Prediction of spontaneous preterm birth in women with previous full dilatation cesarean delivery

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BACKGROUND: A previous term (≥37 weeks' gestation), full-dilatation cesarean delivery is associated with an increased risk for a subsequent spontaneous preterm birth. The mechanism is unknown. We hypothesized that the cesarean delivery scar characteristics and scar position relative to the internal cervical os may compromise cervical function, thereby leading to shortening of the cervical length and spontaneous preterm birth.

OBJECTIVE: This study aimed to determine the relationship of cesarean delivery scar characteristics and position, assessed by transvaginal ultrasound, in pregnant women with previous full-dilatation cesarean delivery with the risk of shortening cervical length and spontaneous preterm birth.

STUDY DESIGN: This was a single-center, prospective cohort study of singleton pregnant women (14 to 24 weeks' gestation) with a previous term full-dilatation cesarean delivery who attended a high-risk preterm birth surveillance clinic (2017−2021). Women underwent transvaginal ultrasound assessment of cervical length, cesarean delivery scar distance relative to the internal cervical os, and scar niche parameters using a reproducible transvaginal ultrasound technique. Spontaneous preterm birth prophylactic interventions (vaginal cervical cerclage or vaginal progesterone) were offered for short cervical length (≤25 mm) and to women with a history of spontaneous preterm birth or late miscarriage after full-dilatation cesarean delivery. The primary outcome was spontaneous preterm birth; secondary outcomes included short cervical length and a need for prophylactic interventions. A multivariable logistic regression analysis was used to develop multiparameter models that combined cesarean delivery scar parameters, cervical length, history of full-dilatation cesarean delivery, and maternal characteristics. The predictive performance of models was examined using the area under the receiver operating characteristics curve and the detection rate at various fixed false positive rates. The optimal cutoff for cesarean delivery scar distance to best predict a short cervical length and spontaneous preterm birth was analyzed.

RESULTS: Cesarean delivery scars were visualized in 90.5% (220/243) of the included women. The spontaneous preterm birth rate was 4.1% (10/243), and 12.8% (31/243) of women developed a short cervical length. A history- (n=4) or ultrasound-indicated (n=19) cervical cerclage was performed in 23 of 243 (9.5%) women; among those, 2 (8.7%) spontaneously delivered prematurely. A multiparameter model based on absolute scar distance from the internal os best predicted spontaneous preterm birth (area under the receiver operating characteristics curve, 0.73; 95% confidence interval, 0.57−0.89; detection rate of 60% for a fixed 25% false positive rate). Models based on the relative anatomic position of the cesarean delivery scar to the internal os and the cesarean delivery scar position with niche parameters (length, depth, and width) best predicted the development of a short cervical length (area under the receiver operating characteristics curve, 0.79 [95% confidence interval, 0.71−0.87]; and 0.81 [95% confidence interval, 0.73−0.89], respectively; detection rate of 73% at a fixed 25% false positive rate). Spontaneous preterm birth was significantly more likely when the cesarean delivery scar was <5.0 mm above or below the internal os (adjusted odds ratio, 6.87; 95% confidence interval, 1.34−58; P=.035).

CONCLUSION: In pregnancies following a full-dilatation cesarean delivery, cesarean delivery scar characteristics and distance from the internal os identified women who were at risk for spontaneous preterm birth and developing short cervical length. Overall, the spontaneous preterm birth rate was low, but it was significantly increased among women with a scar located <5.0 mm above or below the internal cervical os. Shortening of cervical length was strongly associated with a low scar position. Our novel findings indicate that a low cesarean delivery scar can compromise the functional integrity of the internal cervical os, leading to cervical shortening and/or spontaneous preterm birth. Assessment of the cesarean delivery scar characteristics and position seem to have use in preterm birth clinical surveillance among women with a previous, full-dilatation cesarean delivery and could better identify women who would benefit from prophylactic interventions.

Key words: cesarean scar position, full dilatation cesarean delivery, pregnancy, preterm birth, transvaginal ultrasound

Introduction

Preterm birth (PTB), which is delivery before 37 weeks' gestation, is a major global health burden.[1] Although a precise mechanism is unclear in many cases, women with previous term (≥37 weeks' gestation) deliveries are considered to be at a reduced risk for subsequent spontaneous PTB (sPTB).[2] However, recent studies reported a significant association between a previous term full-dilatation (cervical dilation of 10 cm) cesarean delivery (FDCD) and subsequent sPTB.[3−9] When compared with a first stage CD, FDCD has been associated with as high as a 6-fold increased risk for subsequent sPTB.[6] More concerningly, studies found that these women are at an increased risk for recurrent sPTB and a transvaginal cervical cerclage may be less effective.[10,11] With the rising rates of CD worldwide, there is a worrying trend of increasing FDCD.[12−16] Therefore, it is vital to evaluate the mechanisms behind the associated complications.

Transvaginal ultrasound assessments of CD scars have shown that women with a CD that was performed in the

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AJOG MFM at a Glance

Why was this study conducted?

Full dilatation cesarean delivery (CD) increases the risk for spontaneous preterm birth (sPTB) in subsequent pregnancies. The mechanism is unknown but is considered to be the consequence of trauma that weakened cervical function.

Key findings

Using a reproducible transvaginal ultrasound technique in the second trimester of pregnancy, we prospectively measured CD scar characteristics and the distance from the internal cervical os and subsequently assessed cervical length shortening and pregnancy outcome. A low CD scar (within the cervix or <5.0 mm above the internal cervical os) significantly increased the risk for developing a short cervical length (≤25 mm) and/or sPTB in a subsequent pregnancy.

What does this add to what is known?

The mechanism of sPTB among women following a previous full-dilatation CD is likely to be related to trauma near or within the cervix that compromises the function of the internal os, thereby affecting its ability to maintain a long, closed cervix.

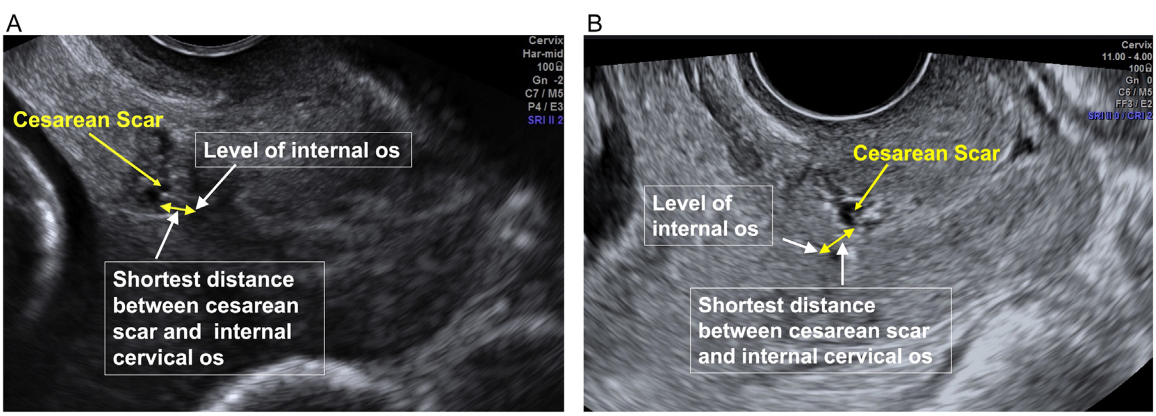
later stages of labor have lower uterine scars, and lower scars are associated with larger niche development.[17–20] A low uterine or cervical incision, CD incision extensions, and the development of a CD scar niche may affect the integrity of the cervix and compromise its function. We hypothesized that the CD scar position and niche characteristics in relation to the uterine internal cervical os may influence the risk for a subsequent sPTB. In addition, we considered that obstetrical events and previous FDCD complications might impact this risk. The objective of this study was to assess the CD scar distance and niche characteristics among women with a previous FDCD using a reproducible standardized transvaginal ultrasound protocol in the second trimester of pregnancy[21] and to develop multiparameter screening models for the prediction of sPTB and the risk for shortening cervical length (CL).

Materials and Methods

This prospective cohort study recruited pregnant women with a singleton pregnancy and a previous lower-segment FDCD at term who were referred to a preterm birth surveillance clinic at the University College London Hospital (UCLH), United King (January 2017 to April 2021). Women were excluded if they had a termination of the current pregnancy (eg, for fetal anomaly), an iatrogenic preterm birth, and a prepregnancy transabdominal cerclage. Women with a history of sPTB or late miscarriage (spontaneous mid-trimester loss, 14–24 weeks) before the FDCD delivery were also excluded. If a woman had more than 1 pregnancy during the study period, only the first pregnancy was included. The demographic characteristics, obstetrical history, and surgical complications during the previous FDCD were collected from the patient records.

Eligible women underwent a serial assessment for CL and CD scar characteristics every 2 to 3 weeks between 14 and 24 weeks' gestation using a validated transvaginal ultrasound technique without saline or gel contrast enhancement (Voluson E8 Expert ultrasound system, 4–9-MHz transvaginal probe; GE Healthcare, Zipf, Austria,).[21] Senior

FIGURE 1
Cesarean scar distance to the internal cervical os in the sagittal plane



A, Cesarean scar above the internal os. **B,** Cesarean scar in cervix.

Images adapted from Banerjee et al.[21]

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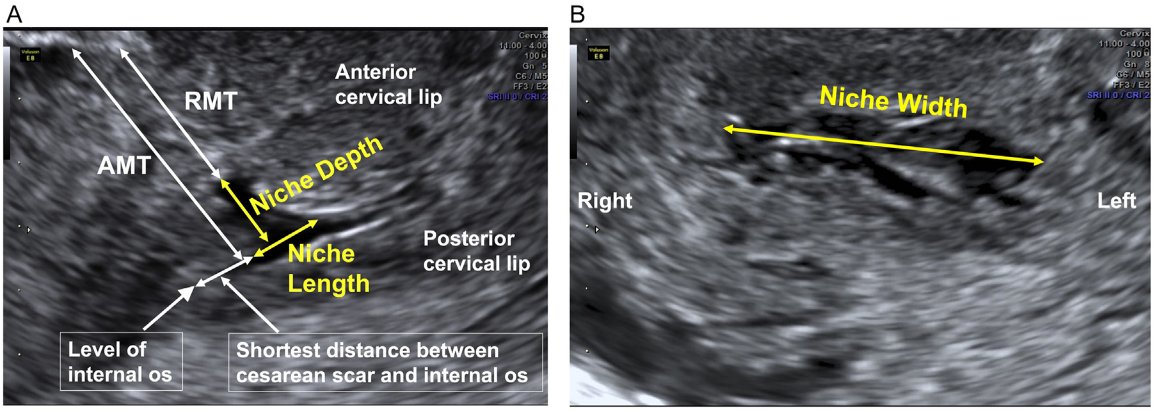
FIGURE 2
Measurements of cesarean scar niche



A, Measurement in the sagittal plane indicating the largest length, largest depth, RMT, and AMT. **B,** Measurement in the transverse plane indicating the largest width. Images adapted from Banerjee et al[21]

AMT, adjacent myometrial thickness; *RMT*, residual myometrial thickness.

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clinicians who were trained in standardized transvaginal ultrasound identification and measurements of CD scar characteristics performed the assessments. A CD scar was defined as a hypoechogenic (or rarely hyperechogenic) discontinuity of the myometrium at the anterior wall of the lower uterine segment or cervix. A niche was defined as an indentation at the CD scar site with a depth of ≥2mm. The presence of a CD scar and/or niche in or near the endocervical canal can make it difficult to identify the internal os, because the anterior portion of the lower segment or anterior cervix is often distorted because of scarring. Therefore, the relative position of the internal os was identified by visualizing the whole cervical canal, the endocervical mucosa, and by using color Doppler to identify the uterine arteries bilaterally in the paracervical region as a landmark from which the internal os position was assessed using a reproducible method.[21] To identify the position of the uterine arteries, color flow mapping was applied and the transducer was gently moved slightly laterally to the right and then to the left in the sagittal plane relative to both paracervical regions. The uterine artery was identified at the level where it straightens out. The transducer was then moved back to visualize the endocervical canal, and the relative position of the internal os was then marked with calipers at this level of the uterine arteries. The CL was recorded as the linear distance between the marked position of the internal os and the external os. CD scar position was recorded in the sagittal plane as the shortest distance from the CD scar base to the internal cervical os position.

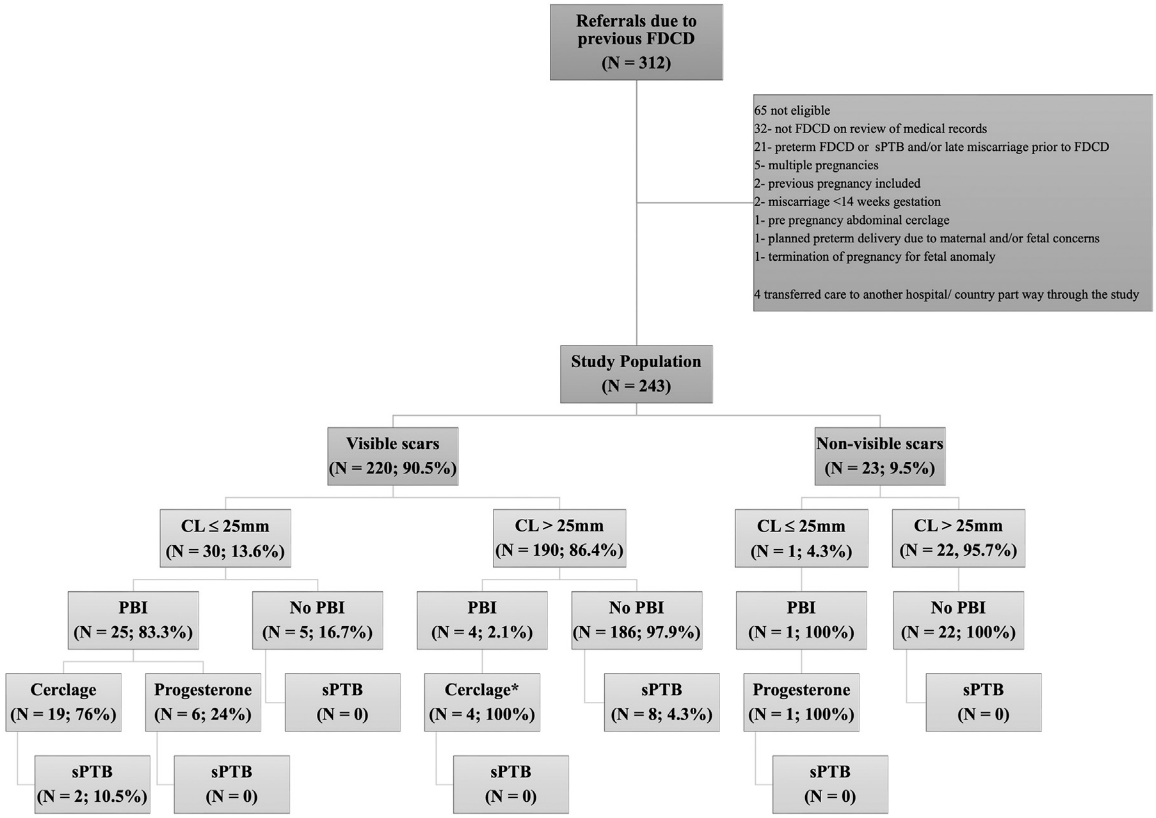
In the presence of a niche, the CD scar position was the shortest distance from the niche base to the internal os (Figures 1 and 2). The relative position of the CD scar from the internal os was defined as the anatomic distance, in millimeters, above (+mm) or below (−mm) the internal os or as the absolute distance, in millimeters, from the internal os (Supplemental Figure S1). The niche parameters (length, depth, width, residual, and adjacent myometrial thickness) were recorded in the sagittal and transverse planes (Figure 2).

Prophylactic interventions (vaginal cervical cerclage and/or vaginal progesterone) for sPTB were offered to women with a CL ≤25 mm. Women with a history of sPTB and/or late miscarriage following an FDCD were also offered prophylactic interventions irrespective of CL measurements. The primary outcome was sPTB at <37 weeks' gestation. Secondary outcomes included shortening of CL (≤25 mm) and prophylactic intervention. Maternal outcome data were collected up to discharge following delivery. Neonatal outcomes were collected up to discharge or 28 days after birth (whichever was sooner). This study was registered and approved by the UCLH clinical governance as a service evaluation project of routinely collected clinical data, therefore ethical approval was not required. No additional tests were undertaken for the purpose of this study.

Statistical analysis

Statistical analysis was performed using R version 4.0.2 (The R Foundation for Statistical Computing, Vienna, Austria). Categorical variable data were presented as numbers and percentages and continuous variables were expressed as the median and interquartile range (IQR). A comparison of the demographic characteristics was performed using chi-square tests for categorical variables and

FIGURE 3
Flowchart summarizing the study population and outcomes



(*) Four women with CL >25 mm had a cervical cerclage because of poor obstetrical history.

CL, cervical length; *FDCD*, full dilatation cesarean delivery; *PBI*, preterm birth intervention (vaginal progesterone and/or vaginal cervical cerclage); *sPTB*, spontaneous preterm birth.

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Wilcoxon Rank Sum Tests for continuous variables.

A multivariable logistic regression analysis was undertaken on data from women with visible CD scars. First, multiparameter models were developed and validated using a leave-one-out cross-validation scheme. Models for sPTB were built on the following parameters in a stepwise manner: (1) scar visualization; (2) scar distance; (3) scar distance and niche; (4) scar distance, niche, and CL; (5) scar distance, niche, CL, and previous FDCD; and (6) scar distance, niche, CL, previous FDCD, and maternal characteristics.

Prediction models for a short CL were built as above with exclusion of the CL parameters, which were outcome measures. For missing values on FDCD history, the mean was used for continuous variables, and categorical variables were coded as not present. The lowest recorded position of the CD scar and the shortest CL during mid-trimester screening were used for analysis. Prediction models were built separately using both anatomic distance and absolute scar distance from the internal os.

The predictive performance of the models was assessed using the area under the receiver operating characteristic (ROC) curve (AUC) with the 95% confidence interval (CI). The detection rate (DR) at a fixed false positive rate (FPR) of 10%, 15%, 20%, and 25% was obtained from the ROC curves.

Second, to assess the significance of parameter contributions, odds ratios (ORs) and 95% CIs were calculated based on coefficients of multivariable logistic regression models.

Third, the best threshold for CD scar distance to internal os to predict sPTB or a short CL was obtained from the ROC curve using the Youden index. Logistic regression analysis was used to demonstrate the risk for sPTB or short CL using an overall optimum CD scar distance cutoff while adjusting for certain maternal characteristics. A post hoc power analysis showed that the power to detect the difference in sPTB rate between those with CD scars located <5.0 mm above or below the internal os and those with scars situated further away was >80%.

Results

In total, 247 women were eligible for the study with complete primary and secondary outcome data available for 243 women (study flowchart in Figure 3).

TABLE 1
Primary and secondary outcomes

Outcomes	N=243
sPTB	
<37 wk	10 (4.1)
<34 wk	3 (1.2)
<28 wk	2 (0.8)
<24 wk	1 (0.4)
PPROM	2 (0.8)
CL ≤25 mm	31 (12.8)
Gestational age at delivery (wk)	39.1 (38.6−39.7)
Gestational age at CL ≤25 mm (wk)	20.4 (17.4−22.4)
Preterm birth prophylactic intervention	30 (12.3)
Vaginal cervical cerclage (total)	23 (9.6)
Ultrasound indicated	19 (7.8)
History indicated	4 (1.6)
Vaginal progesterone only	7 (2.9)

The data are presented as number (percentage) or median (interquartile range).

CL, cervical length; *PPROM*, preterm prelabor rupture of the membranes; *sPTB*, spontaneous preterm birth.

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The maternal and pregnancy demographic characteristics of the study population are summarized in Supplemental Table S1. A total of 834 transvaginal ultrasound assessments were undertaken among the 243 women (average 3.4/pregnancy) during 14 to 24 weeks' gestation.

Overall, 4.1% (10/243) of women had an sPTB. In addition, 12.8% (31/243) of women developed a short CL (≤25 mm) at a median gestation of 20 weeks and 3 days (Table 1). Furthermore, 83.9% (26/31) of women with a short CL had a prophylactic intervention for preterm birth (vaginal progesterone and/or cervical cerclage). Among the 5 women who had a short CL but did not receive any prophylactic intervention, their CL of 24 to 25 mm remained stable and lengthened in subsequent CL assessments. Overall, 23 women underwent a cervical cerclage; 19 had an ultrasound-indicated cerclage following detection of a short CL on transvaginal ultrasound, and 4 had a history-indicated elective cerclage because of previous poor obstetrical history with a CL >25 mm. In total, 8.7% (2/23) of women with a cervical cerclage had an sPTB.

The CD scar was visualized in 91% (220/243) of women. Among women with visualized scars, 6.8% (15/220) had multiple CDs, which included a CD at less than full dilatation and an FDCD, but only 1 CD scar was visualized in each case. The CD scar and niche characteristics are described in Supplemental Table S2. The CD scar distance to internal cervical os was measured for all women with a visible scar. The CD scar was located within the cervix (at the level of internal cervical os or distal to it) in 26% (57/220) of women. The CD scar location was not associated with previous FDCD characteristics, such as the duration of labor and attempt of instrumental delivery (Supplemental Table S3). Overall, in the previous FDCD delivery, a trial of vaginal instrumental delivery was attempted in 40% (91/227) of cases, and uterine extension was reported in 17% (37/224) of cases. A CD scar niche was identified in 52% (115/220) of cases. The presence of a niche was more common when the CD scar was located within the cervix as opposed to above the cervix (90% (51/57) vs 39% (64/163); *P*<.001). Scars with a niche were also noted to have a shorter interpregnancy interval than those without a niche (1 year 9 months vs 2 years 4 months; *P*=.047) (Supplemental Table S4). The median difference between repeat measurements of scar distance to internal os at 14 to 18 +6 weeks' gestation and at 19 to 24 weeks' gestation was an increase of 0.5 mm (IQR, −1.3 to 2.7; *P*=.016) (Supplemental Table S5). In a small cohort (n=40) with multiple measurements of scar distance, the mean distance increased by 0.7 mm (95% CI, −0.5 to 2.0) between 14 to 17+6 and 18 to 20+6 weeks' gestation and by 0.8mm (95% CI, −0.7 to 2.4) between 18 to 20 +6 and 21 to 24 weeks' gestation.

Because the nonvisible CD scar group had no measurable scar characteristics, the subsequent analyses included only the 220 women with visible scars. None of the 20 women for whom the CD scar was not visible delivered prematurely.

In a univariate analysis (Table 2 and 3), women who had an sPTB were more likely to have had a previous sPTB (20% [2/10] vs 2% [4/210]; *P*=.015) and multiple FDCDs (30% [3/10] vs 1% [2/210]; *P*<.0001). The absolute scar distance from the internal os was significantly associated with sPTB (median, 2.5 mm vs 6.5 mm; *P*=.016), whereas a CL ≤25 mm was significantly associated with a lower anatomic position of the CD scar (median, 0 mm vs 5.9 mm; *P*<.0001) (Table 4).

The predictive performance of multiparameter screening models for sPTB is summarized in Table 5. Model 2, based on absolute CD scar distance, performed best at predicting sPTB with an AUC of 0.73 (95% CI, 0.57−0.89) and a DR of 60% for a fixed 25% FPR. For prediction of CL ≤25 mm (Supplemental Table S6), models based on the anatomic CD scar distance were better at predicting the outcome. Model 2, based on anatomic CD scar distance, had an AUC of 0.79 (95% CI, 0.71−0.87), and model 3, with addition of the niche parameters, had an AUC of 0.81 (95%

TABLE 2
Demographic characteristics of women with visualized cesarean scars, stratified according to pregnancy outcomes

Characteristics	Gestational age at delivery: Term birth ≥37 wk (n=210)	Gestational age at delivery: sPTB <37 wk (n=10)	*P* value	Cervical length: CL >25 mm (n=190)	Cervical length: CL ≤25 mm (n=30)	*P* value
Maternal age (y)	35 (32–37)	33 (30–37)	.342	35 (32–38)	34 (31–37)	.225
BMI (kg/m^2)	24 (22–27)	26 (24–30)	.159	24 (22–27)	24 (22–27)	.611
Ethnicity						
White	151 (72)	7 (70)	1	141 (74)	17 (57)	.077
Black	14 (7)	2 (20)	.335	14 (7)	2 (7)	1
South-East Asian	26 (12)	1 (10)	1	20 (11)	7 (23)	.092
Others	19 (9)	0 (0)	.675	15 (8)	4 (13)	.525
Current smokers	11 (5)	0 (0)	1	11 (6)	0 (0)	.367
Parity						
1	179 (85)	4 (40)	.001[a]	156 (82)	27 (90)	.417
2	26 (12)	6 (60)	<.0001[a]	29 (15)	3 (10)	.63
≥3	5 (2)	0 (0)	1	5 (3)	0 (0)	.811
Previous sPTB	4 (2)	2 (20)	.015[a]	6 (3)	0 (0)	.701
Previous PPROM	1 (1)	1 (10)	.163	1 (1)	1 (3)	.638
Previous spontaneous late miscarriage	2 (1)	0 (0)	1	1 (1)	1(3)	.638
Cervical surgery	11 (5)	1 (10)	1	9 (5)	3 (10)	.455
Uterine anomaly	4 (2)	1 (10)	.554	5 (3)	0 (0)	.811
Number of previous FDCDs						
1	208 (99)	7 (70)		186 (98)	29 (97)	
2	2 (1)	3 (30)	<.0001[a]	4 (2)	1 (3)	1

The data are presented as median (interquartile range) or number (percentage).

BMI, body mass index; *CL*, cervical length; *FDCD*, full dilatation cesarean delivery; *PPROM*, preterm prelabor rupture of membranes; *sPTB*, spontaneous preterm birth.

[a] *p* value <0.05.

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CI, 0.73–0.89). Both models had a DR of 73% for a fixed 25% FPR. The ROC curves for an sPTB and a CL ≤25 mm by the competing predictive models are presented in Figure 4.

Multivariable logistic regression analysis was used to determine which characteristics significantly and independently contributed to the prediction outcomes (Supplemental Tables S7 and S8). Absolute and anatomic CD scar distance from the internal os remained consistently significant across the models for prediction of sPTB and a short CL, respectively. The number of previous FDCDs had a significant association with prediction of sPTB in model 5. Niche length and width and uterine incision extensions had a significant association with the prediction of CL ≤25 mm in certain models.

Using ROC curves, we determined that the best threshold of CD scar distance to internal os in prediction of sPTB was 4.9 mm, and to predict shortening of CL to ≤25 mm, the best threshold was 3.6 mm (Figure 5). An optimal CD scar distance threshold of <5.0 mm was considered clinically practical for prediction of both outcomes. When the CD scar was located <5.0 mm above or below the level of the internal cervical os, the sPTB rate was significantly higher than when the CD scar was further away (10.5% vs 1.4%; aOR, 6.87; 95% CI, 1.34–58; *P*=.035).

When the CD scar was located within the cervix or <5.0 mm above the internal cervical os, the risk for a shortening CL was significantly increased when compared with a higher CD scar (26.5% vs 3.3%; aOR, 17.27; 95% CI, 5.52–77.4; *P*≤.0001) (Table 6). Figure 6 demonstrates the relationship between CD scar distance, CL, and sPTB.

The maternal and neonatal outcomes are presented in Supplemental Tables S9 and S10. Two of 243 (0.8%) women were diagnosed with CD scar dehiscence and 1 of 243 (0.4%) woman had placenta accreta. There were no

TABLE 3
Previous full dilatation cesarean delivery characteristics of women with visualized cesarean scars, stratified according to pregnancy outcomes

	Gestational age at delivery			Cervical length		
Previous FDCD[a]	Term birth ≥37 wk (n=210)	sPTB <37 wk (n=10)	*P* value	CL >25 mm (n=190)	CL ≤25 mm (n=30)	*P* value
Gestational age at delivery (wk)	40 (40–41; n= 209)	40 (39–41; n= 10)	.073	40 (40–41; n=189)	41 (39–41; n=30)	.829
Birthweight (g)	3500 (3200–3845; n=204)	3635 (2938–4033; n=9)	.914	3525 (3200–3899; n=184)	3290 (3104–3595; n=29)	.03[b]
Trial of instrumental delivery	80/199 (40)	3/10 (30)	.755	69/181 (38)	14/28 (50)	.323
Duration of first and second stage of labor (h)	12.1 (8.8–17.0; n=109)	8.1 (4.7–14.6; n=4)	.167	12.2 (8.8–16.5; n=95)	11.1 (8.5–17.8; n=18)	.698
Duration of first stage of labor (h)	9.0 (4.3–12.9; n=106)	3.5 (3.3–10.4; n=4)	.119	9.0 (4.1–12.7; n=94)	7.3 (4.4–13.7; n=16)	.970
Duration of second stage of labor (h)	3.8 (2.5–4.8; n=124)	3.0 (1.5–5.7; n=4)	.641	3.7 (2.4–4.8; n=111)	3.8 (2.5–4.9; n=17)	.947
Duration of active second stage of labor (h)	1.4 (0.8–2.0; n=114)	1.9 (0.9–2.5; n=5)	.374	1.4 (0.8–2.0; n=102)	1.5 (0.8–2.3; n=17)	.436
Uterine incision extension	31/197 (16)	2/8 (25)	.835	26/176 (15)	7/29 (24)	.318
Cervical laceration	3/195 (2)	0/7 (0)	1	3/174 (12)	0/28 (0)	1
Interpregnancy interval, months	23 (16–38; n= 174)	37 (18–93; n=7)	.313	24 (16–38; n=155)	20 (17–30; n=26)	.488

The data are presented as median (interquartile range) or number/total number (percentage).

CL, cervical length; *FDCD*, full dilatation cesarean delivery; *sPTB*, spontaneous preterm birth.

[a] Data from most recent FDCD; [b] *p* value <0.05.

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TABLE 4
Transvaginal ultrasound–measured cesarean delivery scar characteristics in women with visualized scars, stratified according to pregnancy outcomes

	Gestational age at delivery			Cervical length		
TVUS CD scar characteristics	Term birth ≥37 wk (n=210)	sPTB <37 wk (n=10)	*P* value	CL >25 mm (n=190)	CL ≤25 mm (n=30)	*P* value
Scar visualization	210/233 (90.1)	10/10 (100)	.622	190/212 (89.6)	30/31 (96.8)	.346
CD scar position						
Anatomic scar distance relative to internal cervical os (mm)	5.6 (0.0–8.9)	2.5 (0.0–5.8)	.186	5.9 (3.2–9.5)	0.0 (−6.1 to 3.1)	<.0001[a]
Absolute scar distance from internal cervical os (mm)	6.5 (3.5–10.0)	2.5 (0.0–5.8)	.016[a]	6.7 (4.1–10.2)	3.1 (1.1–7.2)	.002[a]
In cervix (at or below internal os)	53 (25.2)	4 (40)	.502	38 (20.0)	19 (63.3)	<.0001[a]
In cervix or <5.0 mm above internal os	90 (42.9)	8 (80)	.047[a]	72 (37.9)	26 (86.7)	<.0001[a]
<5.0 mm above or below internal os	68 (32.4)	8 (80)	.006[a]	58 (30.5)	18 (60)	.003[a]
Presence of niche	112 (53.3)	3 (30)	.263	96 (50.5)	19 (63.3)	.268
Niche length (mm)	3.6 (2.9–5.0, n=112)	4.7 (2.7–4.7[b], n=3)	.823	3.6 (2.9–4.7; n=96)	4.1 (2.8–7.0; n=19)	.230
Niche depth (mm)	5.3 (4.2–7.3, n=112)	6.0 (3.4–11.5[b], n=3)	.709	5.5 (4.3–7.4; n=96)	4.8 (3.8–6.0; n=19)	.249
Niche width (mm)	7.5 (5.0–9.6, n=70)	8.3 (4.4–12.1[b], n=2)	.986	7.6 (5.0–10.3; n=60)	6.4 (4.6–7.8; n=12)	.162

The data are presented as median (interquartile range), number (percentage) or number/total number (percentage).

CD, cesarean delivery; *CL*, cervical length; *TVUS*, transvaginal ultrasound.

[a] *p* value <0.05; [b] Indicates range.

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TABLE 5
Performance of multiparameter screening models for the prediction of spontaneous preterm birth

	Model based on absolute scar distance					Model based on anatomic scar distance				
		Sensitivity (95% CI) at fixed FPR of:					Sensitivity (95% CI) at fixed FPR of:			
Model	AUC (95% CI)	25%	20%	15%	10%	AUC (95% CI)	25%	20%	15%	10%
1. Scar visualization[a]	0.52 (0.36–0.69)	0.2 (0–0.5)	0.11 (0–0.4)	0.05 (0–0.24)	0 (0–0.07)	0.52 (0.36–0.69)	0.2 (0–0.5)	0.11 (0–0.4)	0.05 (0–0.24)	0 (0–0.07)
2. Scar distance[b]	0.73 (0.57–0.89)	0.6 (0.3–0.9)	0.5 (0.2–0.8)	0.5 (0.2–0.8)	0.3 (0–0.7)	0.66 (0.55–0.77)	0.3 (0.1–0.6)	0.3 (0–0.6)	0.1 (0–0.5)	0 (0–0.2)
3. Scar distance and niche[b]	0.68 (0.46–0.90)	0.5 (0.2–0.8)	0.5 (0.2–0.8)	0.5 (0.2–0.8)	0.4 (0.1–0.7)	0.63 (0.39–0.87)	0.6 (0.3–0.9)	0.5 (0.1–0.8)	0.3 (0.1–0.7)	0.3 (0–0.6)
4. Scar distance, niche, and CL[b]	0.69 (0.52–0.87)	0.5 (0.1–0.8)	0.4 (0.1–0.7)	0.4 (0.1–0.7)	0.3 (0.1–0.6)	0.61 (0.37–0.86)	0.6 (0.3–0.9)	0.5 (0.2–0.8)	0.4 (0.1–0.7)	0.4 (0.1–0.7)
5. Scar distance, niche, CL and FDCD history[b]	0.71 (0.54–0.89)	0.5 (0.2–0.8)	0.4 (0.1–0.7)	0.4 (0.1–0.7)	0.4 (0.1–0.7)	0.62 (0.38–0.86)	0.6 (0.2–0.9)	0.5 (0.2–0.8)	0.4 (0.1–0.7)	0.3 (0.1–0.6)
6. Scar distance, niche, CL, FDCD, and maternal characteristics[b]	0.67 (0.49–0.85)	0.5 (0.20–0.8)	0.4 (0.1–0.7)	0.27 (0–0.6)	0.17 (0–0.38)	0.65 (0.44–0.86)	0.6 (0.2–0.9)	0.4 (0.1–0.8)	0.3 (0–0.6)	0.2 (0–0.5)

The model parameters are as follows: (1) scar visualization; (2) scar distance (scar distance in relation to internal cervical os and gestation at measurement); (3) scar distance and niche (step 2 parameters plus presence of niche, niche length, niche depth, and niche width); (4) scar distance, niche, and CL (step 3 parameters and shortest CL and gestation at measurement); (5) scar distance, niche, CL, and previous FDCD (step 4 parameters and previous FDCD: gestation at delivery, birthweight, trial of instrumental delivery, uterine incision extensions, cervical lacerations, number of FDCDs); 6) scar distance, niche, CL, FDCD history, and maternal characteristics (step 5 parameters and maternal age, body mass index, ethnicity, smoking status, parity, previous spontaneous preterm birth, previous spontaneous late miscarriage, previous preterm prelabor rupture of membranes, uterine anomaly, cervical surgery, recurrent urinary tract infection in pregnancy).

AUC, area under the receiver operating characteristics curve; *CI*, confidence interval; *CL*, cervical length; *FDCD*, full dilatation cesarean delivery; *FPR*, false positive rate.

[a] n=243; [b] n=220 (visualized scars).

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stillbirths or neonatal deaths. As expected, neonatal adverse outcomes were significantly higher among women who delivered prematurely.

Comments

Principal findings

After an FDCD, with the use of a validated transvaginal ultrasound technique, we have shown that a CD scar located <5.0 mm above or below the internal cervical os is associated with an increased risk for subsequent sPTB, whereas a CD scar located within the cervix or <5.0 mm above the internal cervical os was associated with shortening CL.

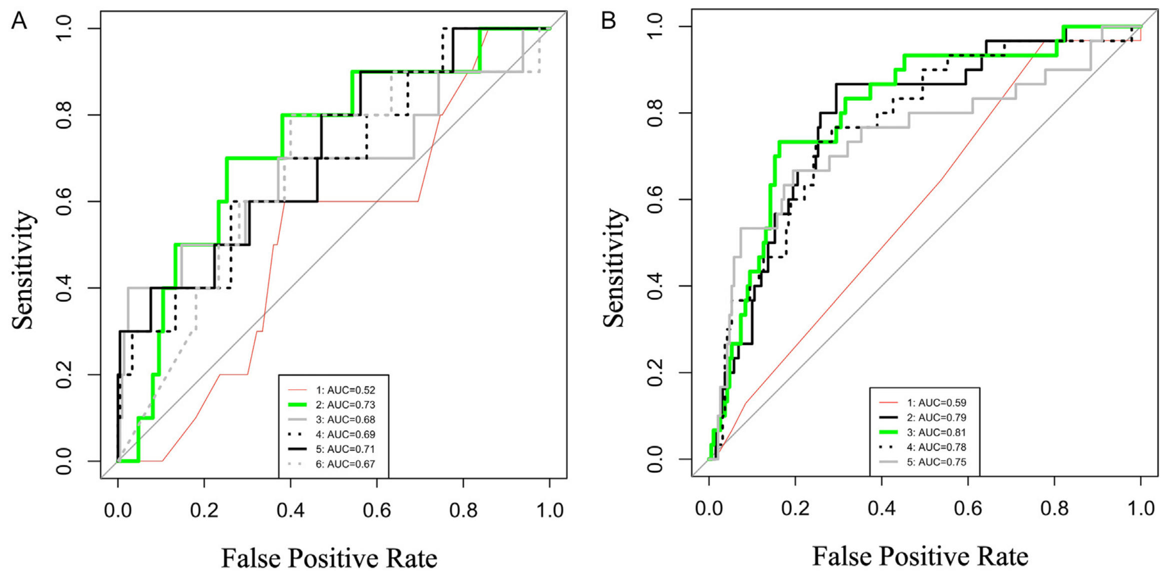
In pregnancies after an FDCD, multiparameter models had a moderate ability to predict a shortening CL and had a relatively underwhelming performance in predicting sPTB. However, in our cohort of women with a previous FDCD, 83.9% (26/31) of women with a short CL had a prophylactic intervention for preterm birth, and the sPTB rate of 4.1% was far lower than that published in international cohorts. Therefore, the type and timing of treatment for women with a previous FDCD are important confounding factors in determining the true predictive ability of the multiparameter models for sPTB.

Overall, a CD scar distance of <5.0 mm above the internal cervical os was identified as an optimal threshold in the prediction of sPTB and/or CL ≤25 mm.

Results in the context of what is known

We used a recently validated, reproducible, midtrimester transvaginal ultrasound technique to assess the CD scar position and the niche in relation to the internal cervical os.[21] We are not aware of any previous studies that investigated the association between specific CD scar characteristics assessed during pregnancy by ultrasonography and the subsequent risk for sPTB. Previous studies have explored the prognostic value of CD scar characteristics to predict obstetrical complications, such as uterine dehiscence or rupture and placenta accrete spectrum disorders.[22–24]

FIGURE 4
Receiver operating characteristic curves for competing prediction models



A, Prediction of sPTB based on absolute cesarean scar distance to internal cervical os. The models evaluated were (1) scar visualization; (2) scar distance; (3) scar distance and niche; (4) scar distance, niche, and CL; (5) scar distance, niche, CL, and previous FDCD; and (6) scar distance, niche, CL, FDCD history, and maternal characteristics. **B,** Prediction of shortening cervical length (≤25 mm) based on anatomic cesarean scar distance to internal cervical os. The models evaluated were (1) scar visualization; (2) scar distance; (3) scar distance and niche; (4) scar distance, niche, and previous FDCD; and (5) scar distance, niche, FDCD history, and maternal characteristics.

AUC, area under the receiver operating characteristic curve; *CL*, cervical length; *FDCD*, full dilatation cesarean delivery; *sPTB*, spontaneous preterm birth.

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This was not the primary aim of our study and because of small numbers, we did not evaluate these obstetrical outcomes.

Similar to our findings, Naji et al[25] reported a rate of 88.8% for CD scar visualization in pregnancy using a transvaginal ultrasound, and Savukyne et al[26] reported a niche prevalence of 51.6%. A CD scar niche was more common in cases with low scars. This is consistent with previous studies, including a randomized trial in which large CD scar defects were more common among cases with low CD scar incisions than among those with high CD scar incisions, defined as an incision that is 2 cm below or 2 cm above the uterovesical fold (41% vs 7%; P<.001).[17,20]

The cervix is crucial in continuing the pregnancy against the increasing intrauterine pressure with advancing gestation and to withstand uterine contractions. The cervix may have a specialized sphincter at the internal os with evidence of smooth muscle cells and a system of dense, well-defined, encircling fibers in the proximal region of the cervix.[27,28] Presence of a CD scar and niche, especially at the level of the internal cervical os, could therefore account for the increased risk for sPTB we identified.

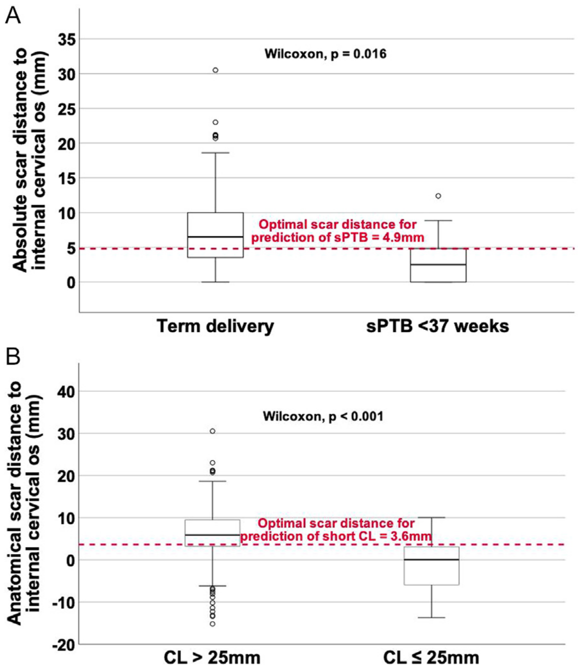
Clinical implications

The association between sPTB and a previous FDCD is well known, and national maternity care programs, such as the United Kingdom Saving Babies Lives Care Bundle 3, recommend preterm birth surveillance for women who underwent an FDCD.[29,30] It is not only an FDCD that confers an increased risk for subsequent sPTB. CD performed at a low fetal head station has been associated with a higher rate of subsequent sPTB (aOR, 1.6; 95% CI, 1.23−2.11) when compared with a CD at high fetal head station.[31] Our findings suggest that the etiology is iatrogenic trauma associated with a CD incision placed at or extending close to the internal os and cervix. Preventing sPTB in these pregnancies will require the development of CD incision, delivery, and repair techniques to prevent iatrogenic cervical injury and re-evaluation of our management of labor to reduce the need for an FDCD. Our findings show that assessing the CD scar position using a transvaginal ultrasound in pregnancy can predict the risk for a shortening CL and sPTB. This could guide serial CL screening to identify those who would benefit most from prophylactic interventions.

Research implications

Although our multiparameter models show promise, the predictive ability of the models should be externally validated before introduction into clinical

FIGURE 5
Cesarean scar height and CL shortening or preterm birth



A, Absolute scar distance to internal cervical os and sPTB. **B,** Anatomic scar distance to internal cervical os and shortening of CL.

CL, cervical length; *sPTB*, spontaneous preterm birth.

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practice. Assessment of the CD scar position and its characteristics from the postnatal period through to the subsequent pregnancy may provide individualized risk assessment and personalized antenatal surveillance. Our findings in this study and our previous reproducibility study highlighted that using a transvaginal ultrasound and having the probe in direct proximity to the cervix allows optimal visualization and precise characterization of the CD scar because of the enhanced resolution.[21] Future studies would therefore need to be conducted with the use of transvaginal ultrasonography to reliably assess the scar characteristics because the reduced resolution of a transabdominal ultrasound would lead to less accurate assessments. Further studies are also required to assess the use of predictive markers, such as fetal cervicovaginal fibronectin concentration.

Optimal management of women with a previous FDCD is currently unknown. Although 91.3% (21/23) of women in our study with a vaginal cervical cerclage had a term delivery, the ideal management options still need further evaluation.

Strengths and limitations

In this study, real-time, 2-dimensional ultrasound assessment of CD scar

TABLE 6
Prediction of spontaneous preterm birth (sPTB) and short cervical length (≤25 mm) according to cesarean scar position relative to the internal cervical os

	sPTB			CL ≤25 mm			sPTB and/or CL <25 mm		
FDCD scar location	Yes (n=10)	No (n=210)	[a]aOR (95% CI)	Yes (n=30)	No (n=190)	[a]aOR (95% CI)	Yes (n=38)	No (n=182)	[a]aOR (95% CI)
Scar <5.0 mm above or below the internal cervical os	8	68	6.87 (1.34–58); *P*=.035	18	58	3.87 (1.66–9.4); *P*=.002	24	52	4.13 (1.87–9.08); *P*≤.0001
Scar ≥5.0 mm above or below the internal cervical os	2	142		12	132		14	130	
Scar in cervix or <5.0 mm above internal cervical os	8	90	4.91 (0.98 –39.3); *P*=.076	26	72	17.27 (5.52–77.4); *P*≤.0001	32	66	12.65 (4.45-–36.0); *P*≤.0001
Scar >5.0 mm above internal cervical os	2	120		4	118		6	116	

aOR, adjusted odds ratio; *CI*, confidence interval; *CL*, cervical length; *FDCD*, full dilatation cesarean delivery; *PPROM*, preterm prelabor rupture of membranes; *sPTB*, spontaneous preterm birth.

[a] Adjusted for the following maternal characteristics: age, body mass index, ethnicity, smoking status, parity, previous sPTB, previous PPROM, previous late miscarriage, cervical surgery, and uterine anomaly.

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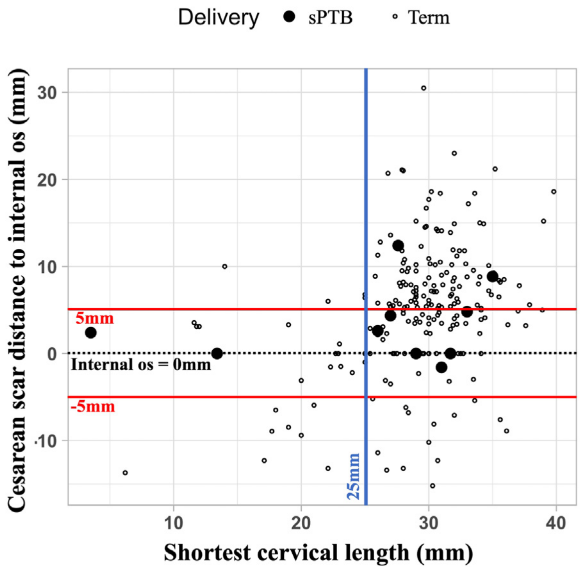
FIGURE 6
Scatterplot of Cesarean scar height and pregnancy outcome



sPTB, spontaneous preterm birth.

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characteristics was performed by experienced operators in a routine, busy, preterm surveillance clinic, thus the findings are robust and the technique is feasible for routine clinical application. Follow-up rates were high with obstetrical outcomes available for >98% of the women, and CD scar position measurement was obtained in 90.5% of the women. Limitations of our study include the single-institution study design and the small numbers of women who had sPTB. Our study did not have adequate power to evaluate individual niche characteristics. We noted that women who developed a short CL had a tendency of having a higher prevalence of a niche than women with a long CL (63.3% vs 50.5%; *P*=.27). This may be clinically important, because it has been hypothesized that a niche may alter immunobiology, increase inflammation, and distort the function of the uterus and cervix.[32–34] Among women with visualized scars, 6.8% (15/220) had multiple CDs, including a CD at less than full dilatation and an FDCD. Although it is not possible to ascertain if the scar that was visualized was from the FDCD, we consider it unlikely that this would have had a significant impact on the results. Only 1 CD scar was visualized among women who had more than 1 CD, and CD performed at full dilatation is associated with lower scars with larger niches that are easier to visualize.[17–20]

Because 83.9% of women with short CL had a prophylactic intervention for preterm birth, the true clinical use of CD scar position and niche as a predictive marker for sPTB remains to be evaluated.

Conclusion

A low CD scar (within the cervix or <5.0 mm above the internal cervical os) significantly increased the risk for shortening CL and/or subsequent sPTB. These findings suggest that a low scar, which commonly occurs following an FDCD, compromises the structural and functional integrity of the internal cervical os, leading to cervical shortening and sPTB.

Although further validation is required, assessment of CD scar characteristics and position relative to the internal cervical os seems to be useful for clinical surveillance among women with a previous FDCD and to identify those who would benefit from prophylactic interventions for sPTB. ■

CRediT authorship contribution statement

Amrita Banerjee: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Validation. **Maria Ivan:** Conceptualization, Data curation, Validation, Writing – review & editing, Investigation. **Tatiana Nazarenko:** Formal analysis, Writing – review & editing. **Roberta Solda:** Investigation, Writing – review & editing. **Emmanouella F. Bredaki:** Data curation, Investigation, Writing – review & editing. **Davide Casagrandi:** Investigation, Validation, Writing – review & editing. **Amos Tetteh:** Investigation, Validation, Writing – review & editing. **Natalie Greenwold:** Data curation, Investigation, Validation, Writing – review & editing. **Alexey Zaikin:** Formal analysis, Writing – review & editing. **Davor Jurkovic:** Conceptualization, Supervision, Writing – review & editing. **Raffaele Napolitano:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing. **Anna L. David:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing. ■

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.ajogmf.2024.101298.

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