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REVIEW ARTICLE

Three-dimensional Ultrasonography and Three-dimensional Power Doppler in the Evaluation of Placenta Accreta Spectrum

[1]Giuseppe Calì, [2]Francesco Forlani, [3]Gabriella Minneci

ABSTRACT

Due to the increased rate of cesarean sections in the last decades, the anomalies of placental implantation and invasion have become an emerging pathology. Undetected prenatally, severe forms of invasive placentation can lead to dramatic consequences such as a uterine rupture in labor, peripartum hemorrhage, necessity of hysterectomy and massive blood transfusions. That is the reason why the prenatal diagnosis of impaired placentation plays a key role to detect patients at risk, who should be referred to tertiary perinatal centers. If the diagnosis of abnormal placentation is confirmed, the next step should be to define the degree of placental invasion. Two-dimensional ultrasonography (2D-US) is the technique mainly used to diagnose the placenta accreta spectrum (PAS), but its accuracy could be possibly increased by the complementary use of the three-dimensional (3D) US and 3D power Doppler. Only a few prospective studies are available on the role of 3D US in the detection of PAS without establishing objective, universally acceptable ultrasonographic diagnostic criteria.

Moreover, diagnosis is subjective with accuracy depending on the experience of the operator. 3D power Doppler technique seems to have a good intraoperator but low interoperator reproducibility, because it needs a rigorous standardization of predetermined machine settings. Multicentric studies are needed to identify common and objective 3D US and 3D power Doppler diagnostic criteria for PAS, to reduce interoperator variability.

Keywords: Diagnosis, Four-dimensional ultrasonography, Impaired placentation, Placenta, Three-dimensional power Doppler.

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INTRODUCTION

Following the constant rise in cesarean deliveries occurred in the last decades, the anomalies of placental implantation and invasion have become an emerging pathology. Severe forms of invasive placentation unexpectedly encountered at the time of delivery can lead to dramatic consequences, such as a uterine rupture in labor, peripartum hemorrhage, necessity of hysterectomy, massive blood transfusions. In this scenario, prenatal diagnosis plays a key role in the individuation of patients at risk, who should be referred to tertiary centers. If the diagnosis of abnormal placentation is confirmed, the next step should be to state the degree of placental invasion. 2D ultrasonography (US) is the technique mainly employed in the diagnosis of PAS disorders, but its accuracy is enforced by the complementary use of 3D US and 3D power Doppler.

[1]Professor and Head, [2,3]Specialist

[1]Department of Obstetrics and Gynecology, ARNAS Civico Di Cristina Benfratelli, Palermo, Italy

[2,3]UOC, Ginecologia e Ostetricia, ARNAS Civico Di Cristina Benfratelli, Palermo, Italy

Corresponding Author: Giuseppe Calì, Professor and Head, Department of Obstetrics and Gynecology, ARNAS Civico Di Cristina Benfratelli, Palermo, Italy, e-mail: pinocali13@gmail.com

Placenta Accreta Spectrum and Ultrasound Diagnosis

PAS disorders include three forms of abnormal placentation:[1]

- Placenta accreta (or adherent), when the villi adhere to the myometrium without invasion.
- Placenta increta, when the villi invade the myometrium.
- Placenta percreta, when villi invade the full thickness of the myometrium including the uterine serosa and sometimes adjacent pelvic organs.

According to the lateral extension of the myometrial invasion and the number of cotyledons involved, PAS disorders can also be divided in focal, partial or total. There is no specific clinical symptomatology of PAS, and in many forms of acretism there is not bleeding during the gestation. So clinicians have to suspect its presence if the patient has recognized risk factors. These include placenta previa, previous curettage, multiparity, maternal age over 35 years, medically assisted reproduction techniques, adenomyosis, hysterotomic scars and above all previous cesarean deliveries (CD), in particular, if associated with placenta previa. The increasing rate of these events has caused the rising incidence of PAS in western countries in the last decades.[2] In the last 40 years, CS rates around the world have risen from less than 10% to over 30%. One of the consequences has been a 10-fold increase in the incidence of PAS.[1] In 2013, a systematic review[3] reported 19% of incidence in women at risk, with a previous caesarian section and with anterior placenta previa diagnosed in the third trimester of pregnancy.

At delivery, PAS disorders expose to a high risk of intra- and postoperative complications, including severe hemorrhage with possible necessity of hysterectomy and massive blood transfusions. So, an accurate prenatal diagnosis is essential to reduce maternal mortality and morbidity. It allows to plan the timing of the delivery, to organize a multidisciplinary team with adequate experience, to predispose the availability of compatible blood, to evaluate the therapeutic options considering the surgical difficulties and the eventual patient's wish of preserving her fertility.

Nowadays ultrasound is the main technique used in the prenatal diagnosis of PAS.

Recently an International AIP expert group has proposed some standardized ultrasound criteria in order to reduce the diagnostic errors linked to the subjective interpretation of the examination:[4]

- *Loss of the clear zone:* Loss or irregularity of hypoechoic area between placenta and myometrium.
- *Placental vascular lacunae:* The presence of numerous lacunae (> 3), some of which wide and irregular, in the placental parenchyma. They often are characterized by turbulent flow visible on grayscale and color Doppler imaging.
- *Interruption of the bladder wall:* Loss or interruption of the hyperechoic line between uterine serosa and bladder lumen (bladder line).
- *Myometrial thinning:* The thickness of the myometrium overlying the placenta is less than 1 mm or undetectable.
- *Placental bulge:* Deformation of the uterine serosa caused by the abnormal protrusion of placental tissue into neighboring organs, typically bladder. Uterine serosa appear distorted.
- *Focal exophytic mass:* Placental tissue breakthrough uterine serosa and extend beyond it. It is visible if the bladder is filled and it is related to the most severe PAS disorders.
- *Uterovesical hypervascularity:* Striking amount of color Doppler signal between myometrium and posterior wall of the bladder, showing closely packed tortuous vessels with the multidirectional flow and aliasing artefact.
- *Subplacental hypervascularity:* The striking amount of color Doppler signal in the placental bed, showing closely packed tortuous vessels with multidirectional flow and aliasing artefact.
- *Bridging vessels:* Vessels appearing to extend from the placenta, across myometrium, and beyond serosa into the bladder or other organs, often running perpendicular to myometrium.
- *Intraplacental hypervascularity:* Complex vascularization with the tortuous and irregular vessel, visible with 3D color Doppler.

In D'Antonio's meta-analysis,[3] the loss of the clear zone showed sensibility of 66.2% and specificity of 95.7%; placental lacunae showed sensibility of 77.4% and specificity of 95%; bladder line anomalies presented sensibility of 49.6% and specificity of 99.7%. Grayscale and color Doppler imaging showed overall sensibility of 90.7%, specificity of 96.9% and an odds ratio of 98.5%.

A recent prospective longitudinal study of 2018[5] highlighted that if ultrasound is employed in a population at risk, its diagnostic accuracy is excellent, with sensibility and specificity of 100%. In particular, the specificity of the examination increases if more diagnostic criteria are used. Probably the increased awareness of the pathophysiology of PAS disorders, the greater attention to the selection of patients at risk, the improvements of ultrasound devices and the bigger experience of operators, have allowed achieving these results in the last years.

Role of 3D Ultrasonography and 3D Power Doppler

Two-dimensional ultrasonography is the gold standard in the diagnosis of PAS disorders. Nevertheless, the importance of an accurate evaluation of the severity of the condition suggests the opportunity to employ all the available imaging techniques in an attempt to improve prenatal diagnostic accuracy.

Surgical complications and hemorrhagic risk associated with PAS vary significantly according to the extent of placental invasion, the severity of uteroplacental hypervascularization and the involvement of bladder and parametrium.

A 3D ultrasonography seems to afford advantages over 2D in the imaging of PAS. It provides images that are not obtainable with the 2D US, thanks to its multiplanar capability which allows the visualization of structures from multiple viewpoints. 3D power Doppler permits the dynamic assessment of uteroplacental vascularity, leading to a more accurate and clearer configuration of the abnormal placentation. So, 3D ultrasonography and 3D power Doppler have become frequent in the study of placental development and vascularization, leading to evaluation not just qualitative but also quantitative.

Three-dimensional power Doppler allows to acquire multiplanar images on coronal, axial and sagittal planes and with rotational technique permits to visualize the placenta–bladder interface more accurately, giving a much more coherent view of the extent of placental invasion. It allows a better study of the degree of bladder invasion, information with great impact on subsequent counseling and management.

Until a few years ago, there were not consistent studies in Literature about the evaluation of the myometrial invasion degree and the possibility to differentiate between

placenta accreta, increta, and percreta before the delivery. In 2000, Chou et al. stated that 3D power Doppler permits quantitative analysis of the level of placental neovascularization, so representing an important examination complementary to 2D ultrasound.[6] In 2009 Chou et al.[7] proposed some 3D US diagnostic criteria in case of suspect abnormal placental invasion and bladder involvement:

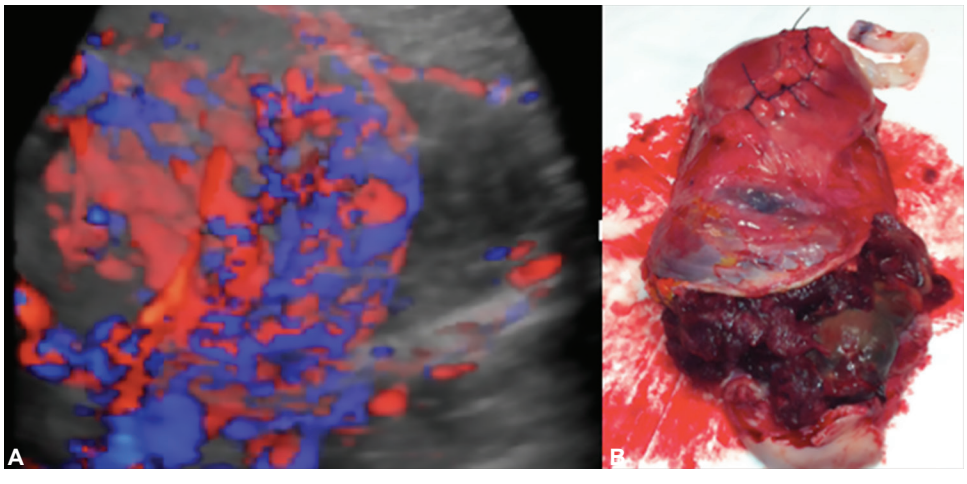
- Loss of the echolucent space between the bladder and the placenta in coronal and axial scans.
- Invasion of the bladder by the infiltrating placenta with irregularity and disruption of the normal bladder wall architecture and/or a focal exophytic placental mass projecting into the bladder in coronal and axial scans.
- Aberrant blood vessels extending into the bladder in the rotational technique.

In 2009, Shih et al. published a prospective study about the role of 3D power Doppler in the diagnosis of PAS versus 2D Ultrasound and color Doppler.[8] In 39 cases of PAS histologically confirmed, the best diagnostic sign was the presence of chaotic vascularization with confluent and tortuous vessels, with a sensitivity of 97% and specificity of 92%. The employment of 3D ultrasound with power Doppler increased the diagnostic information obtainable with 3D technique. The same study also discussed the method limitations, particularly those resulting from signal post-processing, such as the threshold and transparency settings, as well as those related to the relative weighting of the power Doppler signals in the elaboration of data with "glass-body" technique.

In 2013 these results were confirmed in a prospective study we conducted on 187 patients with placenta previa and previous cesarean delivery, among which 41 with placenta accreta histologically confirmed.[9] We used a 3D Ultrasound system with transabdominal and transvaginal transducers. Transabdominal 3D power Doppler was employed to map the vascularization of the placental parenchyma and the uterine serosa–bladder interface. 3D volumes were obtained and processed, either on the ultrasound monitor or using the 4D view software application. With a 180° rotation process, we visualized the sagittal and coronal sections. 3D power Doppler showed that the hypervascularization observed in the uterus–bladder interface extended from side to side in all cases of placenta percreta, with the sensibility of 90% and specificity of 100% (Fig. 1). We used the bladder filling of 300 mL for evaluating the uterine serosa–bladder interface. In this condition, the irregular and tortuous vascularization of the whole placental thickness and the vascularization of the whole uterine serosa–bladder interface strongly suggested the most severe forms of PAS.

This result should be interpreted with caution because the prospective studies in literature are few. Moreover, 3D power Doppler is usually employed after 2D color Doppler, and this could be a bias in the comparison between the techniques. So further studies are required to evaluate the diagnostic performance of 3D ultrasonography used as the main instrument in the examination of PAS.

A few years ago, Collins et al.[10] proposed a new quantitative 3D ultrasound technique permitting reliable prenatal identification of PAS, in an attempt to obtain adequate preparation and management. The technique puts in evidence the largest area of confluent power Doppler signal, called "area of confluence" (Acon). It can differentiate between the presence and absence of PAS and is associated with the histopathologic and clinical severity of the condition, thus predicting the clinical risk. The parameter shows 100% sensitivity and 8% false-positive rate, suggesting that this technique could be useful for an accurate prenatal diagnosis or screening. Acon could help in removing subjectivity in the evaluation of the increased vascularity associated with PAS. However, further validation is necessary before it could be clinically available.



Figs 1A and B: (A) 3D power doppler image showing a remarkable vascularization involving the total bladder–uterine interface from side-to-side; (B) Surgical specimen showing the loss of myometrial tissue in the anterior uterine wall in the case of placenta percreta

Virtual Cystoscopy

A careful study of the degree of bladder involvement is information with great impact on the subsequent surgical management of PAS disorders. Preoperative knowledge about the degree of bladder invasion can be useful to predict the risk of bladder injury, to estimate the entity of bleeding during surgery, to predict technical surgical difficulties and to evaluate the possible insertion of ureteral stents before surgery.

Conventional cystoscopy can identify lesions occupying the full thickness of the bladder wall but does not provide details on vascularization of the placental basal layer adjacent to the urothelium, whose extent is directly related to the degree of PAS disorders.

In the diagnostic workup of our patients with a diagnosis of PAS disorders, we introduced in 2014[11] the 3D high-definition flow "sonographic virtual cystoscopy", employed for the analysis of the vascular topography of the uterine–bladder interface. We filled the bladder with 300 mL of liquid for optimal evaluation of the uterine–bladder interface and, after volume acquisition, we analyzed the image with glass-body rendering, observing the contiguity of the posterior bladder wall with the abnormal site of placental insertion in case of placenta percreta. So the hypervascularization of the serosa–bladder interface under the urothelial tissue was documented allowing the preoperative detection of the degree of myometrial infiltration and involvement of the bladder mucosa (Fig. 2). Very clear details of the same district can be observed employing a 3D volume-rendering technology called "Crystal Vue". This emerging technology is based on image-contrast enhancement and can be used for processing and rendering of acquired 3D volumes. In our experience, we used Crystal Vue in the study of the hypervascularization of the bladder wall, creating a highly detailed virtual cystoscopy. As shown in Figure 3, Crystal Vue puts in evidence the irregularity and disruption of the normal bladder wall architecture in the case of percretism.[12]

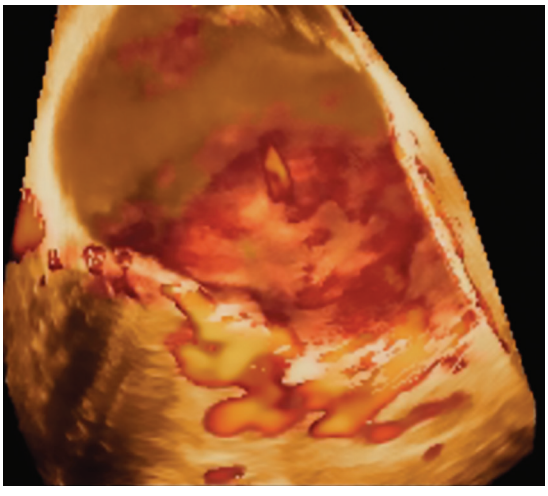


Fig. 2: Virtual cystoscopy: This technique allows to state the extent of vascularization below the bladder mucosa, before bladder wall perforation

The accurate preoperative knowledge of the degree of bladder wall invasion is important for planning the timing of delivery and the surgical approach and to anticipate potential technical difficulties. 3D ultrasonography has a key role for this purpose.

2D and 3D Ultrasound Detection of Bladder–Uterovaginal Anastomoses

High degrees of PAS is often characterized by the presence of a rich vascular anastomotic system between bladder, uterus, and vagina. Normally the connection between uterine arteries and bladder arteries is microscopic, while in case of PAS these vessels enlarge and present important neovascularization. The result is a complex vascular network involving the superior, medial, and inferior vaginal and the lower vesical arteries (Fig. 4).[13]

The role of the interventional radiologist is fundamental in the multidisciplinary team required for optimal management of PAS disorders. Thanks to the employment of embolization techniques we can reach vascular

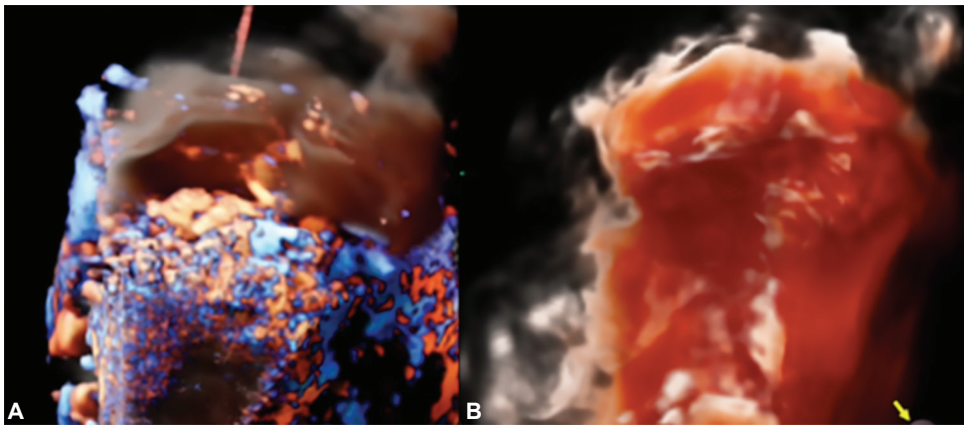


Fig. 3: Virtual cystoscopy realized with Crystal Vue technology: The images show with great detail and efficacy the extensive and chaotic hypervascularization (A)and the disruption (B) of the uterine serosa–bladder interface, strongly suggesting percretism

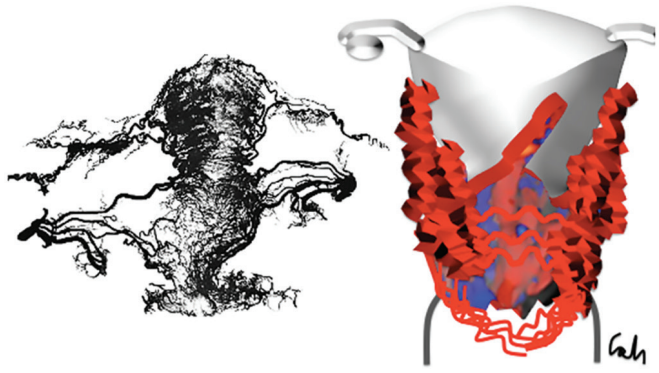


Fig. 4: Complex vascular anastomotic system between bladder, uterus, and vagina. In normal circumstances, the connection between bladder and uterine arteries is microscopic (*Courtesy:* Prof Palacios Jaraquemada), while in the presence of abnormal placentation these vessels enlarge and present important neovascularization

control, an important step to reach satisfactory results in the surgical treatment of PAS. Since the vessels involved arise from the internal pudendal artery, endovascular hemostasis is not possible through a ligation or other methods of closure of the uterine arteries or the anterior divisions of the iliac internal artery. To obtain a targeted embolization, it is necessary to identify the presence of the abnormal vascular connections of the genital tract. A study of 2016 reported the feasibility of ultrasound evaluation of bladder–uterovaginal anastomoses (the "BUV system") in patients with suspect of PAS disorder, using 2D greyscale, color Doppler and 3D power Doppler US. The ultrasound equipment used was a Samsung WS80A with Elite with a 3D transabdominal transducer of 3.8 MHz and a transvaginal transducer of 6.5 MHz. The power Doppler setting was pulse repetition frequency of 0.9 kHz, with the wall filter set to "low". Ultrasound images were evaluated using the 3D multiplanar and the 3D color and power Doppler angiographic application software performed off-line. On conventional 2D ultrasound, patients showed the classic signs of PAS (placental lacunae, loss of the hypoechoic space between the bladder and the myometrium, Doppler abnormalities involving the uterus-bladder interface). The vascular inflow to the lower uterine segment was evaluated with transvaginal scans. 3D power Doppler was applied on sagittal images showing the lower uterine segment and the vagina, with a partially full bladder. On color Doppler, large anastomotic connections between lower uterine segment, vagina, and bladder were visualized, presenting a low-resistance blood flow (Fig. 5). Via axial views through the vaginal fornix, the abnormal anastomotic connections appeared as diffuse pericervical vascularization with multiple anastomotic connections extending superiorly to the bladder and inferiorly through the vagina (Fig. 6). To detect the BUV anastomoses in a patient with PAS disorder is important information which can improve the prenatal diagnosis, potentially anticipating technical difficulties during surgery and post-surgical outcomes.

CONCLUSION

Nowadays no single diagnostic technique affords complete assurance for the diagnosis of PAS. From literature data, diagnostic accuracy seems to increase using more ultrasound criteria. 2D ultrasonography is the gold standard in the diagnosis of abnormal placentation, but 3D US represents an important complementary examination for making or excluding PAS disorders and for stating the degree of placental invasion of the myometrium and the neighboring

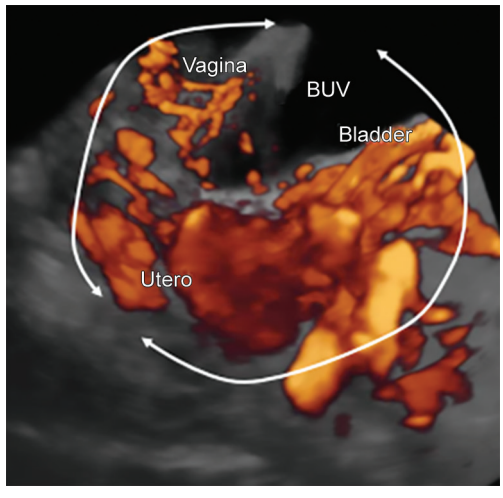


Fig. 5: Transvaginal sagittal lateral scan: The picture shows the large anastomoses characterizing the bladder–uterus–vagina system

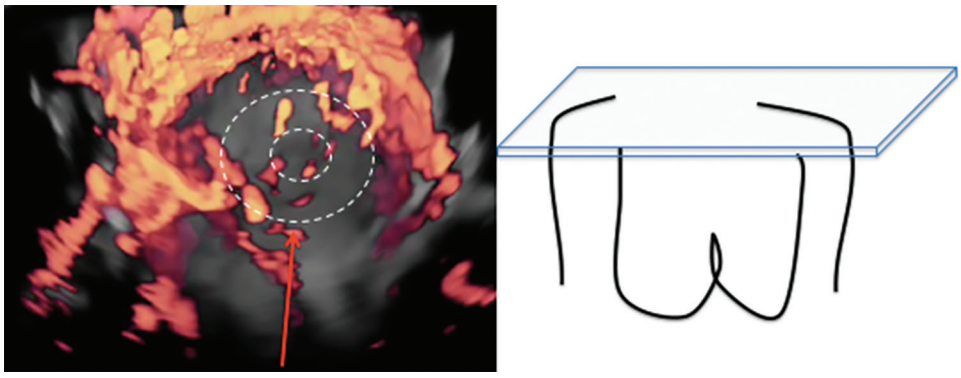


Fig. 6: Transvaginal axial scan: Vascularity of vagina and vaginal fornix in an axial section

organs. Literature presents just a few prospective studies about the role of 3D in this pathologic condition, and objective diagnostic criteria have not been defined yet.

Moreover, diagnosis is subjective with accuracy depending on the experience of the operator.[10] 3D power Doppler technique seems to have got good intraoperator but low interoperator reproducibility because it needs a rigorous standardization of predetermined machine settings. We need new confirmatory, multicenter studies to identify common and objective 3D ultrasound criteria, to reduce interoperator variability.[9]

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