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Routine screening for placenta accreta spectrum

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A B S T R A C T

Screening for clinically significant placenta accreta spectrum (PAS) is possible with a high degree of accuracy (both sensitivity and specificity >90–95%). The group of women to focus on are those with placenta previa and one or more prior Cesarean deliveries. Screening for PAS not associated with placenta previa is not as productive, and several false negatives have been described. The results of the screening program indicate that women have a low or high probability of PAS. Screen-positive women or those with uncertain ultrasound features should be referred to a center of excellence. Those confirmed to have a high probability of PAS should electively be delivered at such centers.

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Questions.

Question 1.

In order to screen for placenta previa, the RCOG recommends a follow-up scan after the anomaly scan, where:

a The placenta is within 5 cm of the internal os
b The woman has had one or more prior Caesarean section
c The placenta is within 1 cm of the internal os
d The pregnancy was conceived through IVF
e There is a history of placenta previa in a previous pregnancy

Question 2.

For ultrasound assessment when screening for PAS:

a The urinary bladder should be empty
b Trans-abdominal scan is sufficient
c All women considered at high risk for PAS should undergo an MRI
d The report indicates a low or high probability of PAS
e Transvaginal scan is risky

Question 3.

Which of the following is a reliable sign of PAS not associated with placenta previa?

a Presence of multiple lacunae
b Increased vascularity in the utero-vesical interface
c Previous Caesarean delivery
d Presence of bridging vessels
e All of the above
f None of the above

Introduction

Placenta accreta spectrum (PAS) is a group of disorders where the placental implantation is in the basal layer of the decidua or deeper in the myometrium [1]. The definition needs to be modified in the context of a previous Cesarean section. A significant proportion of women (25–43%) who have undergone one or more Cesarean sections show a defect in the scar [2]. The prevalence is dependent on the technique used for diagnosis and the definition used to define a "defect." This defect has been termed a "niche" or an "isthmocele." The decidua is deficient, and the myometrium in the niche is replaced by fibrous tissue to a variable extent. Therefore, the traditional criteria for histopathological diagnosis (implantation in the basal layer or in the myometrium) need to be modified.

The histopathology of the uterine niche in the non-pregnant state reveals that it is lined by endocervical mucosa in the vast majority of cases, which is cystically dilated and/or atrophic disorganized endometrial mucosa, probably of lower uterine segment origin [3]. Pregnancy is associated with profound remodeling of the lower uterine segment and the Cesarean scar. The myometrium is further thinned during pregnancy. Prior Cesarean delivery is associated with a thinner lower uterine segment on transvaginal ultrasound assessment compared with the thickness in women with prior vaginal delivery [4]. The mean lower uterine segment thickness in the third trimester is 3.3 ± 1.3 mm [5]. The traditional histopathological criteria for the diagnosis of PAS are no longer a "gold standard" for Cesarean section-associated PAS. The clinical criteria suggested by the International Federation of Obstetrics and Gynecology (FIGO) guidelines [6] are also valid in making this diagnosis. Spontaneous separation and expulsion of the placenta associated with post-partum uterine contraction effectively

excludes this diagnosis, irrespective of the histopathological findings. We made a case of "clinically relevant PAS [7]," which stipulated that the placenta should not separate spontaneously, the condition should be associated with difficulty for access to the baby as well as definitive treatment (low anterior placenta), and a higher morbidity, thereby excluding co-incidental histopathological diagnosis such as basal plate myometrial fibers (BPMF, please see later).

Cesarean section-associated PAS

Prior Cesarean delivery is a well-known risk factor for PAS. A combination of a prior lower segment Cesarean delivery and anterior placenta previa is associated with a high risk of not only PAS but also increased maternal morbidity and is therefore clinically relevant [7]. Screening for placenta previa in pregnancy is recommended in the UK [8] and is part of routine ultrasound screening protocol. The overwhelming majority of Cesarean sections are of the lower segment type. The scar is located on the lower anterior uterine wall. For the placenta to be implanted in the Cesarean section scar, the placental location will have to be on the anterior lower uterine segment. Screening for placenta previa is likely to be useful for the antenatal identification of the large majority of Cesarean section-associated PAS.

Non-cesarean section-associated PAS

A majority of the ultrasound signs described in the literature deal with PAS in the setting of previous Cesarean sections and placenta previa. The features of non-previa PAS or PAS not associated with previous Cesarean deliveries have not been well validated. Although series describing prospective antenatal diagnosis of PAS have women with placenta previa and lower segment Cesarean section in the large majority of cases, one population-based study reported that 51% of cases of PAS did not have placenta previa [9] and 49% had not undergone a prior Cesarean delivery. Even then, the authors recommended concentrating on women with placenta previa or Cesarean delivery to increase the antenatal detection of cases of PAS. It should be noted that the definition of "abnormally invasive placenta (AIP)" was: a woman with delivery by Cesarean section in current pregnancy and assessed by the obstetrician to be AIP or a vaginal delivery assessed to be AIP, where blood transfusion and laparotomy were needed. This definition is rather unusual, and it is possible that not all cases included in this study may have involved placental implantation in the basal layer of the decidua or deeper in the myometrium.

Whom to screen

The two most important risk factors are placenta previa and women with one or more prior Cesarean births. Therefore, it makes sense to focus on this group. Screening for placenta previa is already implemented in many developed countries. For example, the Royal College of Obstetricians and Gynaecologists recommends a follow-up scan for all women in whom the placenta is either covering the internal os or the leading edge is within 2 cm of it [8]. In this subgroup, women with previous Cesarean births are particularly at risk of PAS.

A recently published systematic review [10] reported on cases of PAS in women without a placenta previa or low-lying placenta. The authors reported that antenatal detection was unlikely without placenta previa. They also reported that PAS without placenta previa is associated with lower morbidity (lower blood loss and fewer hysterectomies). The risk factors associated with PAS without placenta previa were different in that previous uterine procedures and the use of assisted reproduction were much more important than a previous Cesarean delivery. Inability of antenatal detection makes screening for this type of PAS an unproductive exercise.

When to screen

The answer to when to screen depends on the strategy used for the identification of cases. Coutinho et al. [11] used screening for PAS on the back of the screening program for placenta previa. Consequently, the first step was the identification of all cases of placenta previa/low placenta at the time of

the routine anomaly scan, which is 18–22 weeks in the UK. The second stage of screening took place at 32–34 weeks. On the other hand, the screening study reported by Baumann et al. [12] reported evaluation in the first, second, and third trimesters.

It is now fairly well accepted that a Cesarean scar pregnancy is a precursor of PAS [13,14]. However, whether it is a good policy to screen for Cesarean scar pregnancies by targeting all women who are pregnant following one or more Cesarean births is not clear. To the best of our knowledge, no study has demonstrated the benefits of screening for Cesarean scar pregnancy by scanning in the first trimester all women pregnant after a Cesarean section. One of the reasons for this is that not all Cesarean scar pregnancies progress to PAS in the later part of the pregnancy.

How to screen

The Society of Maternal and Fetal Medicine special report [15] recommends starting the assessment with *trans*-abdominal imaging to obtain an overview of placental location and to start assessing the regions of concern. Transvaginal ultrasound is strongly recommended for the assessment of PAS. They recommend keeping the urinary bladder partially full. They recommend using the highest frequency transducer that does not compromise the depth of scanning, the use of color Doppler ultrasound, and appropriate magnification to enhance the region of interest. When assessing the retroplacental region, perpendicular orientation of the angle of insonation and applying minimal transducer pressure are recommended. The ultrasound markers for PAS are quite well known by now. The EW-AIP reported a list of 11 ultrasound markers [16]: six in 2D grayscale, four using color Doppler ultrasound, and one in 3-dimensional power Doppler mode. These are listed below:

Markers evident on 2D ultrasound:

- Loss of the clear zone
- Placental lacunae (Please see Fig. 1)

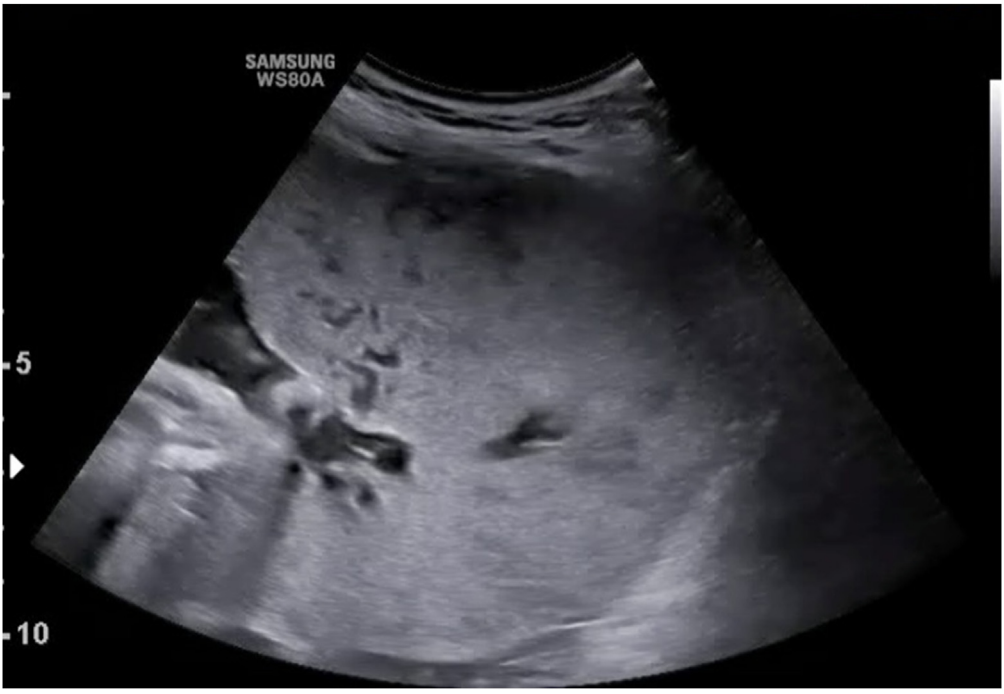


Fig. 1. Presence of multiple lacunae in the placenta.

- Bladder wall interruption
- Myometrial thinning
- Bladder bulge
- Focal exophytic mass

Markers evident on color Doppler:

- Utero-vesical vascularity
- Sub-placental vascularity
- Bridging vessels
- Lacunar feeder vessels

Marker evident on 3D power Doppler mode:

- Intra-placental hyper-vascularity

In addition to these, an increase in the placental thickness in the lower uterine segment (Please see Fig. 2) has also been described as a feature of PAS [17]. Although many ultrasound markers have been described, the most reproducible ones are the presence of lacunae and an increase in the utero-vesical or sub-placental vascularity [18] (Please see Fig. 3).

Magnetic resonance imaging (MRI) has been reported for the diagnosis of PAS by many authors. However, MRI is not a primary imaging technique in pregnancy, and its use is restricted to selected cases. This is not a technique useful for "routine screening for PAS" and is out of the scope of the present study.

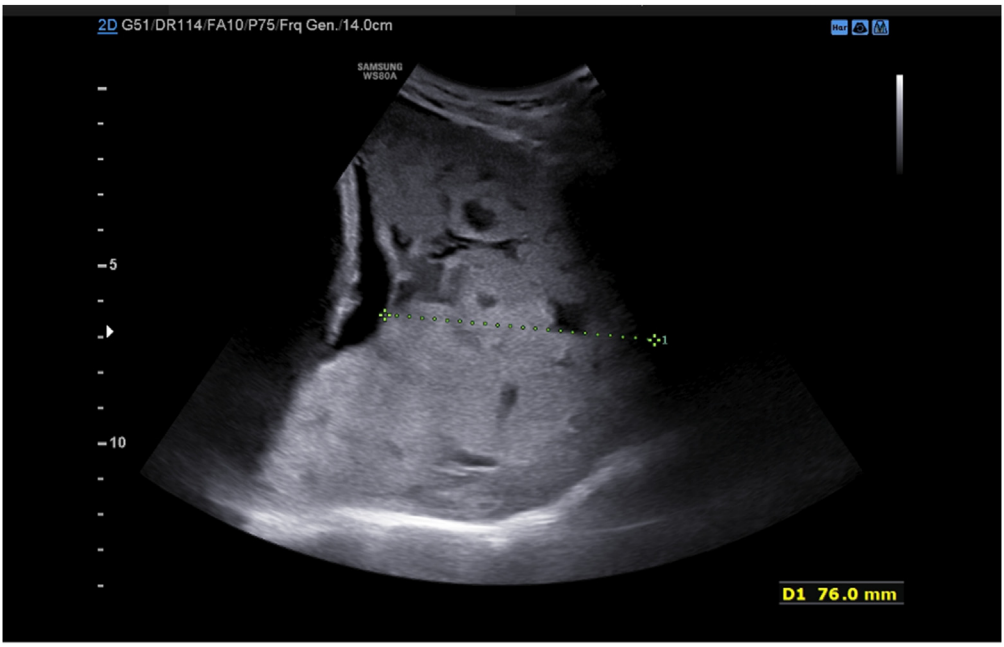


Fig. 2. Increased placental thickness in the lower uterine segment.

Screening performance

Data regarding population screening for PAS are limited. Most publications are case series and are subject to referral bias. One of the first screening studies was reported by Coutinho et al. [11]. In this historical cohort study, the authors reported their experience with 57,179 women undergoing routine mid-trimester ultrasound assessment (Please see Fig. 4). Women with placenta previa (n = 415) underwent a follow-up scan in the third trimester. The placenta previa persisted in roughly half. No woman from this subgroup developed PAS in the absence of previous uterine surgery.

Twenty-two women with PAS were encountered during this time period, 21 of whom were detected on antenatal ultrasound assessment (sensitivity, 95.45% [95% confidence interval (CI), 77.16–99.88%] and specificity, 100% [95% CI, 99.07–100%]). This study reported excellent sensitivity for prenatal detection of PAS using ultrasound in a population screening study. The authors used intraoperative clinical findings and histopathological examination of the surgical specimen as the gold standard for the final diagnosis of PAS. A histological diagnosis was possible only when hysterectomy or partial myometrial resection specimens were available for examination. A surgical record of adherent placenta was used if a pathology specimen was not available.

Baumann et al. [12] reported their experience of screening for PAS. They did not restrict their search to cases with placenta previa. It is not clear at what stage of pregnancy the women underwent an ultrasound scan. Antenatal suspicion of PAS was raised in all three trimesters, but predominantly in the second and third trimesters. In this series of 5219 women, 191 cases of PAS (this included all severities of PAS) were observed. The sensitivity of prenatal ultrasound was 25.8% and the specificity was 99.8% for all cases of PAS, in contrast to the results from the earlier study. However, the sensitivity was 100% and the specificity was 99.9% for the severe cases (placenta increta/percreta). The authors included

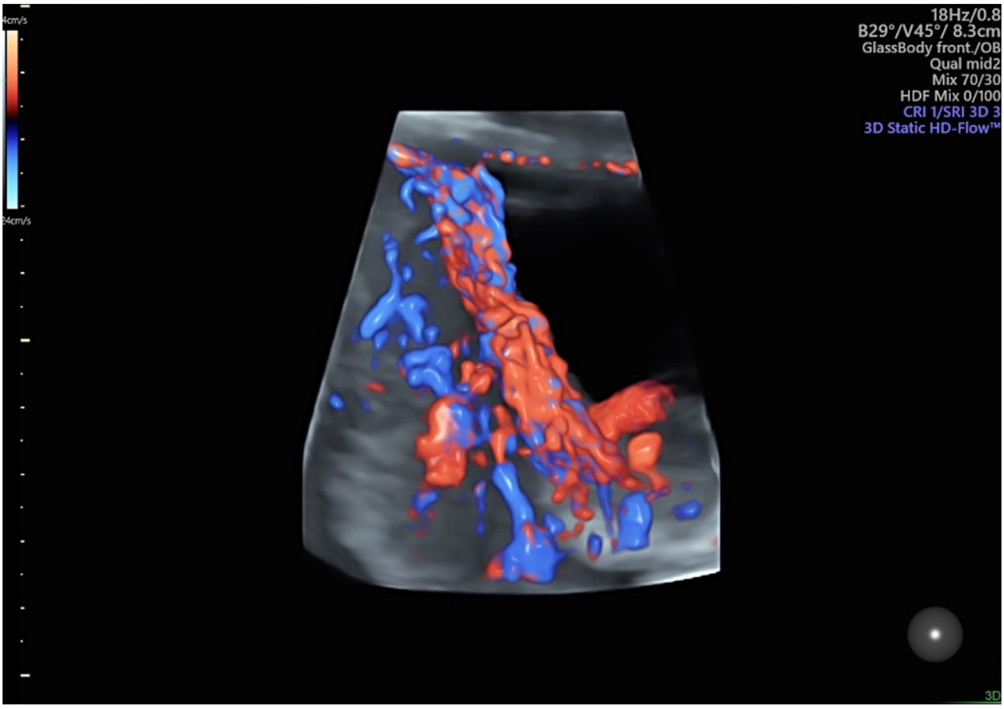
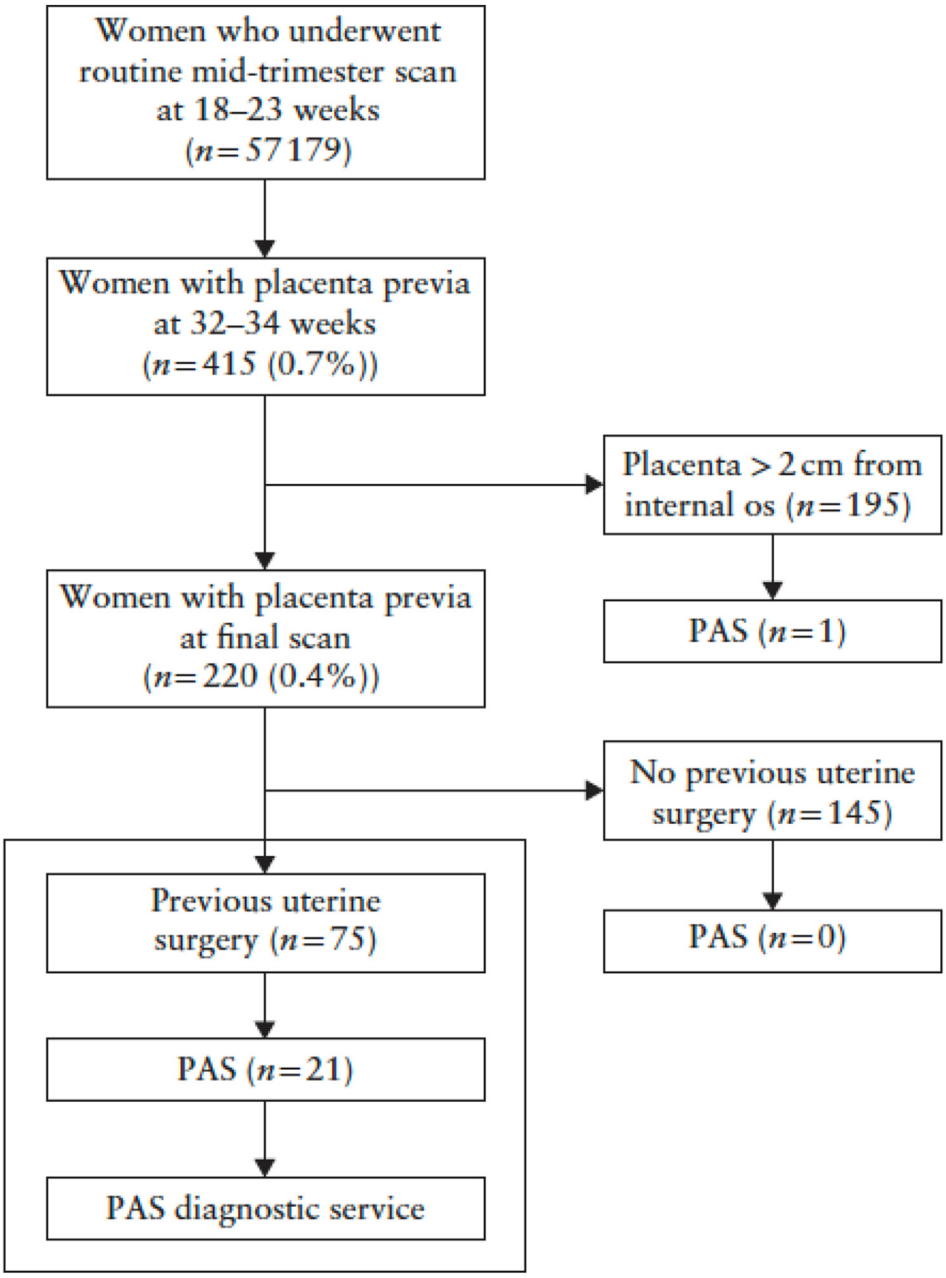


Fig. 3. Increased vascularity in the vesico-uterine area.



Flowchart of unselected women in routinely screened cohort, in which those with diagnosis of placenta previa and history of uterine surgery were referred to placenta accreta spectrum (PAS) diagnostic service for further management.

Fig. 4. Reproduced from Coutinho et al., 2021 [11].

cases with delivered placenta showing adherent myometrial fibers to the basal plate (BPMFs) as evidence of PAS contrary to the consensus document. This states that "the pathologic diagnosis of PAS is restricted to hysterectomy or partial myometrialresection specimens and cannot be made on placental tissue alone or on biopsies of the placental bed [19]." It is not surprising that the prevalence of "PAS" in this series was a whopping 3.5%. None of the "milder cases of PAS" required a hysterectomy for postpartum hemorrhage. Whether BPMFs should be taken as evidence for PAS is controversial. The differences in sensitivity are likely to be related to the differences in the definition of PAS. We would like to argue that "clinically significant placenta previa [7]" is the only variety worth detecting prior to birth. A study from 2015 [20] suggested referral to a center of excellence for further imaging evaluation in the presence of a set of criteria as below:

Clinical risk factors

a. Prior Cesarean delivery (especially multiple Cesareans)
b. Placenta previa
c. History of endometrial ablation
d. Previous uterine surgery
e. First- or second-trimester bleeding with other risk factors for placenta accreta

Sonographic risk factors

a. Abnormal placental appearance
b. Abnormal uterine shape
c. Abnormal vascularity of the myometrial wall
d. Current or previous Cesarean scar was ectopic

The above criteria are useful but do not fit into the purview of "routine screening." Moreover, the performance of this protocol in terms of sensitivity and specificity is not known.

Care of screen-positive cases

It is preferable for screen-positive women to give birth at an appropriate place. The qualifiers for an "appropriate place" have also been described [20]. They focus on the following three aspects:

1. A multidisciplinary team of imaging experts, experienced surgeons, anesthesiologists, neonatologists, and urologists
2. Intensive care facilities such as surgical, medical, and neonatal intensive care units and interventional radiology facilities
3. Blood services with the capability and experience of massive transfusions, the availability of cell-saver and alternative transfusion products, and the backing of transfusion medicine experts

There is accumulating evidence that the majority of maternal deaths associated with PAS are preventable [21], and that antenatal knowledge reduces the morbidity associated with PAS [22].

Not all cases of placenta previa with or without prior Cesarean sections are associated with PAS. Many of these cases are correctly judged to have a low probability of PAS on antenatal assessment. However, it should be remembered that maternal morbidity, although lower than those associated with PAS, is still significantly higher than those not associated with placenta previa; moreover, nearly one in five women required a blood transfusion in one study [17]. Therefore, the availability of an experienced surgeon and adequate blood products should still be ensured.

Practice points

- A combination of a prior lower segment Cesarean delivery and anterior placenta previa is associated with a high risk of not only PAS but also of increased maternal morbidity and is therefore clinically relevant.
- There is insufficient evidence to recommend screening for Cesarean scar pregnancies as a precursor to PAS.
- The use of both *trans*-abdominal and transvaginal imaging is strongly recommended.
- The antenatal detection of PAS is unlikely without placenta previa.
- The results of the screening program identify women with a low or high probability of PAS.
- When the category of BPMFs is not included in the diagnosis of Placenta Accreta Spectrum, screening for PAS has high sensitivity and specificity.
- Screen-positive women or those with uncertain ultrasound features should be referred to a center of excellence. Those confirmed to have a high probability of PAS should electively be delivered at such centers.

Research agenda

- Agree on the gold standard diagnostic criteria for PAS.
- Validate the reported high performance of antenatal screening for C-section-associated PAS.
- Investigate the performance of screening for Cesarean scar pregnancy and whether such a screening program does more good than harm.
- Develop teaching methods for clinicians engaged in effective screening for PAS and for those dealing with operative management of screen-positive cases.
- The antenatal identification of cases suitable for one stage resection and repair of PAS associated with Cesarean section and placenta previa.
- Study the psychological impact of the diagnosis of high suspicion of PAS on women and their partners.

Answers

Q1. Answer is c

Q2. Answer is d

Q3. Answer is f

Declaration of competing interest

Amarnath Bhide authored the guidelines on PAS produced on behalf of the Royal College of Obstetricians and Gynaecologists (RCOG), UK; International Federation of Obstetrics and Gynecology (FIGO); and Society of Maternal and Fetal Medicine (SMFM), USA.

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