The importance of a full bladder in the ultrasound diagnosis of Abnormally Invasive Placenta (AIP)

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Synopsis: *An adequately filled bladder is vital to visualise signs of AIP, bladder volume also has a quantifiable effect on the vascularity of the placental bed.*

Type of Article: Clinical Article

Abstract:

Objective: The diagnosis of AIP is difficult, relying on subjective interpretation of imaging signs. Only one quantifiable marker has been described. This uses the appearance of abnormally confluent vascularity seen in the sub-placental myometrium with 3D power Doppler ultrasound to identify AIP. We sought to discuss how the appearance of the subjective ultrasound signs employed to diagnose AIP change with filling the bladder and examine how the objective measure of vascularity, Acon, changed with different bladder volumes.

Methods: Discussion regarding subjective signs with example images. The largest area of confluent 3D-PD signal (Acon) at the utero-placental interface (UPI) was estimated for women with bladder volumes which differed by at least 200mls.

Results: Acon was calculated for 14 women, 7 of whom had AIP. In women with AIP, $\log(A_{con})$ was significantly greater with a 'filled' bladder when compared to that with an 'unfilled' bladder ($P<0.0005$).

Conclusion: We provide subjective evidence for the need for a full bladder to ensure that signs of AIP can be properly assessed as well as objective evidence for a quantifiable change in the vascularity seen in the myometrium of women with AIP at different bladder volumes. This difference is of sufficient magnitude to influence the potential of this as a diagnostic marker.

Introduction:

Maternal mortality and morbidity are reduced when women with AIP deliver in a tertiary care hospital with a multidisciplinary care team who have experience in managing the risks and challenges presented by the condition[1-4]. Transfer to an experienced team however, relies on accurate antenatal diagnosis. Recent studies have shown that AIP remains undiagnosed before delivery in half[5] to two-thirds of cases[6]. Even In specialist centres, around a third of cases of AIP were not correctly diagnosed during pregnancy[7].

Current antenatal diagnosis relies on the subjective interpretation of sonographic findings with 2-dimensional (2D) greyscale and colour Doppler ultrasound. Most of the signs suggested in the literature have varying reports as to their sensitivity and specificity[8]. In an attempt to improve consistency, and allow appropriate comparison of different imaging markers, panels of experts have published consensus statements aiming to both standardise the descriptions and minimum requirements for an ultrasound scan to diagnose AIP[9, 10]. Magnetic resonance imaging (MRI), although widely employed, has yet to clearly demonstrate an improvement in management or pregnancy outcomes[11]. Irrespective of the imaging modality used, diagnosis is entirely subjective with accuracy depending on the experience of the operator, which is limited by the rarity of the condition. It is vital therefore, that the techniques employed are clearly described in the literature including explaining the effect simple changes such as filling or emptying the urinary bladder can have on the appearance of the images and the assessment of the underlying vascularity, which is arguably the most difficult and subjective of all the signs.

The only objective, quantifiable tool for diagnosing AIP suggested in the literature to

date, uses Power Doppler (PD) to estimate the size of the abnormal hypervascularity seen with colour Doppler[12]. This technique produces an estimation of the largest area of confluent 3D-PD signal (Acon) seen at the utero-placental interface (UPI) and is thought to represent the abnormal flow arising from placental invasion into the myometrial anastomoses[13]. In a pilot study of 93 women at risk of AIP, the size of the Acon was seen to correlate not only to a diagnosis of AIP but to the reported severity at delivery[12].

This article is therefore presented in two parts. In the first we discuss, and demonstrate with examples, how the filling of the woman's urinary bladder affects the subjective appearance of many of the recognised signs of AIP. In the second part, we investigate whether there is a quantifiable difference in the vascularity at the UPI, measured with 3D-PD, as a result of different levels of urinary bladder fullness.

Part 1: Subjective change in appearance of AIP signs related to bladder fullness

AIP can occur anywhere within the uterus. However, it usually only becomes highly clinically significant in combination with an anterior low lying placenta or placenta previa as this also poses other problems at delivery including potentially transecting the placenta at caesarean delivery (CD) to gain access to the baby and the relatively poor contractility of the lower segment leading to greater blood loss increasing the likelihood of emergency hysterectomy. Also, as the single greatest risk factor is previous CD, AIP in the anterior lower segment is not only the most hazardous but probably the most commonly occurring. It is unsurprising therefore, that the majority of the commonly accepted signs for AIP relate to the anterior lower segment such as 'bladder wall interruption' (loss or interruption of the bright bladder wall (the

hyperechoic band or ‘line’ between the uterine serosa and the bladder lumen))[10]. Figure 1 shows a midline sagittal 2D B-mode image of major placenta previa with a virtually empty (Fig 1A) and an adequately filled bladder (Fig 1B). It is evident that without a filled bladder it is almost impossible to identify the bright bladder wall let alone comment on its integrity. The myometrium would be extremely difficult to measure and clear zone is difficult to identify. Interestingly, even in just an anterior placenta, with no previa, an empty bladder causes the clear zone to be more difficult to visualize (Figure 2).

The ‘placental bulge’ sign (deviation of the uterine serosa away from the expected plane, caused by an abnormal bulge of placental tissue into a neighboring organ, typically the bladder)[10] represents a loss of structural integrity in the muscle of the uterus resulting in that area ‘bulging’ away from the rest of the uterus. This most commonly occurs in the anterior lower segment and is extremely difficult to detect without a full bladder as the ‘bulge’ is less evident into surrounding tissue than it I into a full bladder.

Probably the most difficult signs to assess are the highly subjective hypervascularity markers. The sign relating to the bladder is ‘utero-vesical hypervascularity’ (striking amount of colour Doppler signal seen between the myometrium and the posterior wall of the bladder)[10]. This is almost impossible to assess with an empty bladder and difficult with a relatively empty one (Figure 3 B) as the bladder outline is required to demarcate the area between the anterior uterine wall and the posterior wall of the bladder (Figure 3A). In Fugure 3, the fuller bladder allows a clearer picture of the uterovesical vascularity showing the cluster of vascularity around the small bladder bulge and the increased vascularity in the region of the cervix. What remains unclear is whether filling of the bladder in itself directly affects the vascularity seen.

Part 2: Quantifiable estimate of changes in vascularity associated with bladder fullness

Methods

Women were recruited from the John Radcliffe Hospital Fetal Medicine Unit Placenta Clinic (Oxford, UK). They had been referred by their primary health care provider if abnormally invasive placentation was suspected. Written informed consent was obtained in accordance with local research ethics approval (14/NS/0069). The exclusion criteria were: multiple gestation, age younger than 16 years, and inability to provide informed consent.

The women were managed according to local unit protocol. The presence and severity of abnormally invasive placentation were assessed at delivery by an experienced attending obstetrician, and from histopathology results in cases where hysterectomy was performed. All histopathology was undertaken by senior pathologists with expertise in placentology.

Patients underwent standard diagnostic imaging according to the local unit protocol. In addition, static, transabdominal three-dimensional power Doppler ultrasound volumes of the placental bed were obtained using a RAB4-8-D 3D/4D curved array abdominal transducer (4–8.5 MHz) on a Voluson E8 according to a predefined protocol (see Collins et al 2015)[12]. In summary, predetermined machine settings with sub-noise gain were selected, and sagittal volumes were captured in the midline under the uterovesical fold. Actual bladder volume was estimated online in 2D B-mode using the Voluson 3 distance generic volume tool (General Electric Healthcare, Milwaukee, WI, USA.) and measuring the following 3 distances: first in sagittal midline view 1) Utero-vesical fold to the base of bladder and 2) anterior

bladder wall to posterior wall at the midpoint of the bladder. In coronal view 3) distance from side to side through the middle of the bladder.

Two 3D-PD scans were taken at the same visit of exactly the same region of interest which focused on the area of suspected AIP. The first 3D-PD scan volume was captured when the patient reported a sensation of a 'full' bladder, and the actual US bladder volume was estimated to be >200mls. The other volume was captured after she had micturated and reported an 'empty bladder'. To ensure an appropriate difference the woman was asked to try to void again if the estimated difference in volumes was <200mls between the two scans. The data were stored anonymously using Sonoview.

A_{con} was measured offline according to a pre-defined protocol[12]. In summary, volumes were manipulated in 3D using 4D View™ (General Electric Healthcare, Milwaukee, WI, USA.) The colour-only 'Magicut™' tool was used to sequentially remove maternal, fetal, and placental bed vasculature outside a 1cm signal (A_{con}) was then identified and measured using the 4D View™ generic area tool. The operator was blinded to the delivery outcome but as they were examining the images, could not be blinded to the fullness of the bladder.

As A_{con} has previously been found to be right-skewed[12], A_{con} was log-transformed to normalised, and $\log(A_{con})$ was tested for normality using the Shapiro-Wilk method. A paired Student's T test was used to test for a difference between $\log(A_{con})$ with full bladder and unfilled bladder. Patients with AIP and non-AIP controls were analysed separately. Statistical significance was assumed at a p value ≤ 0.05. All statistical

analyses were carried out using SPSSv.22 (IBM Corporation, NY, USA.) Figures were constructed using Prism v.6 (GraphPad software, CA, USA.)

Results

15 patients were recruited between August 2015 and May 2017. Of these, a bladder volume difference of >200ml was achieved in 14 patients (7 confirmed AIP at delivery, 7 no evidence of AIP). Log(A_{con}) was confirmed to be normally distributed in both patient groups and with filled and unfilled bladder (Shapiro-Wilk method: $p>0.05$.)

The values for 'Filled' and 'Unfilled' bladder volumes for both patient groups are reported in Table 1. Two women, one in the AIP and one in the non-AIP group were found to have 'Filled' bladder volumes of ≥800mls. Neither could empty their bladders completely, leaving residuals of 187mls and 326mls. In patients with AIP, the value for log(A_{con}) was significantly greater when measured with a 'Filled' bladder compared to that measured with an 'Unfilled' bladder ($P<0.0005$) Figure 4A and 5. In contrast, no significant difference was detected in measured log(A_{con}) between 'Filled' bladder and 'Unfilled' in patients without AIP ($P=0.9$) (Figures 4B). When the log(A_{con}) was compared between the AIP and not AIP cases with an underfilled bladder there was a significant difference between size of Acon ($p=0.05$). However when the log(A_{con}) of the AIP and not AIP cases were compared with a full bladder the difference between the two groups increased (see Figure 6) and the p value decreased to <0.0001.

Conclusion

We believe that the majority of sonographers with expertise in AIP would agree that it is an extremely difficult, if not impossible, diagnosis to make with an empty bladder and that the figures included demonstrate this point. It is surprising therefore that this is not currently highlighted in the literature or the majority of guidelines published worldwide including in the standardised proforma for reporting ultrasound diagnosis of AIP[9]. We would encourage all sonographers to ensure that women have an adequately filled bladder (in the region of at least 250mls) before attempting to diagnose AIP.

We have also demonstrated a quantifiable effect of adequate bladder filling on A_{con}, an objective ultrasound marker of AIP. Importantly, this effect only seems to occur in patients with AIP. Interestingly, A_{con} is a metric derived from the power Doppler signal which is recording the same vascularity subjectively observed with color Doppler. It therefore stands to reason that the performance of the subjective marker of hypervascularity may also be affected by an inadequately filled bladder.
The mechanism underlying the development of A_{con} is unclear. The most biologically plausible theory is that deep invasion of extravillous trophoblast and subsequent vascular remodelling, causes enlargement and merging of arteriovenous anastomoses found in the subplacental myometrium, producing a large, relatively slow draining aterio-venous sump within the myometrium[12-14]. With this in mind, it is possible that extrinsic pressure within the pelvis from a filled bladder might impair venous outflow from this abnormal vasculature. The subsequent engorgement of these remodelled vessels would be seen as the increase in A_{con} with a filled bladder. In contrast, the small areas of power Doppler signal measured as A_{con} in non-AIP patients are likely to result form measuring artefact seen where arteries cross in the

basal plate. These higher pressure thick walled arterial vessels are less effected by venous engorgement, and so A_{con} will be unaffected by bladder volume in these patients.

This study has several limitations including inherent difficulties with examining the highly subjective signs for AIP. However, we believe that the images given are sufficiently convincing to persuade sonographers of the benefit of encouraging women to attend their ultrasound scan with a full bladder. The sample size for the A_{con} study is small and with no idea of any effect size, a power calculation was impossible to perform. However, the high p-value and clear trend in the AIP group is sufficient to demonstrate that the effect size is large in true cases of AIP. Two women had bladder volumes of >800mls which is an excessively filled bladder and then were unable to completely empty it. The fact that A_{con} increased between 300mls and 800mls in the AIP case hints at a possible dose relationship indicating that an overfilled bladder should also be avoided. Reassuringly despite this excessive bladder volume minimal difference was seen in the woman without AIP. Within the context of a busy ultrasound clinic it is impossible to control the exact amount a woman can fill her bladder by. Our patients reported a full bladder sensation at between 255 and 866mls. However, this small amount of pilot data clearly shows that there is a difference in this novel marker according to bladder volume but more data would be required to fully understand the raltionship..

In summary, these data provide subjective evidence for the need for a full bladder to ensure some of the signs for AIP can be properly assessed as well as objective, quantitative evidence for an effect of bladder volume on 3D-PD signal in AIP that is of sufficient magnitude to influence potential diagnostic markers and the subjective appearance of hypervascularity.

Table 1: Mean bladder volume and log(A_{con}) for the recruited patients by diagnosis

	AIP		**Non-AIP**	
	Unfilled bladder	Filled bladder	Unfilled bladder	Filled bladder
Log(A_{con}) (range)	1.16 (0.61-1.52)	1.56 (1.18-1.95)	0.85 (0.48-1.16)	0.84 (0.46-1.10)
Bladder Volume in mls (range)	79 (13-187)	473 (275-800)	94 (0-326)	584 (351-866)

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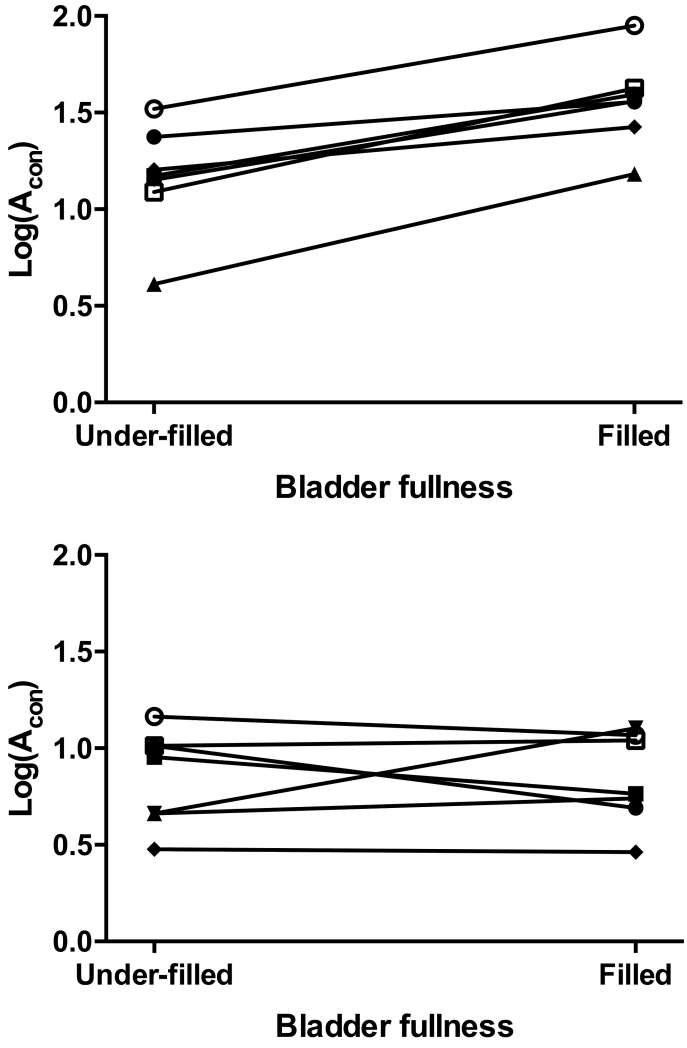
Figure Legends:

Figure 1: Midline sagittal image of the same woman with a placenta previa and an empty and then filled bladder (images taken from an accreta case at 21 weeks gestation)

Figure 2: Clear zone less apparent due to an under filled bladder (images from a non-AIP case at 32 weeks gestation)

Figure 3: Change in the appearance of the vascularity in AIP (Images from a case of increta at 24 weeks gestation)

Fig. 4: Line graph of Log(A_{con}) for under-filled and then filled bladder for A) each patient with AIP B) each non-AIP control



A) Patients with AIP (n=7)

B) Patients who do not have AIP (n=7)

Fig. 5: Comparison of 3D PD signal with filled and under-filled bladder. A, C: sagittal midline 2D view from volumes taken from the same patient with filled and under-filled bladders, respectively. B,D: 3D glass body render in transverse view from the same volumes.

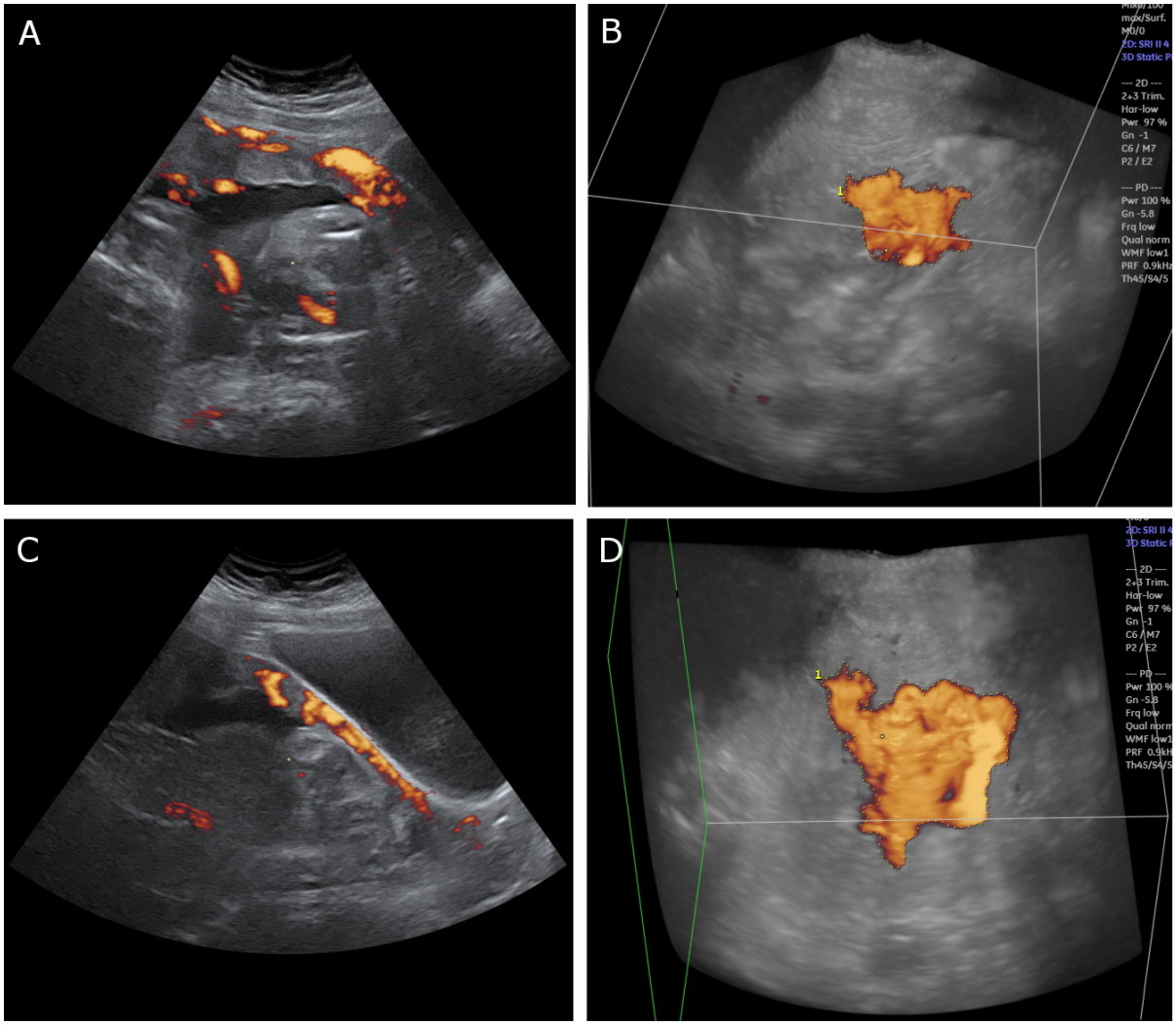
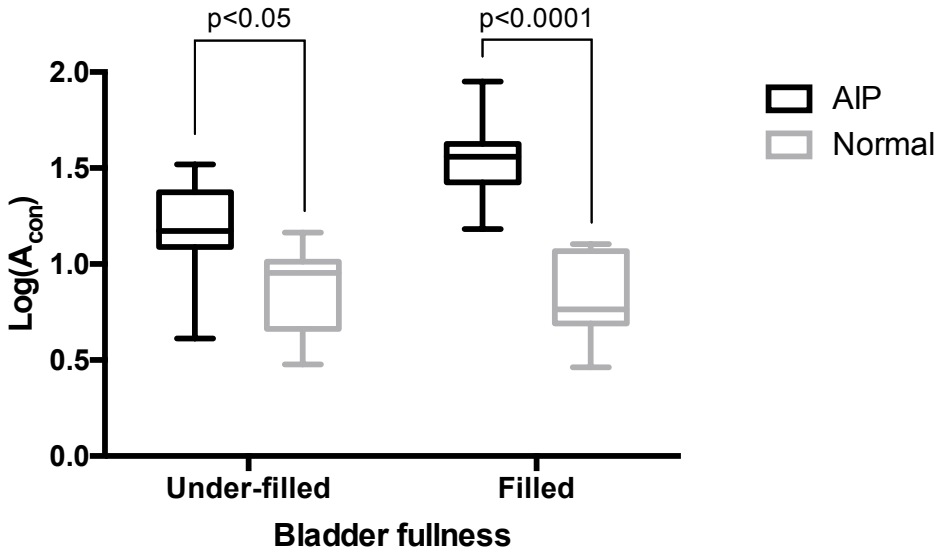


Figure 6: Boxplots showing the mean and range of Log(A_{con}) for both AIP and Non AIP cases with filled and under filled bladders


p<0.05
p<0.0001
2.0
1.5
1.0
0.5
0.0
Log(A_con)
Under-filled
Filled
Bladder fullness
AIP
Normal