

# A. M. HUSSEIN<sup>1</sup>, M. M. THABET<sup>1</sup>, R. A. ELBARMELGY<sup>1</sup>, R. M. ELBARMELGY<sup>1</sup> and E. JAUNIAUX<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Kasr Al Ainy School of Medicine, University of Cairo, Cairo, Egypt; <sup>2</sup>EGA Institute for Women's Health, Faculty of Population Health Sciences, University College London, London, UK

KEYWORDS: bladder injury; complex Cesarean section; placenta previa accreta; ultrasound imaging; uterine dehiscence

## CONTRIBUTION

### What are the novel findings of this work?

Remodeling of the lower uterine segment after Cesarean delivery is associated with anomalies of uterine contour on imaging, independent of evidence of accreta placentation at birth. The severity of these changes on transabdominal ultrasound is associated with an increased risk of intraoperative bladder injury.

#### What are the clinical implications of this work?

Prenatal ultrasound is essential to identify patients with a high probability of placenta accreta spectrum at birth. In addition, and independent of the confirmation of the diagnosis of accreta placentation at delivery, ultrasound imaging can identify signs that are associated with higher risk of intraoperative bladder injury during complex Cesarean section.

## ABSTRACT

**Objective** Intraoperative hemorrhage and peripartum hysterectomy are the main complications in patients presenting with a low-lying placenta or placenta previa undergoing repeat Cesarean delivery (CD). Patients with a high probability of placenta accreta spectrum (PAS) at birth also have a higher risk of intraoperative urologic injury. The aim of this study was to evaluate the ultrasound signs and intraoperative features associated with these injuries.

Methods This was a retrospective case-control study of consecutive singleton pregnancies included in a prospective cohort of patients with a history of at least one prior CD and diagnosed prenatally with an anterior low-lying placenta or placenta previa at 32-36 weeks' gestation. All patients underwent investigational preoperative transabdominal and transvaginal ultrasound examination within 48 h prior to delivery. Ultrasound anomalies of uterine contour and uteroplacental vascularity, and gross anomalies of the lower uterine segment (LUS) and surrounding pelvic tissue at delivery, were recorded using a standardized protocol, which included evaluation of the extent of uterine contour anomalies. The diagnosis of PAS was established when one or more placental lobules could not be separated digitally from the uterine wall at delivery or during the gross examination of the hysterectomy or partial myometrial resection specimens, and was confirmed by histopathology. Data were compared between cases complicated by intraoperative bladder injury and controls from the same cohort matched at a 1:3 ratio by parity and the number of prior CDs using conditional logistic regression.

Check for updates

. 18

**Results** There were 16 (9.4%) patients with an intraoperative bladder injury in a cohort of 170 managed by the same multidisciplinary team during the study period. There were no patients diagnosed with ureteric or bladder trigone damage. There were 14 (87.5%) patients with a bladder injury that had histopathologic evidence of PAS at birth, including 11 (68.8%) cases described on microscopic examination as placenta increta and three (18.8%) as placenta creta. There was a significant (P = 0.03) difference between cases and controls in the distribution of intraoperative LUS vascularity, whereby the higher the number of enlarged vessels, the higher the odds of bladder injury. Multivariable regression analysis revealed that both gestational age at delivery and LUS remodeling on

Correspondence: Prof. E. Jauniaux, Institute for Women's Health, University College London, 86–96 Chenies Mews, London WC1E 6HX, UK (e-mail: e.jauniaux@ucl.ac.uk)

Accepted: 15 January 2024

transabdominal ultrasound were associated with bladder injury. A higher gestational age was associated with a lower risk of injury. A higher LUS remodeling grade on transabdominal ultrasound was associated with an increased risk of bladder injury. Patients with Grade-3 remodeling (involving > 50% of the LUS) had 9-times higher odds of a bladder injury compared to patients with Grade-1 remodeling (involving < 30% of the LUS).

**Conclusions** Preoperative ultrasound examination is useful in the evaluation of the risk of intraoperative bladder injury in patients with a history of prior CD presenting with a low-lying placenta or placenta previa. The larger the remodeling of the LUS on transabdominal ultrasound, the higher the risk of adverse urologic events. © 2024 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.

## INTRODUCTION

Patients with a history of multiple Cesarean deliveries (CDs) are at high risk of complications in subsequent pregnancies<sup>1</sup>. Compared to classical CD, patients with lower uterine segment (LUS) CD are at lower risk of spontaneous uterine rupture during pregnancy, but as the LUS is thinner and contains less myofibers than the upper segment, it is at higher risk of Cesarean scar defect (CSD)<sup>2</sup> and the development of large areas of dehiscence during the third trimester<sup>3,4</sup>. Epidemiologic studies have systematically shown a strong association between LUS-CD and abnormally low placentation in subsequent pregnancy<sup>5,6</sup>. Depending on the number of prior CDs, between 40% and 70% of patients develop a large CSD or niche, which favors implantation and placentation in the LUS<sup>1</sup>.

A CSD often occupies the entire thickness of the LUS, with permanent loss of the normal myometrium anatomy, including the endometrium, the spiral circulation and the junctional zone that controls the physiologic invasion of the extravillous trophoblast during the first trimester of pregnancy<sup>1,7</sup>. Very often, the thickness of the remaining layer at the bottom of a CSD is  $\leq 1$  mm, made of collagen, elastosis and fibrous tissue<sup>8</sup>. This creates an environment that is not favorable for pregnancy development and around 70% of Cesarean scar ectopic pregnancies miscarry during the first trimester<sup>9</sup>. Cesarean scar ectopic pregnancies that continue into the second trimester will present with a low-lying placenta or placenta previa, of which 50% develop into placenta previa accreta<sup>6,10</sup>.

Independent of evidence of accreta placentation at birth, placental development under a large LUS dehiscence often leads to a placental bulge or hernia of one or more placental lobules towards the bladder and other pelvic structures<sup>1</sup>. Multiple CDs are also associated with the development of thick pelvic adhesions, adding to the complexity of the surgical procedure in general and, in particular, separation of the bladder from the LUS<sup>1</sup>. A recent systematic review has shown that intraoperative urologic complication occurs in 15.3% of patients with PAS at birth<sup>11</sup>. The purpose of this preliminary study was to assess the role of ultrasound imaging in the preoperative evaluation of the risk of urologic injury in patients with a history of multiple CDs presenting with low placentation.

## METHODS

## Study design and participants

This was a retrospective case–control study of data collected prospectively between September 2018 and July 2023 at Cairo University Hospital, Cairo, Egypt. All patients in the prospective cohort presented with a singleton pregnancy, a history of at least one prior CD, a low-lying placenta or placenta previa on ultrasound examination and were referred for delivery by an expert specialist multidisciplinary team (MDT) at 32–36 weeks' gestation<sup>12</sup>. Patients with multiple pregnancy or requiring emergency delivery before 32 weeks were excluded from the prospective cohort.

All patients were managed by the same MDT, according to local protocols, including either hysterectomy or conservative management, i.e. partial myometrial resection (PMR) and uterine anterior wall repair when sufficient myometrial tissue was available for reconstruction after dissection of the LUS<sup>13</sup>.

An image-capture digital photographic protocol was used to record the macroscopic features during the different phases of the surgery and gross examination of the hysterectomy specimens (Figure 1)<sup>14</sup>. Intraoperative findings at laparotomy included LUS dehiscence, which was recorded as: focal (Grade 1), if involving < 30% of the lower segment surface; large (Grade 2), if involving 30-50% of the lower segment surface; and extended (Grade 3), if involving > 50% of the LUS and changes in the LUS vascularity, i.e. the number of enlarged vessels running craniocaudally and laterally in the anterior uterine serosa found over the placental bed or in the parametria. A diagnosis of PAS was recorded when one or more placental lobules could not be separated digitally from the uterine wall at delivery or during the gross examination of the hysterectomy or PMR specimen (Figure 1).

Samples were taken at the placental–uterine interface of the abnormally attached cotyledons for histologic confirmation of diagnosis. The PAS cases were described as creta (adherenta) or increta when placental villi were implanted superficially or deeply, respectively, into the uterine wall. Basal plate areas of excessive fibrinoid deposition on microscopic examination were reported as previously described<sup>15</sup>.

Ethical committee approval was obtained prior to the start of this study (Scientific and Research Ethical Committee approval at University of Cairo RSEC 021001). Clinical data were collected using a standard clinical audit protocol and all data and images were fully anonymized for further analysis.

### Ultrasound protocol

а

All patients had a least one detailed transabdominal (TAS) and transvaginal (TVS) sonographic examination by the MDT, including color Doppler image (CDI) mapping of the placenta and uteroplacental interface (GE Voluson E10; GE Medical Systems, Zipf, Austria) and within 48 h before surgery. The placenta was recorded as low-lying when the edge was 0.5-2 cm from the internal os of the uterine cervix on TVS. When the placenta was < 0.5 cm from the internal os or completely covering it, it was defined as placenta previa (marginal or covering)<sup>12</sup>. Cervical length was measured in all cases by TVS.

Ultrasound findings were recorded using a standardized protocol, including anomalies of uterine contour (loss of clear zone, myometrial thinning and placental bulge) and anomalies of the uteroplacental, intraplacental and cervical circulation<sup>16</sup>. The score proposed by Finberg

and Williams<sup>17</sup> was used to record placental lacunae (Grade 0, no lacunae; Grade 1+, 1–3 lacunae; Grade 2+, 4–6 lacunae; Grade 3+, > 6 lacunae). The presence of feeder vessels to the lacunae was also recorded. The residual myometrial thickness (RMT) was measured at the thinnest site perpendicular to the long axis of the LUS, placing one caliper at the interface between the LUS and bladder walls and the other at the interface between the LUS wall and the placental bed or the amniotic cavity.

On TAS, the RMT was measured with a full bladder at the thinnest site of the upper, middle and lower edges of the bladder–LUS wall junction and myometrial thinning was defined as RMT  $\leq 1$  mm. Anomalies of uterine contour, including loss of clear space and myometrial thinning, were graded based on the extension of the remodeling<sup>4</sup>: focal when involving < 30% of the LUS, large if involving 30–50% and extended if involving > 50% of the LUS, as evaluated from the total distance



b

delivery, showing large areas of lower uterine segment dehiscence (\*). (e) Patholo attached (\*) (not detachable digitally) to uterine wall (U). AC, amniotic cavity.

between the upper uterine–bladder junction and the inner os of the uterine cervix (Figure S1). On TVS, the RMT was measured at the thinnest site within 5 cm from the cervix internal os (distal part of the LUS). Myometrial thinning was recorded when the RMT was <2 mm anywhere on TAS and categorized on TVS as normal when >2 mm, thin when 1-2 mm and very thin when <1 mm, as previously described<sup>18</sup>. All measurements were obtained prospectively by the same operator (A.M.H.) and the corresponding images and videoclips were reviewed independently by another operator (E.J.).

## Statistical analysis

Each case of bladder injury was matched to three controls from the same cohort by parity and the number of prior CDs. Categorical variables are summarized by the number and percentage of subjects in each category. Standard kurtosis analysis indicated a normal distribution and, therefore, continuous variables are presented as mean  $\pm$  SD. Differences between cases and controls were examined using linear mixed models. Matching intraoperative variables group (each combination of one case and three controls) was included as a random factor in the analysis. All further analyses examined factors associated with bladder injury. To allow for the matched case-control design, the analysis was performed using conditional logistic regression. The analysis for both outcomes was performed in two stages. First, the separate association between each ultrasound sign and intraoperative gross feature and bladder injury was examined separately in a series of univariable analyses. Subsequently, the joint association between the features and the outcome was examined in a multivariable analysis. To reduce the number of factors in this stage of the analysis, only ultrasound findings and intraoperative features showing some association with the outcome from the univariable analyses (P < 0.2) were included. Patient parameters found to vary between cases and controls were also included in this stage of the analysis. A backwards selection procedure was used to retain only the significant parameters in the final model. SPSS version 28.0.1.1 (IBM Corp., Armonk, NY, USA) was used to analyze the data. A P-value < 0.05 was considered significant.

## RESULTS

### Study group demographics

There were 170 patients in the cohort during the study period, including 16 (9.4%) with a bladder injury during delivery. There were no patients diagnosed with ureteric or bladder trigone damage. Table 1 presents the preoperative ultrasound findings, intraoperative gross features and outcomes of the study group. In all cases, the bladder cystotomy involved the upper half of the bladder. In one case, the cystotomy was intentional to allow surgical access to the lower pelvis (Case 14), as no dissection plane between the LUS and the bladder could be identified at laparotomy. There were 14 (87.5%) cases with confirmed histopathologic evidence of PAS at birth, including 11 (68.8%) cases described on microscopic examination as placenta increta and three (18.8%) as placenta creta. All patients in the study group required a peripartum hysterectomy, including the two patients with no evidence of PAS at birth, due to intraoperative bleeding (Case 11) and failure to reconstruct an extended dehiscence of the LUS after complete delivery of the placenta (Case 16).

In the control group (n = 48), there were 39 (81.3%) patients with histopathologic evidence of PAS at birth, including 29 (74.4%) cases described on microscopic examination as placenta increta and 10 (25.6%) as placenta creta. A peripartum hysterectomy was performed in 41 (85.4%) patients, including in five with no evidence of PAS at birth, due to failure to reconstruct an extended dehiscence of the LUS after complete delivery of the placenta. There was no difference in the mean  $\pm$  SD maternal age at the time of delivery between the study cases and the controls  $(33.1 \pm 6.2 \ vs \ 32.6 \pm 4.5 \ years; P = 0.70)$ . The mean  $\pm$  SD gestational age at delivery was significantly lower in the cases compared with controls  $(35.9 \pm 0.7 \ vs \ 36.4 \pm 0.8 \ weeks); P = 0.02)$ .

## Preoperative ultrasound findings, gross intraoperative features and outcomes associated with bladder injury

Table 2 summarizes and compares the preoperative ultrasound findings and gross intraoperative findings in both cases and controls. All patients in both groups presented with a lack of clear space and myometrial thinning on TAS. The finding of a large or extensive dehiscence of the LUS involving > 30% on TAS and on gross intraoperative examination was more common in the study cases, but the results of the univariate analysis indicated that none of the ultrasound variables was associated significantly with bladder injury.

There was a significant (P = 0.03) difference in the distribution of intraoperative LUS vascularity, whereby the higher the number of enlarged vessels running craniocaudally and laterally in the anterior uterine serosa, the higher the odds ratio (OR) for bladder injury (Table 2). There was also an increase in the odds of bladder injury according to the extension of the LUS dehiscence, but the results did not reach statistical significance.

Multivariable regression analysis (Table 3) revealed that both gestational age at delivery and LUS remodeling on TAS were associated with bladder injury. A higher gestational age was associated with a lower risk of injury. Every additional week of gestation was associated with the odds of bladder injury being only 0.4-times as high (or 60% lower). A higher LUS remodeling grade on TAS was associated with an increased risk of bladder injury. Patients with Grade-3 remodeling (involving > 50% of the LUS) had 9-times higher odds of a bladder injury than patients with Grade 1 (involving < 30% of the LUS).

			TAS-LUS			Uteropl	acental circula	tion anomaly	LUS	feature		De	livery outcome	
Caco	Prior CD	Placental Location	remodeling	Placental bulgg	TW-SVT	Lacunae	Subplacental	Cervical	Dehiscence	Vacaulanitut+	Carronan	Fetal	GA (11100bc - Jane)	Histotototoo
7426	(11)	100411011	graue	vuige	(mm)	score	разсанатиу	разсанатиу	graue	v uscaturity	yngery	weigni (g)	$(weeks \pm uays)$	111stopution0gy
1	2	Low-lying	2	No	1 - 2	3+	Increased	Normal	3	1 - 3	CSH	3200	36 + 3	PAS (PI)
7	2	Previa covering	33	No	$\sim$	3+	Increased	Increased	3	> 3	CSH	3100	36 + 0	PAS (PI)
б	2	Previa covering	3	Yes	$^{\prime}$	3+	Increased	Increased	С	> 3	CSH	2700	35 + 5	PAS (PI)
4	3	Previa covering	2	Yes	>2	$^{2+}$	Increased	Normal	2	1 - 3	CSH	3000	37 + 0	PAS (PC)
5	33	Previa marginal	ŝ	Yes	1 - 2	$^{+1}$	Normal	Normal	33	1 - 3	CSH	2850	36 + 0	PAS (PC)
9	ŝ	Previa covering	1	Yes	>2	3+	Increased	Normal	2	> 3	CSH	2900	35 + 0	PAS (PI)
	ŝ	Previa covering	2	Yes	1 - 2	3+	Increased	Increased	33	1 - 3	CSH	2550	36 + 0	PAS (PI)
8	С	Low-lying	2	Yes	$\stackrel{\wedge}{-}$	3+	Increased	Normal	1	1 - 3	CSH	3200	36 + 0	PAS (PI)
6	4	Previa covering	1	No	1 - 2	$^{2+}$	Normal	Normal	1	1 - 3	CSH	2350	35 + 0	PAS (PI)
10	4	Previa covering	ŝ	Yes	1 - 2	$^{2+}$	Increased	Increased	ŝ	> 3	CSH	3080	36 + 5	PAS (PI)
11	4	Previa covering	2	No	$^{\prime}$	$^{1+}$	Increased	Normal	С	1 - 3	CSH	3300	36 + 2	Not PAS
12	5	Previa covering	2	No	1 - 2	3+	Increased	Normal	2	Normal	CSH	2500	36 + 5	PAS (PC)
13	5	Previa covering	2	No	$^{\prime}$	$^{2+}$	Increased	Normal	С	× 3	CSH	2700	34 + 0	PAS (PI)
14	2	Previa covering	ŝ	No	1 - 2	$^{1+}$	Increased	Increased	ŝ	> 3	CSH	2600	36 + 5	PAS (PI)
15	5	Previa covering	33	Yes	$\stackrel{\wedge}{-}$	$^{2+}$	Increased	Increased	С	> 3	CSH	2720	36 + 2	PAS (PI)
16	4	Previa covering	33	Yes	$^{\prime}$	$\frac{1}{1}$	Normal	Normal	3	1 - 3	CSH	2850	36 + 0	Not PAS
*Grae	de 1, focal (	< 30%); Grade 2,	large (30-50	%); Grade 3	, extended	(> 50%). †	Number of en	larged vessels ru	inning cranioc	audally and lat	erally in ar	iterior uterin	ie serosa found o	ver placental bed
or in incret	parameuria. a; TAS, trar	UND, UESATEAN SC 15abdominal sono;	sction hystered graphy; TVS,	transvaginal), נוסא	gestationai ; l sonograph	age; LU3, 1 y.	ower uterine s	egment; w11, m	yometriai unic	kness; ľað, piad	centa accre	ta spectrum;	; ru, placenta cre	ta; F1, piacenta

Table 1 Preoperative ultrasound findings, intraoperative gross features and delivery outcome in 16 cases complicated by bladder injury during Cesarean delivery (CD)

## © 2024 The Authors. *Ultrasound in Obstetrics & Gynecology* published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.

Variable	Cases $(n = 16)$	Controls $(n = 48)$	OR (95% CI)*	Р
Ultrasound finding				
Placental location				0.62
Placenta previa	14 (87)	44 (92)	1	
Low-lying	2 (13)	4 (8)	1.59 (0.25-9.95)	
Cervical length (mm)	$42.3 \pm 12.6$	$45.8 \pm 10.3$	0.74 (0.43-1.28)‡	0.28
Cervical vascularity				1.00
Normal	10 (62)	30 (62)	1	
Increased	6 (38)	18 (38)	1.00 (0.31-3.26)	
TAS-LUS remodeling grade <sup>+</sup>				0.07
Grade 1	2 (13)	14 (29)	1	
Grade 2	7 (44)	27 (56)	1.65 (0.33-8.21)	
Grade 3	7 (44)	7 (15)	5.78 (1.00-33.3)	
TVS-MT (mm)				0.44
> 2	2 (13)	13 (27)	1	
1-2	7 (44)	16 (33)	2.76 (0.51-15.1)	
< 1	7 (44)	19 (40)	5.58 (0.42-15.9)	
Placental bulge				0.48
No	7 (44)	26 (54)	1	
Yes	9 (56)	22 (46)	1.51 (0.49-6.66)	
Subplacental vascularity				0.48
Normal	3 (19)	13 (27)	1	
Increased	13 (81)	35 (73)	1.70 (0.39-7.48)	
Lacunae score				0.85
Grade 1+	4 (25)	15 (31)	1	
Grade 2+	5 (31)	15 (31)	1.30 (0.30-5.64)	
Grade 3+	7 (44)	18 (38)	1.55 (0.34-7.13)	
Feeder vessels				0.28
No	6 (37)	25 (52)	1	
Yes	10 (63)	23 (48)	2.03 (0.56-7.38)	
Gross feature				
LUS dehiscence grade <sup>+</sup>				0.09
Grade 1	2 (13)	16 (33)	1	
Grade 2	3 (19)	14 (29)	1.62(0.23 - 11.4)	
Grade 3	11 (69)	18 (38)	4.43 (0.89-22.1)	
LUS vascularity				0.03
Normal	1 (6)	14 (29)	1	
1-3 vessels	8 (50)	23 (48)	8.33 (0.90-77.3)	
> 3 vessels	7 (44)	11 (23)	18.5 (1.53-224)	
Histopathology	× /	× /	· · · · ·	0.54
PAS	14 (87)	39 (81)	1	
Not PAS	2 (13)	9 (19)	0.57 (0.10-3.34)	
Fetal weight (g)	$2850 \pm 280$	$2988 \pm 245$	0.83 (0.66-1.03)	0.09

Table 2 Preoperative ultrasound findings and intraoperative gross features in 16 cases complicated by bladder injury at Cesarean deliveryand 48 matched controls

Data are given as n (%) or mean  $\pm$  SD, unless stated otherwise. \*Odds of bladder injury. †Grade 1, focal (< 30%); Grade 2, large (30–50%); Grade 3, extended (> 50%). ‡Odds ratio (OR) given per 10-mm increase in cervical length. §OR given per 100-g increase in fetal weight. LUS, lower uterine segment; MT, myometrial thickness; PAS, placenta accreta spectrum; TAS, transabdominal sonography; TVS, transvaginal sonography.

 Table 3 Multivariable regression analysis, following backwards

 selection of variables

Variable	OR (95% CI)*	Р
Gestational age at delivery (in weeks)	0.39 (0.17-0.89)	0.03
TAS-LUS remodeling grade <sup>+</sup>		0.05
Grade 1	1	
Grade 2	1.77 (0.31-10.0)	
Grade 3	9.25 (1.23-69.8)	

\*Odds of bladder injury. †Grade 1, focal (< 30%); Grade 2, large (30–50%); Grade 3, extended (> 50%). LUS, lower uterine segment; OR, odds ratio; TAS, transabdominal sonography.

## DISCUSSION

## Main findings

The present data confirm and add to recently published data highlighting the role of imaging, both ultrasound<sup>18–21</sup> and magnetic resonance imaging<sup>22–24</sup>, in the preoperative evaluation of surgical outcome in patients with a high probability of PAS at birth. In particular, anomalies of the uteroplacental circulation i.e. subplacental hypervascularity and high lacunae scores on TAS have been associated with higher odds of multiple transfusions and peripartum hysterectomy<sup>20</sup>. The OR for peripartum hysterectomy is also higher for a very thin (< 1 mm) distal LUS on TVS<sup>18</sup>. The data of the present study indicate that

© 2024 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.

the intraoperative risk of bladder injury during Cesarean hysterectomy increases with the extent of the LUS remodeling on TAS, independent of the confirmation of the diagnosis of PAS at birth.

#### Strengths and limitations

This study has several strengths. As far as we know, this is the first study to evaluate the risk of intraoperative urologic injury using well-defined protocols to report on preoperative standardized ultrasound signs and gross pelvic features at laparotomy in patients with a high probability of PAS at birth. In addition, our protocols included quantification of the extent of the ultrasound signs and gross changes associated with LUS remodeling. Detailed histopathologic examination of samples of abnormally attached placental lobules in all cases of hysterectomy and PMR allowed us to confirm accurately the diagnosis of PAS and identify non-PAS cases that may present with major uterine remodeling without any abnormal placental attachment.

The primary limitation of this study lies in its retrospective design. However, all cases were obtained prospectively from the same cohort and all patients were managed by the same MDT, which was established 10 years ago. The use of three controls for each individual case, matched for the main risk factors of PAS in subsequent pregnancy, should limit the risk of bias in the present analysis of the data. Another limitation is the exclusion of cases requiring emergency delivery prior to planned surgery, which are known to be associated with a higher risk of intraoperative urologic complications<sup>11</sup>. The single-institution study design may also limit the generalizability of our results.

### Comparison with other studies

The upper uterine segment is less prone to remodeling after surgery than the LUS because it is made of three thick layers of dense smooth muscle cells<sup>25</sup>. Surgical procedures such as myomectomy, with opening of the upper segment uterine cavity, or accidental perforation during curettage rarely lead to the development of PAS in subsequent pregnancy<sup>26,27</sup>. When it happens, thick myometrial tissue around the scar area often allows for a conservative surgical management<sup>28</sup>. By contrast, LUS remodeling after CD often leads to the formation of CSD with progressive dehiscence of the LUS as pregnancy advances<sup>4</sup>. Major dehiscence of the lower half of the LUS, making reconstruction of the corresponding uterine wall after delivery difficult, often leads to hysterectomy, even in patients with non-PAS placenta previa<sup>7,20</sup>.

The incidence of intraoperative urologic complication in the present study was lower than that reported in a recent systematic review and meta-analysis (9.4% *vs* 15.3%)<sup>11</sup> and involved only the upper part of the bladder. This can be explained by the high volume of cases and MDT expertise of nearly a decade in managing complex CDs<sup>13</sup>. A single-center cohort study of 292 patients in the USA reported an incidence of 19.9% urologic morbidity, with a higher incidence in those patients diagnosed with placenta percreta<sup>29</sup>. Similarly, a single-center cohort study of 312 patients in Germany found a bladder-injury incidence of 9.3% with a higher risk in patients with ultrasound imaging suggesting a placenta percreta<sup>30</sup>. In view of recent evidence, indicating that normal villous tissue does not cross the uterine serosa<sup>3,31</sup>, these cases are likely to be the consequence of surgical dissection of a dehiscent LUS covered only by a thin layer of scar myometrium and single-cell layer of serosa epithelium<sup>32</sup>. These findings and our data support the association between a thin uterine LUS with loss of clear zone and myometrial thinning on preoperative TAS and the risk of intraoperative bladder injury during delivery.

## Future perspectives

Anomalies of uterine contour, including the loss of clear zone, myometrial thinning and a bulge-like appearance of the LUS on ultrasound, are reported commonly in the literature as essential signs for the prenatal diagnosis and/or to predict the severity of PAS<sup>33-35</sup>. However, the abnormal attachment of placental lobules to the uterine wall is a clinical diagnosis at birth and these ultrasound features are secondary to scarification and remodeling of the anterior LUS<sup>1,13,20</sup> and, thus, not specific to clinic-pathologic diagnosis of PAS<sup>31</sup>. Similarly, abnormalities of uteroplacental circulation, in particular, retroplacental hypervascularity, are not always specific of PAS, but when concomitant with the presence of placental lacunae<sup>36</sup> and anomalies of the uterine contour in patients with prior CD presenting with a low-lying placenta or placenta previa, increase the probability not only of PAS at birth<sup>16</sup>, but also the risk of intraoperative hemorrhage and peripartum hysterectomy<sup>18–21</sup>. The association of extended uterine dehiscence and thick adhesions between a highly vascularized LUS (Table 2) and the bladder serosa or the lateral pelvic vasculature make the access to the lower pelvis difficult and increases the risk of injury to the lower urinary tract, particularly in case of placental bulge. Except for number of lacunae, anomalies of the uteroplacental circulation cannot be quantified accurately on ultrasound<sup>16</sup>. In contrast, as suggested by the present data, the severity of uterine remodeling can be graded on ultrasound (Table 3) and could be used prenatally to evaluate the risk of surgical complications, such as bladder injury, in particular when the surgical procedure is performed earlier in the third trimester.

### Conclusions

PAS is the consequence of parts of the definitive placenta developing within a uterine scar area and the severity of the condition is secondary to the lateral extension of the uterine dehiscence and RMT of the scar tissue under the placental bed, rather than the depth of abnormal villous attachment. Prenatal imaging, both ultrasound and magnetic resonance imaging, may quantify the severity of the uterine remodeling and future studies should include these parameters in the preoperative evaluation of the complexity of the surgical procedure. This approach can improve the overall assessment of patients at risk of PAS at birth and is essential to the development of new imaging protocols and tailored management strategies.

## ACKNOWLEDGMENT

We are grateful to Mr Paul Bassett, M.Sc. (Statsconsultancy Ltd, Amersham, UK) for his help with the statistical analysis.

### REFERENCES

- Jauniaux E, Fox K, Einerson B, Hussein A, Hecht JL, Silver RM. Perinatal assessment of complex cesarean delivery: beyond placenta accreta spectrum. Am J Obstet Gynecol. 2023;229:129-139.
- Jauniaux E, Jurkovic D, Hussein AM, Burton GJ. New insights into the etiopathology of placenta accreta spectrum. Am J Obstet Gynecol. 2022;227:384-391.
- Jauniaux E, Hecht JL, Elbarmelgy RA, Elbarmelgy RM, Thabet MM, Hussein AM. Searching for placenta percreta: a prospective cohort and systematic review of case reports. *Am J Obstet Gynecol.* 2022;226:837.e1-837.e13.
- Hussein AM, Elbarmelgy RA, Elbarmelgy RM, Thabet MM, Jauniaux E. Prospective evaluation of impact of post-cesarean section uterine scarring in perinatal diagnosis of placenta accreta spectrum disorder. Ultrasound Obstet Gynecol. 2022;59:474-482.
- Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: systematic review and meta-analysis. *PLoS Med.* 2018;15:e1002494.
- Jauniaux E, Chantraine F, Silver RM, Langhoff-Roos J, FIGO Placenta Accreta Diagnosis and Management Expert Consensus Panel. FIGO consensus guidelines on placenta accreta spectrum disorders: epidemiology. Int J Gynaecol Obstet. 2018;140:265-273.
- Jauniaux E, Zosmer N, De Braud LV, Ashoor G, Ross J, Jurkovic D. Development of the utero-placental circulation in cesarean scar pregnancies: a case-control study. *Am J Obstet Gynecol.* 2022;226:399.e1-399.e10.
- Karpathiou G, Chauleur C, Dridi M, et al. Histologic findings of uterine niches. Am J Clin Pathol. 2020;154:645-655.
- Jauniaux E, Mavrelos D, De Braud LV, Dooley W, Knez J, Jurkovic D. Impact of location on placentation in live tubal and cesarean scar ectopic pregnancies. *Placenta*. 2021;108:109-113.
- Calì G, Timor-Tritsch IE, Palacios-Jaraquemada J, et al. Outcome of cesarean scar pregnancy managed expectantly: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2018;51:169-175.
- Lucidi A, Jauniaux E, Hussein AM, et al. Urological complications in women undergoing cesarean section for placenta accreta spectrum disorders: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2023;62:633-643.
- Reddy UM, Abuhamad AZ, Levine D, Saade GR, Fetal Imaging Workshop Invited Participants. Fetal imaging: executive summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound Fetal Imaging Workshop. J Ultrasound Med. 2014;33:745-757.
- Hussein AM, Momtaz M, Elsheikhah A, Abdelbar A, Kamel A. The role of ultrasound in prediction of intra-operative blood loss in cases of placenta accreta spectrum disorders. Arch Gynecol Obstet. 2020;302:1143-1150.
- 14. Jauniaux E, Hussein AM, Zosmer N, et al. A new methodologic approach for clinico-pathologic correlations in invasive placenta previa accreta. *Am J Obstet Gynecol*. 2020;222:379.e1-379.e11.

- Jauniaux E, Hussein AM, Elbarmelgy RM, Elbarmelgy RA, Burton GJ. Failure of placental detachment in accreta placentation is associated with excessive fibrinoid deposition at the utero-placental interface. *Am J Obstet Gynecol.* 2022;226:243.e1-243.e10.
- Jauniaux E, D'Antonio F, Bhide A, et al. Modified Delphi study of ultrasound signs associated with placenta accreta spectrum. Ultrasound Obstet Gynecol. 2023;61:518-525.
- Finberg HJ, Williams JW. Placenta accreta: prospective sonographic diagnosis in patients with placenta previa and prior cesarean section. J Ultrasound Med. 1992;11:333-343.
- Jauniaux E, Hussein AM, Thabet MM, Elbarmelgy RM, Elbarmelgy RA, Jurkovic D. The role of transvaginal ultrasound in the third-trimester evaluation of patients at high risk of placenta accreta spectrum at birth. *Am J Obstet Gynecol.* 2023;229:445.e1-445.e11.
- 19. Cali G, Forlani F, Lees C, et al. Prenatal ultrasound staging system for placenta accreta spectrum disorders. *Ultrasound Obstet Gynecol.* 2019;53:752-760.
- Hussein AM, Fox K, Bhide A, et al. The impact of preoperative ultrasound and intraoperative findings on surgical outcomes in patients at high risk of placenta accreta spectrum. *BJOG*. 2023;130:42-50.
- Bhide A, Hussein AM, Elbarmelgy RM, Elbarmelgy RA, Thabet MM, Jauniaux E. Assessment of ultrasound features of placenta accreta spectrum in women at high risk: association with outcome and interobserver concordance. Ultrasound Obstet Gynecol. 2023;62:137-142.
- Finazzo F, D'Antonio F, Masselli G, et al. Interobserver agreement in MRI assessment of severity of placenta accreta spectrum disorders. Ultrasound Obstet Gynecol. 2020;55:467-473.
- Mufti N, Chappell J, O'Brien P, et al. Use of super resolution reconstruction MRI for surgical planning in Placenta accreta spectrum disorder: case series. *Placenta*. 2023;142:36-45.
- Pan W, Chen J, Zou Y, et al. Uterus-preserving surgical management of placenta accreta spectrum disorder: a large retrospective study. *BMC Pregnancy Childbirth*. 2023;23:615.
- 25. Schwalm H, Dubrauszky V. The structure of the musculature of the human uterus--muscles and connective tissue. Am J Obstet Gynecol. 1966;94:391-404.
- Thurn L, Lindqvist PG, Jakobsson M, et al. Abnormally invasive placenta-prevalence, risk factors and antenatal suspicion: results from a large population-based pregnancy cohort study in the Nordic countries. *BJOG*. 2016;123:1348-1355.
- Gyamfi-Bannerman C, Gilbert S, Landon MB, et al. Risk of uterine rupture and placenta accreta with prior uterine surgery outside of the lower segment. Obstet Gynecol. 2012;120:1332-1337.
- Jauniaux E, Toplis PJ, Nicolaides KH. Sonographic diagnosis of a non-previa placenta accreta. Ultrasound Obstet Gynecol. 1996;7:58-60.
- Erfani H, Salmanian B, Fox KA, et al. Urologic morbidity associated with placenta accreta spectrum surgeries: single-center experience with a multidisciplinary team. *Am J Obstet Gynecol*. 2022;226:245.e1-245.e5.
- Friedrich L, Mor N, Weissmann-Brenner A, et al. Risk factors for bladder injury during placenta accreta spectrum surgery. Int J Gynaecol Obstet. 2023;161:911-919.
- Einerson BD, Kennedy A, Silver RM, Branch DW, Comstock J, Woodward PJ. Ultrasonography of the explanted uterus in placenta accreta spectrum: correlation with intraoperative findings and gross pathology. *Obstet Gynecol.* 2023;141:544-554.
- Jauniaux E, Hussein AM, Einerson BD, Silver RM. Debunking 20<sup>th</sup> century myths and legends about the diagnosis of placenta accreta spectrum. Ultrasound Obstet Gynecol. 2022;59:417-423.
- Morel O, van Beekhuizen HJ, Braun T, et al. Performance of antenatal imaging to predict placenta accreta spectrum degree of severity. *Acta Obstet Gynecol Scand*. 2021;100(Suppl 1):21-28.
- Gatta LA, Ellestad SC, Boyd BK, et al. Validation of a sonographic checklist for the detection of histologic placenta accreta spectrum. Am J Obstet Gynecol MFM. 2023;5:101017.
- Sargent W, Gerry S, Collins SL. A Risk-Prediction model for placenta accreta spectrum severity from standardized ultrasound markers. Ultrasound Med Biol. 2023;49:512-519.
- Jauniaux E, Zosmer N, D'Antonio F, Hussein AM. Placental lakes vs lacunae: spot the differences. Ultrasound Obstet Gynecol. 2023;63:173-180.

## SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 Preoperative transabdominal ultrasound of uteroplacental interface with full bladder, showing anomalies of uterine contour, including loss of clear space and myometrial thinning (< 1 mm), at 35 ± 5 weeks' gestation. (a) Myometrium is not visible for > 90% of the length of the distance between upper uterine-bladder (B) junction and the inner os of the uterine cervix (Cx). Myometrial thickness at level 3 (calipers) was 2.8 mm. (b) Remodeling involving 30-50% of lower uterine segment (LUS). Clear zone and thin myometrium are visible in upper part of LUS (arrow). (c) Remodeling involving > 50% of LUS with placental bulge (\*). Clear zone and thin myometrium are only visible in upper part of LUS (arrow). P, placenta.