

ORIGINAL RESEARCH

Prediction of preterm birth using 3D volume cesarean scar morphology in pregnant women with previous advanced labor cesarean delivery

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Abstract

Introduction: This study aimed to develop a multiparameter predictive model for spontaneous preterm birth in pregnant women with a history of advanced labor cesarean delivery, using cesarean scar ultrasound characteristics.

Material and Methods: This prospective observational cohort study included pregnant women with a history of advanced labor cesarean delivery (≥ 8 cm cervical dilatation) at University College London Hospitals (August 2019–August 2023). Participants underwent transvaginal ultrasound using validated protocols for cesarean scar evaluation. Measurements included scar distance to the internal os, niche dimensions (length, depth, and width), residual and adjacent myometrial thickness, and 3D niche and cervical volumes. Predictive models for spontaneous preterm birth and short cervical length ≤ 25 mm were developed using multivariable logistic regression, adjusting for potential confounders.

Results: During the surveillance period, 12.6% (21/166) of women developed a short cervix, and 23.5% (39/166) received preterm birth prophylactic interventions. Spontaneous preterm birth rate was 7.8% (13/166) < 37 weeks and 4.8% (8/166) < 34 weeks. The cesarean scar was visualized in 89.8% (149/166), with a niche identified in 48.3% (72/149) of women. Scars positioned at or caudal to the internal cervical os were associated with significantly higher risks of short cervix and/or spontaneous preterm birth compared to scars cranial to the internal os (aOR 5.26, 95% CI 1.59, 17.32, $p = 0.006$; aOR 5.00, 95% CI 1.10, 22.78, $p = 0.037$, respectively). Traditional predictive models based on cervical length and obstetric history demonstrated modest performance. Scar distance to the internal os consistently emerged as the strongest independent predictor of short cervix across all models ($p < 0.001$ – 0.005). Models

Abbreviations: AMT, Adjacent myometrial thickness; AUC, Area under the receiver operator characteristic curve; CL, Cervical length; CD, Cesarean delivery; FPR, False positive rate; GA, Gestational age; ROC, Receiver operator characteristic; RMT, Residual myometrial thickness; sPTB, Spontaneous preterm birth.

UCLH Preterm Birth Clinic Research Group includes Amos Tetteh, Natalie Greenwold, Kasya Maksym, Davide Casagrandi.

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incorporating 3D ultrasound scar parameters improved predictive accuracy, with the final model achieving AUC 0.91 (95% CI 0.81, 0.98) and 91% (95% CI 0.73, 1.00) sensitivity at FPR of 25% for spontaneous preterm birth. For short cervix prediction, the AUC was 0.89 (95% CI 0.80, 0.96), at 88% (95% CI 0.62, 1.00) sensitivity for the same FPR.

Conclusions: 3D transvaginal ultrasound assessment of cesarean scar morphology was associated with improved prediction of spontaneous preterm birth in pregnant women with a history of advanced labor cesarean delivery; however, scar position relative to the internal os remained the strongest individual predictor.

KEYWORDS

3D ultrasound, cesarean, niche, preterm birth, scar, volume

1 | INTRODUCTION

Preterm birth (PTB) remains a significant global health challenge, despite extensive research into its risk factors^{1,2} and the implementation of preventative strategies.^{3–5}

The estimated global PTB reduction rate was –0.14% from 2010 to 2020.⁶ While a history of spontaneous PTB (sPTB) is recognized as the strongest predictor of subsequent PTB,² this pattern does not apply to women who have undergone term advanced labor cesarean delivery (CD). Studies in the last decade have identified advanced labor CD as a distinct risk factor for subsequent late miscarriage or sPTB, increasing the risk up to threefold compared to having a prior term vaginal birth.^{7–14} In a recent systematic review, pooled estimates indicated that the rate of sPTB in subsequent pregnancies was 6.9% after full dilatation CD and 2.6% following operative vaginal birth.¹⁵ Increasing cervical dilatation at the time of CD has been independently associated with a higher risk of subsequent sPTB,^{7,11} with evidence suggesting that this risk is greatest following CD in advanced labor (≥ 8 cm dilatation).¹⁴ A recent postnatal ultrasound study¹⁶ showed that CD in advanced labor, compared with early labor CD, more frequently results in low-positioned hysterotomy incisions involving the cervix, which may influence cervical function in subsequent pregnancies. With the prevalence of CD on the rise, especially in late stages of labor,^{17,18} this association needs closer attention to refine screening and management strategies for at-risk populations.

Current methods for PTB surveillance—such as transvaginal cervical length (CL) ultrasound measurement, obstetric history assessment, and point-of-care biomarker testing—have not been validated for women with previous advanced labor CD. One promising approach to address this gap is the use of transvaginal ultrasound to evaluate CD scar morphology and location.^{19–21} Our previous research has found that a CD scar within 5 mm of the internal os on 2D ultrasound is linked to a higher risk of sPTB, suggesting that scar location may affect cervical function.²² CD scar ultrasound appearance may vary depending on the acquisition plane and may be influenced by factors such as irregular scar niche configuration and branching morphology, and defects related to hysterotomy extensions. Compared to 2D ultrasound, 3D

Key message

Ultrasound assessment of the scar distance to the internal os may be considered for inclusion in spontaneous preterm birth risk stratification for women with advanced labor cesarean delivery.

ultrasound offers additional benefits, including superior visualization through coronal plane reconstruction²³ and accurate volume assessment,^{24–26} which enables a more comprehensive evaluation of scar niche volume characteristics.²⁷ To our knowledge, no previous studies have directly evaluated associations between 3D ultrasound advanced labor CD scar parameters in pregnancy and subsequent sPTB. We hypothesized that CD scar position and morphology assessed using 3D transvaginal ultrasound are associated with subsequent CL shortening and sPTB in women with advanced labor CD, and assessment of these ultrasound parameters may improve risk stratification in this high-risk group of women. The aim of this study was to evaluate the factors, including 3D ultrasound scar morphology, that could be applied in a multiparametric approach to predict the development of a short CL and/or sPTB in pregnant women with a history of advanced labor CD.

2 | MATERIAL AND METHODS

This single-center prospective observational cohort study included consecutive singleton pregnant participants with a history of previous term advanced labor emergency CD (cervical dilatation ≥ 8 cm) who received PTB surveillance at the University College London Hospitals NHS Foundation Trust, London, UK, between August 2019 and August 2023. Participants were monitored and clinically managed within a dedicated specialist antenatal service every 2–3 weeks between 12 and 24 weeks of gestation, following local and national clinical care pathways for women considered at increased risk of sPTB. Participants who terminated the pregnancy or experienced iatrogenic PTB in the

studied pregnancy were excluded, as were women with a history of sPTB or late miscarriage prior to the advanced labor CD or with pre-pregnancy transabdominal cerclage placement. Cases of late miscarriage or sPTB occurring after the advanced labor CD were included in the study. If a participant experienced more than one pregnancy during the study period, only the pregnancy with complete data and closest to the advanced labor CD was included.

Prophylactic interventions for sPTB, such as vaginal cervical cerclage and/or progesterone, were offered based on detection of a short CL (≤ 25 mm) and/or a history of late miscarriage or sPTB following the advanced labor CD. Three types of vaginal cervical cerclage were performed under regional anesthesia: McDonald, Shirodkar, and modified Wurm technique,²⁸ selected according to previous clinical history, surgeon's or patient's preference. Micronized vaginal progesterone at a dose of 200–400 mg vaginally or rectally was offered to women as an alternative to cervical cerclage if the CL was ≤ 25 mm; however, if the CL was < 15 mm, cerclage was prioritized. No additional tests beyond standard sPTB surveillance screening were conducted.

2.1 | Examination ultrasound protocol of cesarean scar morphology

Transvaginal 3D ultrasound volumes were acquired by four fetal medicine specialists (MI, AB, ALD, and RN) using a Voluson E8 or E10 Expert ultrasound system (GE® Healthcare, Austria) equipped with a 4–9 MHz 3D TV probe. The region of interest for volume acquisition encompassed the entire cervix and lower uterine segment in a longitudinal view, along with three key anatomical landmarks: the internal cervical os, cervical canal, and external cervical os. The location of the internal cervical os was further confirmed through 2D color Doppler mapping of the uterine arteries in the paracervical region.^{21,29}

The automatic volume capture was set with a 120° acquisition angle and high image resolution. The acquisition time for each volume was 4–5 s, during which time participants were instructed to remain still to minimize motion artifacts. The 3D volumes were processed offline by a single operator (MI) using the VOCAL imaging function in the 4D View software (GE® Healthcare) on a Windows® 10 platform, following a validated and highly reproducible CD scar examination protocol.²⁷ The recorded volumes were displayed in three reference planes: sagittal (A), transverse (B), and coronal (C). The CD scar was identified by manipulating the sagittal plane (A) along the x-, y-, and z-axis and using the “parallel shift” function to move front to back through the volume. A CD scar niche was defined as an “indentation at the level of the scar with a depth measuring ≥ 2 mm”.²⁰ Measurements of CL, niche dimensions (length, depth, width), residual and adjacent myometrial thickness (RMT and AMT), and scar distance to internal os were recorded. The niche to internal os distance was measured by placing the calipers at the nearest edge of the niche to the internal os and the internal os. The scar distance to the internal os was recorded as an anatomic value—a mathematically positive value indicated that the CD scar was located cranial to the internal os, while a negative value indicated that the CD scar was located caudal to the internal os (Figure 1).²⁷ Niche and cervix volumes were calculated using manual contouring in sic reference planes, spaced at 30° angle intervals.

2.2 | Outcome measures

The primary aim of the study was to evaluate the predictive performance of sPTB screening models for women with a history of advanced labor CD by integrating 3D ultrasound CD scar features and CL alongside clinical history. Secondary outcomes included the prediction of the development of a short CL ≤ 25 mm. For cases with

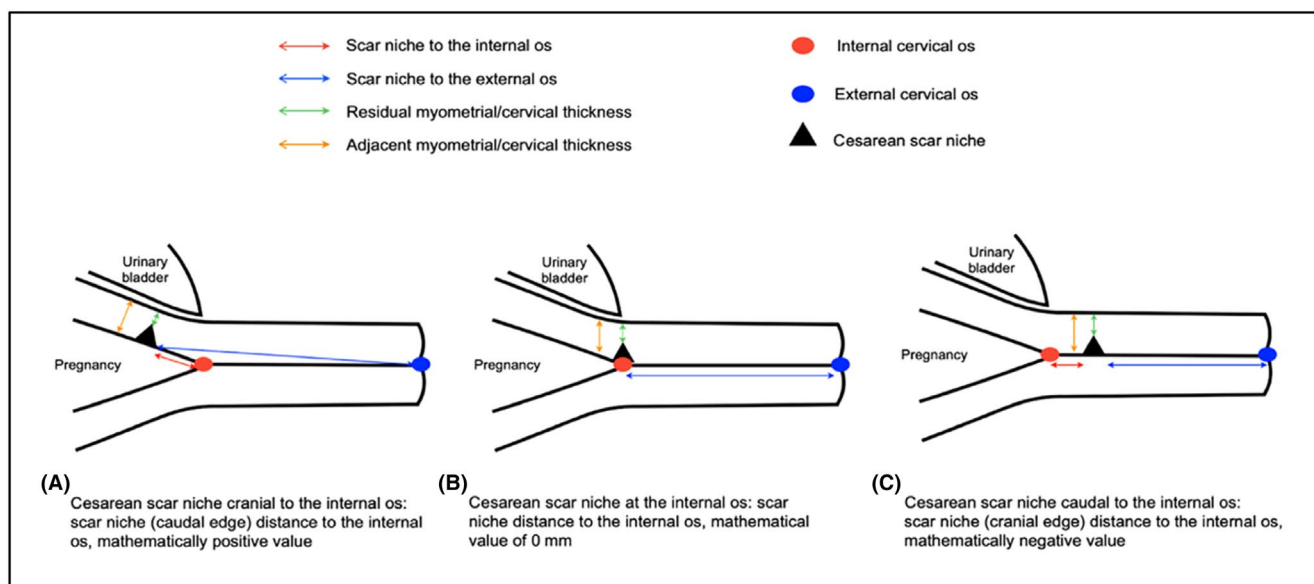


FIGURE 1 Schematic representation of cesarean scar niche measurements according to scar position relative to the internal cervical os.

multiple examinations at different gestational ages (Gas), the examination with the shortest scar distance to the internal os was used in the predictive models, and the shortest CL recorded during the surveillance period was considered. In women who received a cervical cerclage, the CD scar measurements were recorded prior to cerclage placement.

Data were collected during the clinic appointment and from electronic medical records (Viewpoint®, EPIC®), recording demographic details as well as maternal and neonatal clinical characteristics and outcomes. Some data fields relied on detailed information from the time of the index advanced labor CD (e.g., uterine extension, postpartum hemorrhage), which was unavailable for women who gave birth at other hospital facilities. Analyses were restricted to cases with complete data for the main study outcomes.

2.3 | Statistical analyses

Categorical variables were summarized as numbers and percentages, while continuous numeric variables were expressed as median and interquartile range or median and standard deviation, as appropriate. Continuous variables were assessed for normality using visual inspection of histograms and Shapiro–Wilk tests. Demographic

characteristics were compared using Chi-square tests for categorical variables and Wilcoxon Rank Sum tests for continuous variables. The optimal threshold for scar distance to the internal os in predicting sPTB or short CL (≤ 25 mm) was determined using receiver operator characteristic (ROC) curve analysis. Logistic regression models were applied to evaluate the risk for sPTB and short CL, adjusting for potential cofounders (demographics: age, ethnicity, body mass index, smoking status, parity, and mode of birth; risk factors for sPTB: cervical surgery and uterine anomaly).

Exploratory prediction models were constructed using R®, version 4.2.2 (The R Foundation for Statistical Computing, Vienna, Austria). To maximize the data available for training, the bootstrap ROC method (boot.roc function from the fbroc package) was implemented. Models were trained on the full dataset, and their performance was evaluated on random samples with replacement from the same dataset. No imputations were used to estimate or replace missing/irrelevant data points in the analysis (e.g., trial of instrumental birth where CD occurred before full dilatation). Parameters were included in the model in a stepwise manner (Table 1), and their predictive performance was evaluated by calculating the area under the ROC curve (AUC). Detection rates were determined at fixed false positive rates (FPRs) of 10%, 15%, 20%, and 25% based on the ROC curves.

TABLE 1 Summary of parameters included in each predictive model.

	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12
Demographics, sPTB risk factors, CL, fFN	●	●	●	●	●	●	●	●	●	●	●	●
CD clinical data	●	●	●	●	●	●	●	●	●	●	●	●
Scar visualisation	●	●	●	●	●	●	●	●	●	●	●	●
Niche presence	●	●	●	●	●	●	●	●	●	●	●	●
Scar distance to IO – continuous* (mm)	●	●	●	●	●	●	●	●	●	●	●	●
Scar distance to IO – categorical (<5mm)	●	●	●	●	●	●	●	●	●	●	●	●
Niche length, depth, width (mm)	●	●	●	●	●	●	●	●	●	●	●	●
RMT: AMT ratio	●	●	●	●	●	●	●	●	●	●	●	●
Niche volume – continuous (mm ³)	●	●	●	●	●	●	●	●	●	●	●	●
Niche volume – categorical (≤ 0 , 0–125, 125–600, >600 mm ³)	●	●	●	●	●	●	●	●	●	●	●	●
Cervix volume (mm ³)	●	●	●	●	●	●	●	●	●	●	●	●
Niche : cervix volume ratio	●	●	●	●	●	●	●	●	●	●	●	●

Abbreviations: AMT, adjacent myometrial thickness; CD clinical data: interpregnancy interval, trial of instrumental birth; CD, cesarean delivery; CL, cervical length (sPTB models only); fFN, fetal fibronectin; IO, internal cervical os; RMT, residual myometrial thickness; sPTB, spontaneous preterm birth.

*Anatomic value—a mathematically positive value indicates that the CD scar is located cranial to the internal os, and a negative value indicates that the CD scar is located caudal to the internal os.

TABLE 2 Demographic and advanced labor cesarean birth characteristics of the study population.

Demographic characteristics	N = 166
Maternal age (years)	35 (32, 37)
Ethnicity	
White	97 (58.4)
Black	19 (11.4)
Southeast Asian	29 (17.5)
Mixed/Other	21 (12.6)
BMI at booking (kg/m ²)	24.4 (21.9, 27.5), N = 165
Smoker	2 (1.2)
Parity	
1	126 (75.9)
2	35 (21.1)
≥3	5 (3.0)
IVF conception	12 (7.2)
Risk factors for PTB	
Previous sPTB	5 (3.0)
Previous PPROM	3 (1.8)
Previous LM	4 (2.4)
Cervical surgery (LLETZ, cone biopsy)	6 (3.6)
Uterine anomaly	2 (1.2)
Number of advanced labor CD (8–10 cm)	
1	164 (98.8)
2	2 (1.2)
Number of previous CDs	
1	149 (89.8)
≥2	17 (10.2)
Advanced labor CD characteristics	
Cervical dilatation (cm)	
8	6 (3.6)
9	11 (6.6)
10	149 (89.8)
Gestational age at birth (weeks)	40 (39, 41)
Birthweight (g)	3469 ± 485 (2280, 4640)
Active second stage	107 (73.3), N = 146
Trial of instrumental birth	61 (42.4), N = 144
Hysterotomy extensions	15 (20.0), N = 75
Uterine/broad ligament	15 (20.0)
Cervical	0 (0)
Postpartum hemorrhage >1000 mL	17 (15.3%), N = 111
Interpregnancy interval (months)	32 (22, 61)

Note: Data presented as median (IQR, interquartile range), n (%).

Abbreviations: BMI, body mass index; CD, cesarean birth; IVF, in vitro fertilization; LLETZ, large loop excision of the transformation zone; LM, late miscarriage; PPROM, preterm prelabor rupture of membranes; sPTB, spontaneous preterm birth.

TABLE 3 Study outcomes.

Outcome	N = 166
Spontaneous PTB	
<37 weeks' gestation	7.8% (n = 13)
<34 weeks' gestation	4.8% (n = 8)
<28 weeks' gestation	1.8% (n = 3)
<24 weeks' gestation	1.2% (n = 2)
Gestational age at birth	39w1d (38w2d, 39w5d)
PPROM	4.2% (n = 7)
Cervical length ≤25 mm	12.6% (n = 21)
Cervical length ≤15 mm	3.0% (n = 5)
Gestational age at cervical length ≤25 mm	18w6d (15w6d, 22w2d)
Prophylactic preterm birth intervention	23.5% (n = 39)
Vaginal cervical cerclage	9% (n = 15)
Prophylactic progesterone only	14.5% (n = 24)

Note: Data presented as median (IQR, interquartile range), % (n).

Abbreviations: PTB, preterm birth; PPROM, preterm prelabor rupture of membranes.

3 | RESULTS

During the study, 3D ultrasound volumes were acquired for 196 women, with 166 eligible participants included with complete primary and secondary outcome data. This cohort underwent 302 3D transvaginal ultrasound examinations during the PTB surveillance period. The demographic and advanced labor CD characteristics of the population examined in this study are detailed in Table 2. As previous full dilatation CD was a national referral criterion for PTB surveillance before the study period began, most women were in this group—89.8% (149/166) of cases had a full dilatation CD, and the median GA at birth was 40 weeks.

The rate of sPTB <37 weeks' gestation was 7.8% (13/166), with just over half of the PTBs 4.8% (8/166) occurring <34 weeks and 1.2% (2/166) delivering <24 weeks' gestation (Table 3). The median GA at delivery was 39w1d (38w2d, 39w5d). Among women who experienced sPTB, approximately half, 46.1% (6/13), demonstrated no significant CL shortening during the surveillance period and had no other high-risk PTB factors than the previous advanced labor CD. In the study cohort, 12.6% (21/166) of women were identified with a CL ≤25 mm. The median GA at the time of diagnosis was 18w6d (15w6d, 22w2d). Among these women, 4.8% (1/21) opted for no prophylactic intervention for PTB and delivered at term, 33.3% (7/21) received prophylactic progesterone and delivered at term, and 61.9% (13/21) underwent ultrasound indicated cervical cerclage. In the broader cohort, 9% (15/166) of women underwent transvaginal cervical cerclage during pregnancy. Of these, 86.7% (13/15) were ultrasound indicated due to identification of a CL ≤25 mm, while 13.3% (2/15) had a cerclage placed based on a history of prior spontaneous late miscarriage following advanced labor CD. The median GA at cervical

TABLE 4 Characteristics of the cesarean birth scar and cervix measured on 3D ultrasound volumes.

Ultrasound characteristic	N=166
Shortest cervical length (mm)	29.9 (27.9, 32.0)
Gestational age at the shortest cervical length	17w6d (15w3d, 20w6d)
Cesarean scar visualization	89.8% (149/166)
Gestational age at cesarean scar assessment	16w5d (15w1d, 18w5d)
Presence of niche	48.3% (72/149)
Cesarean scar position	N=149
Scars above the internal os	53.7% (80/149)
Scars at the internal os	33.5% (50/149)
Scars below the internal os	12.7% (19/149)
Scar distance to the internal os (mm)	2.3 (0.0, 4.4)
Scars above the internal os	4.2 (2.9, 6.6)
Scars at the internal os	0.0 (0.0, 0.0)
Scars below the internal os	4.5 (3.0, 9.8)
Scar distance to the external os (mm)	32.6 (29.6, 35.9)
Scars above the internal os	35.1 (32.1, 38.3)
Scars at the internal os	31.4 (28.6, 33.9)
Scars below the internal os	22.9 (17.8, 25.9)
Niche measurements (mm, mm ³)	N=72
Niche length	5.2 (3.9, 7.4)
Niche depth	5.6 (4.0, 7.2)
Niche width	6.5 (4.5, 8.6)
Niche volume	65 (30, 143)
Residual myometrial thickness (mm)	6.3 (4.3, 9.7)
Adjacent myometrial thickness (mm)	11.2 (8.3, 14.0)
Cervical length at cesarean scar assessment (mm)	32.0 (29.2, 34.5)
Cervical volume (cm ³)	33.3 (27.1, 38.2)

cerclage insertion was 18w0d (16w0d, 21w0d), and removal occurred at 38w2d (35w5d, 39w0d). Additionally, 80% (12/15) of women who received a cerclage also took supplementary progesterone. In the study cohort, 14.46% (24/166) received prophylactic progesterone until 37 weeks or delivery. Among those who received cervical cerclage, 33.3% (5/15) experienced sPTB, while 8.3% (2/24) of women managed with progesterone alone had sPTB (Figure S1).

A summary of the 3D ultrasound characteristics of the CD scar and cervix in the study cohort is presented in Table 4. The CD scar was visualized in 89.8% (149/166) of cases, and 48.3% (72/149) had a scar niche present. A detailed analysis of CD scar characteristics in relation to maternal demographics, obstetric history, and peripartum factors related to advanced labor CD can be found in Table S1. Multiple CDs were linked to RMT/AMT ≤ 0.5 ($p=0.021$). Significant correlations ($p<0.001$) were identified between individual 2D niche measurements derived from 3D ultrasound volumes and corresponding niche volumes computed through the tracing method (Figure S2).

CD scars positioned at or caudal to the internal cervical os (cervical scars) demonstrated a higher likelihood of developing a niche compared to scars situated cranial to the internal os (uterine scars), with niche rates of 58% (40/69) versus 40% (32/80), RR 1.45 (95% CI 1.04, 2.03; $p=0.029$). There was no statistically significant difference in the median niche volume between scars located at or below the internal os compared to scars located above the internal os: 0.065 cm^3 (0.040, 0.108) versus 0.051 cm^3 (0.024, 0.158); $p=0.813$.

In the sPTB group, the median scar distance to the internal cervical os level was 0.0mm (−3.07, 1.72), whereas in the group with term birth it was 2.6mm (0.00, 4.70); $p=0.042$. Similarly, among women who developed short CL ≤ 25 mm within the surveillance period, the median scar distance to the internal os was −3.4mm (−4.90, 0.00), compared to 2.6mm (0.00, 4.65) in the group that had no significant CL shortening; $p=0.011$ (Figure 2).

Women who had a cesarean scar positioned at or caudal to the internal cervical os had significantly higher risks of sPTB and CL ≤ 25 mm compared to those with scars cranial to the internal os, with aOR of 5.00 (95% CI 1.10, 22.78; $p=0.037$) for sPTB and 5.26 (95% CI 1.59, 17.32; $p=0.006$) for short CL, respectively.

The univariate analysis results for demographic factors, obstetric history, advanced labor CD characteristics, and 3D CD scar ultrasound features in relation to CL during the PTB surveillance period and GA at delivery are presented in the Table S2.

The performance evaluation of screening models for sPTB is summarized in Table 5. The baseline model, which included parameters such as demographics, sPTB risk factors, CL, and fetal fibronectin testing, demonstrated an AUC of 0.69, 95% CI 0.52–0.85, and a sensitivity of 62%, 95% CI 0.31–0.85 at a FPR of 25% (Model 1). Adding clinical data specific to advanced labor CD significantly improved the model's predictive performance, resulting in an AUC of 0.80, 95% CI 0.67–0.91, and a similar sensitivity of 67%, 95% CI 0.33–0.92 at the same FPR (Model 2). However, models investigating basic caesarean scar details such as scar visualization, niche presence, and scar distance to IO (either as an anatomic or categorical variable) demonstrated limited improvement in predictive accuracy. The best performance was achieved by integrating 3D scar data as individual parameters, specifically niche volume and cervical volume, rather than using niche: cervix ratio, with an AUC of 0.91, 95% CI 0.81–0.98, and a sensitivity of 91%, 95% CI 0.73–1.00 (Model 12).

Conventional predictors typically used in PTB surveillance showed modest performance for predicting CL ≤ 25 mm, with an AUC of 0.60, 95% CI 0.47–0.73, and a low sensitivity of 22%, 95% CI 0.06–0.44 at a FPR of 25% (Model 1). Integration of clinical data specific to advanced CD improved model sensitivity, increasing it to 44%, 95% CI 0.22–0.67 at the same FPR, though the overall AUC increased only slightly to 0.64, 95% CI 0.48–0.79 (Model 2). The inclusion of scar distance to the internal os as an anatomic value significantly increased model performance, showing an AUC of 0.84, 95% CI 0.73–0.93, and sensitivity of 82%, 95% CI 0.59–1.00 at a FPR of 25% (Model 5). 2D CD scar niche measurements, such as length, depth, and width, marginally improved the model performance, while the RMT/AMT ratio did not demonstrate

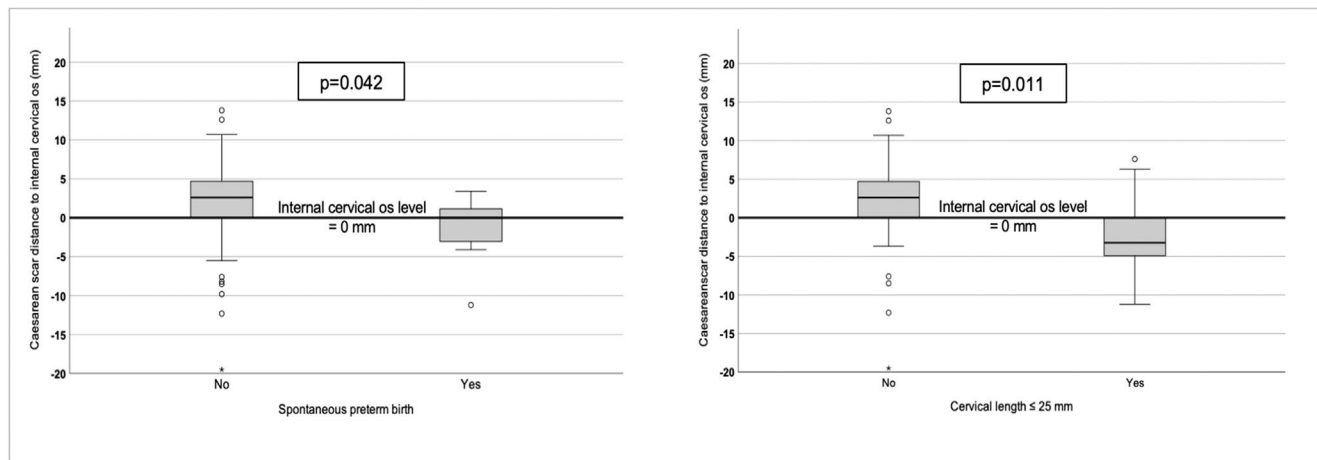


FIGURE 2 Comparison of median cesarean scar distance to internal os measured by 3D transvaginal ultrasound and stratified by risk of spontaneous preterm birth and cervical length shortening.

TABLE 5 Performance analysis of multiparameter screening models for spontaneous preterm birth and short cervical length.

First row: sPTB prediction, Second row: CL ≤25 mm prediction	AUC (95% CI)	Sensitivity (95% CI)			
		FPR 10%	FPR 15%	FPR 20%	FPR 25%
M1—demographics, risk factors sPTB, fFN, CL*	0.69 (0.52, 0.85) 0.60 (0.47, 0.73)	0.38 (0.08, 0.62) 0.17 (0.00, 0.39)	0.38 (0.15, 0.77) 0.22 (0.06, 0.44)	0.38 (0.23, 0.85) 0.22 (0.06, 0.44)	0.62 (0.31, 0.85) 0.22 (0.06, 0.44)
M2—step 1 and CD clinical data	0.80 (0.67, 0.91) 0.64 (0.48, 0.79)	0.50 (0.17, 0.75) 0.17 (0.00, 0.61)	0.58 (0.25, 0.83) 0.44 (0.11, 0.67)	0.58 (0.33, 0.83) 0.44 (0.22, 0.67)	0.67 (0.33, 0.92) 0.44 (0.22, 0.67)
M3—step 2 and scar visualization	0.80 (0.67, 0.91) 0.68 (0.52, 0.82)	0.50 (0.17, 0.75) 0.44 (0.06, 0.67)	0.50 (0.25, 0.83) 0.44 (0.17, 0.67)	0.67 (0.33, 0.92) 0.44 (0.22, 0.67)	0.67 (0.42, 0.92) 0.44 (0.22, 0.72)
M4—step 3 and niche presence	0.78 (0.62, 0.91) 0.69 (0.54, 0.83)	0.50 (0.17, 0.75) 0.28 (0.11, 0.61)	0.50 (0.25, 0.83) 0.44 (0.17, 0.72)	0.58 (0.33, 0.92) 0.50 (0.28, 0.78)	0.75 (0.42, 0.92) 0.61 (0.33, 0.83)
M5—step 4 and scar distance to IO (anatomic value)	0.79 (0.63, 0.93) 0.84 (0.73, 0.93)	0.64 (0.27, 0.91) 0.59 (0.35, 0.82)	0.64 (0.36, 0.91) 0.65 (0.41, 0.88)	0.64 (0.36, 0.91) 0.76 (0.47, 0.94)	0.73 (0.36, 0.91) 0.82 (0.59, 1.00)
M6.1—step 4 and scar distance to IO (categorical, cutoff 0 mm)	0.81 (0.65, 0.94) 0.80 (0.68, 0.90)	0.55 (0.18, 0.82) 0.41 (0.12, 0.76)	0.64 (0.27, 0.91) 0.59 (0.29, 0.82)	0.73 (0.45, 2.00) 0.65 (0.41, 0.88)	0.73 (0.45, 1.00) 0.65 (0.41, 0.88)
M6.2—step 4 and scar distance to IO (categorical, cutoff 5 mm)	0.79 (0.63, 0.92) 0.74 (0.61, 0.85)	0.45 (0.18, 0.82) 0.24 (0.06, 0.53)	0.64 (0.27, 0.91) 0.35 (0.12, 0.65)	0.64 (0.36, 0.91) 0.47 (0.18, 0.76)	0.64 (0.36, 0.91) 0.53 (0.29, 0.82)
M7—step 5 and niche length, depth, width	0.85 (0.72, 0.95) 0.86 (0.73, 0.95)	0.64 (0.36, 0.91) 0.65 (0.41, 0.88)	0.73 (0.45, 1.00) 0.71 (0.47, 0.88)	0.73 (0.45, 1.00) 0.76 (0.53, 0.94)	0.82 (0.55, 1.00) 0.76 (0.59, 0.94)
M8—step 7 and RMT: AMT ratio	0.85 (0.73, 0.95) 0.86 (0.74, 0.95)	0.64 (0.36, 0.91) 0.71 (0.47, 0.88)	0.73 (0.45, 0.91) 0.71 (0.47, 0.88)	0.73 (0.45, 1.00) 0.71 (0.47, 0.88)	0.73 (0.45, 1.00) 0.71 (0.47, 0.94)
M9—step 7 and niche volume (continuous)	0.88 (0.74, 0.98) 0.89 (0.79, 0.96)	0.82 (0.55, 1.00) 0.76 (0.53, 0.94)	0.82 (0.55, 1.00) 0.76 (0.53, 0.94)	0.82 (0.55, 1.00) 0.76 (0.53, 0.94)	0.82 (0.55, 1.00) 0.76 (0.59, 1.00)
M10—step 7 and niche volume (categorical, ≤0, 0–125, 125–600, >600 mm ³)	0.86 (0.73, 0.96) 0.86 (0.76, 0.94)	0.73 (0.27, 1.00) 0.65 (0.41, 0.88)	0.82 (0.45, 1.00) 0.71 (0.47, 0.88)	0.82 (0.55, 1.00) 0.71 (0.47, 0.88)	0.82 (0.55, 1.00) 0.71 (0.47, 0.94)
M11—step 9 and cervix volume	0.91 (0.81, 0.98) 0.89 (0.79, 0.96)	0.73 (0.45, 1.00) 0.62 (0.38, 0.88)	0.82 (0.55, 1.00) 0.69 (0.44, 0.94)	0.91 (0.64, 1.00) 0.81 (0.56, 1.00)	0.91 (0.73, 1.00) 0.88 (0.62, 1.00)
M12—step 7 and niche: cervix ratio	0.87 (0.74, 0.97) 0.89 (0.79, 0.97)	0.73 (0.36, 1.00) 0.69 (0.44, 0.94)	0.82 (0.55, 1.00) 0.81 (0.56, 1.00)	0.82 (0.55, 1.00) 0.81 (0.62, 1.00)	0.82 (0.55, 1.00) 0.81 (0.62, 1.00)

Abbreviations: AMT, adjacent myometrial thickness; AUC, area under the curve; CD, cesarean birth; CL* included only in the sPTB prediction models; CL, cervical length; fFN, fetal fibronectin; FPR, false positive rate; IO, internal cervical os; RMT, residual myometrial thickness; sPTB, spontaneous preterm birth; sPTB, spontaneous preterm birth.

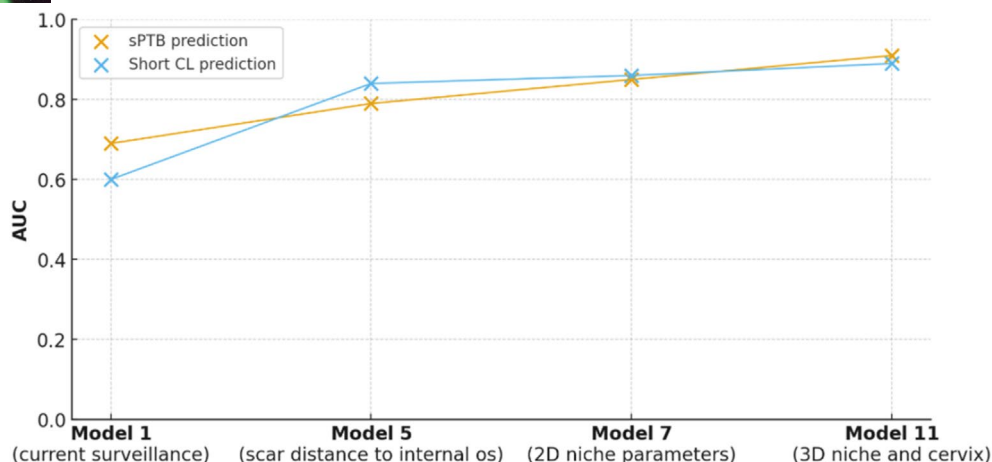


FIGURE 3 Receiver operating characteristic curves for prediction models of spontaneous preterm birth and short cervical length. 2D, two dimensional; 3D, three dimensional; AUC, area under curve; CL, cervical length; sPTB, spontaneous preterm birth.

predictive value for CL shortening ≤ 25 mm. Similar to the predictive models for sPTB, the highest predictive performance was achieved by the inclusion of 3D ultrasound features, niche volume, and cervical volume, as independent predictors. This final model reached an AUC of 0.89, 95% CI 0.80–0.96, with a sensitivity of 88%, 95% CI 0.62–1.00 at a FPR of 25% (Model 12). The ROC curves corresponding to the analyzed models for CL ≤ 25 mm and sPTB prediction are shown in Figure 3.

A multivariable logistic regression analysis was conducted to identify which CD scar ultrasound parameters independently and significantly predicted outcomes (Table S3). Scar distance to the internal os consistently showed statistical significance across all models for short CL ≤ 25 mm. Furthermore, niche depth and length, as well as niche and cervix volume and niche/cervix volume ratio, were significantly associated with short CL prediction in specific models. In the sPTB models, the coefficients that demonstrated statistical significance included scar distance to the internal os, niche volume, and the niche/cervix volume ratio.

Additional maternal and perinatal outcomes are presented in Table S4. Repeat CD accounted for 68.9% (111/161) of cases, and uterine scar dehiscence was documented in 2.5% (4/161) of cases. These instances of scar dehiscence were recorded as incidental findings at the time of surgery and did not represent the indication for birth. No incidents of uterine rupture were observed in this cohort. There were no cases of stillbirth or neonatal death. As anticipated, the incidence of neonatal adverse outcomes was significantly higher in women who experienced PTB.

4 | DISCUSSION

In this prospective observational cohort of women with previous advanced labor CD, the inclusion of mid-gestation 3D transvaginal ultrasound parameters, such as niche volume and cervical volume, was associated with higher predictive performance for subsequent short CL ≤ 25 mm and sPTB and reaching sensitivity of 0.88, 95%

CI 0.62–1.00 and 0.91, 95% CI 0.73–1.00 at FPR 25%, respectively. The improvement over models using 2D cesarean scar measurements alone was marginal, which achieved a sensitivity of 0.76, 95% CI 0.59–0.94 for short CL and 0.82, 95% CI 0.55–1.00 for sPTB, at the same FPR.

No statistically significant differences in median niche volumes were observed between women who experienced sPTB and those who delivered at term, nor between those with a short CL ≤ 25 mm versus normal CL > 25 mm.

CD scar position emerged as a key factor for evaluating the individual risk of sPTB and short CL ≤ 25 mm. The median scar distance to the internal os was significantly more likely to be positioned cranial to the internal os in women who had a term birth or did not experience significant CL shortening. In contrast, for women who delivered preterm or had CL shortening, there was a significantly higher likelihood that the median scar distance was at or caudal to the level of the internal os (i.e., the scar was in the cervix). Scar distance to the internal os demonstrated the strongest association with short CL ≤ 25 mm and remained the most robust individual parameter that consistently showed statistical significance across all short CL models.

Overall we report a sPTB rate of 7.8%, which is comparable to the pooled sPTB rate of 6.9% observed in a recent meta-analysis of 18 retrospective cohort studies evaluating $n = 605\,138$ women with a history of full dilatation CD.¹⁵ Interestingly, a significant proportion of women who experienced sPTB did not demonstrate significant CL shortening during surveillance and we propose several potential explanations for this observation. First, intraoperative cervical trauma during advanced labor CD due to low hysterotomy incision and/or uterine or cervical extensions may lead to cervical dysfunction in subsequent pregnancies.^{7,30} Therefore, CD scar parameters such as scar distance to the internal os can serve as a valuable additional risk stratification tool in this cohort of women. We also noted a tendency towards a higher incidence of unsuccessful attempts at instrumental birth prior to full dilatation CD in the subsequent sPTB group compared to the term birth

group (72.7% vs. 39.8%, $p=0.054$). A study by Eriksson et al.³¹ reported that women having a CD at a low fetal station have a higher risk of subsequent sPTB. Low fetal station in the maternal pelvis at the time of CD results in scars that are more caudal on the uterus or in the cervix on postnatal ultrasound.³² Since instrumental births are safely attempted only if the fetal station is at or below the maternal ischial spines,³³ this may explain the increase in predictive performance for sPTB observed when this information was integrated into the model.

Second, subclinical inflammatory or infection mechanisms could lead to sPTB with rapid CL changes. Observational studies in women with secondary subfertility found a higher rate of bacterial colonization in cases with a CD scar niche present.³⁴ Chronic inflammatory changes have been observed in women with a CD scar niche undergoing niche resection.³⁵ Our study found that CD scars positioned at or caudal to the internal cervical os were more likely to be associated with a niche compared to scars situated cranial to the internal os. This aligns with other studies concluding that women in active labor with advanced cervical dilatation at the time of CD are at a higher risk of developing a scar defect.^{36–39} In this study, IVF conception showed a significant association with the presence of a niche; however, associations with other risk factors for subfertility were not assessed, as this was outside the scope of the study.

A key strength of this research is its novel approach to risk stratification in women with a history of advanced labor CD, using ultrasound assessment of the cesarean scar. We included women who experienced sPTB following a term advanced labor CD, excluding those with sPTB prior to the index CD, to better isolate the effect of advanced labor CD on subsequent sPTB risk without underestimation. Analyses were adjusted for other established PTB risk factors to account for potential confounding.

We acknowledge, however, that the exploratory sPTB predictive models are at risk of bias due to the prophylactic interventions that were often administered to women identified as high risk due to the history of a previous LM or sPTB or the finding of a short CL. This necessitates cautious interpretation and further multicenter validation. The exploratory models for short CL are less prone to bias, since most PTB interventions were initiated in response to the identification of short CL ≤ 25 mm, and adjustments were made for women receiving progesterone. However, even models for the prediction of CL shortening demonstrated that adding CD scar characteristics improves the performance of the model. Study limitations include the observational, clinic-based design, with an inherent risk of selection bias as well as variations in clinical practices across cases, even within the same service, despite standardized protocols. Although the cohort primarily consisted of women with a previous full dilatation CD, potentially limiting the generalizability of the findings across all advanced labor CD, the inclusion of consecutive patients from a tertiary UK clinical setting aligned with national and international PTB prevention standards supports the relevance of these findings to comparable healthcare settings and populations. However, the feasibility and

external validity of this approach across different clinical settings require further evaluation.

Direct comparisons on the effectiveness of PTB prophylactic measures are limited, given the observational nature of the study. Among women receiving an ultrasound indicated cerclage, 30% (4/13) experienced a sPTB, a rate comparable to previously reported effectiveness of cervical cerclage in other high-risk populations with short CL.^{40,41} Addressing the impact of PTB prophylactic interventions in women with advanced labor CD, requires further investigation through multicenter RCTs incorporating data on CD scar characteristics such as position relative to the internal os and niche parameters.

5 | CONCLUSION

This study highlights the importance of transvaginal sonographic assessment of CD scar position relative to the internal os in evaluating the risk of sPTB in pregnant women with a history of advanced labor CD (8–10 cm dilatation). Our findings suggest that scar location may be a more critical determinant of sPTB risk than cervical dilatation alone at the time of surgery.

Although 3D ultrasound assessment of cesarean scar niche morphology demonstrated the highest predictive performance for both sPTB and short CL, the added benefit over assessment of cesarean scar position alone was modest. Given the additional time, specialised training, and software required for 3D volume analysis, its routine application in clinical practice remains limited.

Our findings indicate that routine assessment of the cesarean scar distance to the internal os warrants further evaluation as a potential addition to PTB surveillance in this high-risk population. This clinically accessible strategy may help with early identification of women with a scar located at or caudal to the internal os, who could be considered for closer surveillance, allowing more timely PTB prophylactic interventions.

AUTHOR CONTRIBUTIONS

Maria Ivan: Conceptualization, methodology, data curation, formal analysis, investigation, writing—original draft, validation. Amrita Banerjee: Conceptualization, data curation, investigation, writing—review and editing, validation. Ekaterina Pazukhina: Formal analysis, writing—review and editing. UCLH Preterm Birth Clinic Research Group: Investigation, writing—review and editing, validation. Oleg Blyuss: Formal analysis, writing—review and editing. Alexey Zaikin: Formal analysis, writing—review and editing. Davor Jurkovic: Conceptualization, supervision, writing—review and editing. Anna David: Conceptualization, methodology, formal analysis, investigation, supervision, writing—review and editing, validation, visualization, funding acquisition, project administration, resources, software. Raffaele Napolitano: Conceptualization, methodology, formal analysis, investigation, supervision, writing—review and editing, validation, visualization, project administration, resources, software.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

This study was registered and approved as a clinical governance antenatal service quality improvement project and employed analysis of routinely collected clinical data, thus ethical approval and individual patient consent were not required.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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