterior or located laterally[28] but, importantly, rarely changes decisions about surgical management when used in conjunction with US to assess patients for the diagnosis of PAS. (An exception might lie in the ability of MRI to assess the degree or depth of invasion of the placenta and discerning placenta percreta from placenta accreta.[15])

Enhancement with contrast. Addition of gadolinium-based contrast might improve the ability of MRI to make a diagnosis of PAS, but gadolinium crosses the placenta barrier. Although fetal effects of gadolinium have not been observed, American College of Radiology guidelines recommend avoiding this contrast agent during pregnancy unless absolutely essential.[29]

Specific indications. MRI *without* contrast should be considered 1) when US is inconclusive and 2) to further evaluate a posterior placenta suspicious for invasion, to define the precise topography of extrauterine placental invasion. The additional information offered by MRI might alter surgical planning.[15]

Biomarkers

Multiple serum biomarkers have been proposed to predict PAS in high-risk women. PAS might be associated with increased levels of first-trimester pregnancy-associated plasma protein A, second-trimester maternal serum alpha fetoprotein, and human chorionic gonadotropin, but studies of the utility of these biomarkers have yielded contradictory results.[30,31] Biomarkers are of interest and have significant clinical applicability, but none of the ones identified to date have high sensitivity or specificity for predicting PAS prenatally. Research is ongoing to identify markers of PAS that have sufficient predictive power. ●

FAST TRACK

Standardization of placental marker definitions and placenta evaluation in at-risk pregnancies are initial steps, and prospective studies are needed to refine and evaluate prenatal diagnosis of PAS by US

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