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Techniques for detecting cervical remodeling as a predictor for spontaneous preterm birth: current evidence and future research avenues in patients with multiple pregnancies

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ABSTRACT

Background: Spontaneous preterm birth occurs more frequently in multiple pregnancies. This syndrome has multiple triggers that result in a unified downstream pathway of cervical remodeling, uterine activity, and progressive cervical dilatation. Whilst the triggers for labor in multiple pregnancy may be different from singletons, the downstream changes will be the same. Identifying patients at risk of preterm birth is a priority as interventions to delay delivery and optimize the fetus can be initiated. Methods for screening for risk of preterm birth which focus on the detection of cervical remodeling may therefore have potential in this population.

Methods: This review explores the evidence for the predictive utility for preterm birth of several published techniques that assess the physical, biomechanical, and optical properties of the cervix, with a focus on those which have been studied in multiple pregnancies and highlighting targets for future research in this population.

Results: Fifteen techniques are discussed which assess the physical, biomechanical, and optical properties of the cervix in pregnancy. Of these, only three techniques that evaluated the predictive accuracy of a technique in patients with multiple pregnancies were identified: uterocervical angle, cervical consistency index, and cervical elastography. Of these, measurement of the uterocervical angle has the strongest evidence. Several techniques have shown predictive potential in singleton pregnancies, but have not yet been studied in multiple pregnancies, which would be a logical expansion of research.

Conclusion: Research on techniques with predictive utility for PTB in patients with multiple pregnancies is limited but should be a research priority. Overall, the theory supports the investigation of cervical remodeling as a predictor of PTB, and there are numerous techniques in development that may have potential in this field.

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Introduction

Preterm birth (PTB), delivery before 37 weeks of gestation, occurs at a rate of 7.6% in the UK, with higher rates globally [1,2]. PTB can be medically induced or spontaneous; this manuscript will only consider spontaneous preterm birth. Prematurity is the leading cause of neonatal mortality, with survivors experiencing respiratory, neurological, and gastrointestinal complications [2]. PTB occurs more frequently in multiple pregnancies, with 60% of twins delivering <37 weeks and 75% of triplets delivering <35 weeks, with significantly higher neonatal mortality than singletons [3].

Identifying patients at risk for PTB is a priority, as interventions to delay delivery and optimize the fetus

can be initiated [4]. Identifying those *not* at increased risk reduces unnecessary interventions and the associated economic and emotional tolls. In singleton pregnancies, NICE recommends cervical length (CL) screening in asymptomatic patients at a higher risk and CL ± fetal fibronectin (fFN) screening in symptomatic patients [4]. However, no recommendations exist for asymptomatic patients with multiple pregnancies owing to limited evidence [4].

PTB is a syndrome with multiple triggers that result in a unified downstream pathway involving cervical remodeling, uterine activity, and progressive cervical dilatation [5]. PTB in multiple pregnancies may be due to either “supra-physiological” or pathological stimuli

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Table 1. All techniques included in this review and the level of evidence currently available.

Technique	Level of evidence	References
Physical properties		
Uterocervical angle	Predictive accuracy studies – multiple pregnancy	[12–17]
Cervical consistency index	Predictive accuracy studies – multiple pregnancy	[17–22]
Cervical gland area	Predictive accuracy studies – singleton pregnancy only	[23–32]
Cervical texture analysis	Predictive accuracy studies – singleton pregnancy only	[33,34]
Cervical sliding sign	Predictive accuracy studies – singleton pregnancy only	[35–37]
MRI	Predictive accuracy studies – singleton pregnancy only	[38–41]
Biomechanical properties		
Cervical elastography	Predictive accuracy studies – multiple pregnancy	[37,42–51]
Optical properties		
Electrical impedance	Predictive accuracy studies – singleton pregnancy only	[52–54]
Acoustic attenuation	Cohort studies including preterm birth (not predictive accuracy) – singleton pregnancy only	[55,56]
Backscattered power loss	Cohort study not assessing preterm birth – singleton pregnancy only	[57]
Light induced fluorescence	Cohort study not assessing preterm birth – singleton pregnancy only	[58–60]
Near-infrared spectroscopy	Cohort study not assessing preterm birth – singleton pregnancy only	[61–63]
Raman spectroscopy	Cohort study not assessing preterm birth – singleton pregnancy only	[64,65]
Mueller matrix colposcopy	Cohort study not assessing preterm birth – singleton pregnancy only	[66,67]

[6]. “Supra-physiological” stimuli are physiological triggers that occur at an enhanced level at an earlier gestation in multiple pregnancies. This includes uterine distension, production of corticotrophin-releasing hormone from the larger placental mass, and earlier fetal lung development, resulting in surfactant production [6]. Pathological stimuli include infection, inflammation, cervical weakness, and placental vasculopathy [6].

Whilst the triggers for labor in multiple pregnancy may be different, the downstream changes will be the same, with cervical remodeling occurring prior to dilatation, with or without uterine contractions [5]. Methods for screening for the risk of PTB which focus on the detection of cervical remodeling, may therefore have potential in this population.

Cervical remodeling

The cervix has two primary mechanical functions: to provide a strong outlet to the uterus until an appropriate gestation and then to become compliant and dilate to allow passage of the fetus [7].

The cervix is largely (90%) composed of an extracellular matrix (ECM) containing collagen and proteoglycans and a smaller cellular component, including immune cells, fibroblasts, smooth muscle, and glandular/vascular cells [8]. Collagen is cross-linked, which provides the strength to support the advancing pregnancy; this is mediated by the ground substance composed of glycosaminoglycans [7].

Cervical remodeling occurs in four overlapping phases: softening, ripening, dilation, and repair [9]. Softening is a gradual process beginning in the first trimester that does not result in the loss of cervical integrity. Ripening occurs as gestation advances, resulting in rapid increase in compliance and loss of

strength. Dilatation occurs when uterine contractions occur in the presence of a ripened cervix. The triggers for these changes are variable [4], but the results are immune cell infiltration, matrix metalloproteinase activation resulting in ECM degradation, an increase in hyaluronic acid, increased hydration of the ECM, and weakening of the collagen network [9]. These changes result in reduced cervical stiffness, increased elasticity, and hydration, which are required to facilitate subsequent dilatation and labor progress.

This review explores the evidence for the predictive utility for preterm birth of several published techniques that assess the physical, biomechanical, and optical properties of the cervix (Table 1), with a focus on those which have been studied in multiple pregnancies and highlighting targets for future research in this population.

Physical properties

Cervical length

The most studied predictive tool for PTB in multiple pregnancies is CL. There are review papers and meta-analyses that outline the current evidence, and it is not intended to duplicate this, other than to say that there is evidence that a single CL measurement of <20 mm at 20–24 weeks has a predictive value in asymptomatic patients with multiple pregnancies [10]. The shorter the CL and the earlier the gestation, the higher the risk of PTB [11].

Uterocervical angle

The uterocervical angle (UCA) is the angle between the cervix and the anterior uterine wall measured on a transvaginal sagittal section. Theoretically, the more

obtuse the angle, the more force is transmitted onto the cervix and the higher the propensity for PTB.

A 2021 meta-analysis included 11 studies that reported a second-trimester UCA of 5061 pregnancies. They concluded that a wider UCA significantly increased the risk of PTB in singleton and twin pregnancies [12].

Five studies assessed the association between UCA and PTB in multiple pregnancies. In the largest retrospective cohort study, Vielba assessed UCA in 424 twin pregnancies between 19 + 0-22 + 0 weeks. A UCA $>120^\circ$ was significantly associated with PTB at <28 , <32 , and <34 weeks [13]. The same group also published a smaller ($n=177$) cohort study that demonstrated that a UCA $>117^\circ$ was significantly associated with PTB <28 , <32 , and <34 weeks [14]. A further retrospective cohort study ($n=259$) concluded that a UCA $>110^\circ$ was associated with PTB <32 weeks and $>114^\circ$ with PTB <28 weeks [15]. Lynch concluded that UCA $>110^\circ$ was associated with PTB <37 weeks but this could not be demonstrated at other gestations ($n=137$) [16]. Finally, a prospective cohort study ($n=63$) also demonstrated a significant difference in the UCA between term and PTB <34 and <37 weeks [17].

Whilst the cutoff for prediction remains contentious, the studies are consistent in their findings of an association between a wider angle and PTB in both singleton and multiple gestations.

Cervical consistency index (CCI)

CCI is the ultrasonically determined ratio between the anteroposterior diameter of the cervix when maximal pressure is applied and the same diameter at rest; it reflects cervical compressibility.

Parra-Saavedra described CCI in 2011 in a prospective cross-sectional study of 1115 singletons. They demonstrated an inverse linear correlation between gestational age and CCI and predicted delivery at <32 , <34 , and <37 weeks with an AUROC of >0.9 [18]. A subsequent prospective cohort study ($n=532$) assessing low-risk patients at 19 + 0-24 + 6 weeks also demonstrated predictive potential for PTB at <37 weeks (AUROC 0.84) and <34 weeks (AUROC 0.87) [19]. The same group also studied 82 high risk patients and demonstrated a significantly reduced CCI in patients who delivered <37 weeks, although the AUROC were less robust ($0.73 < 37$ weeks; $0.68 < 34$ weeks) [20].

However, the results in multiple pregnancies were less consistent. A gestational decrease in CCI has been

observed [21] but two prospective cohort studies have reported differing results. Rosen ($n=80$) identified no significant difference between mid-trimester CCI and gestation at delivery and very poor predictive capacity, [22] whilst Van Der Merwe ($n=63$) identified a significant difference in those who delivered <34 and <37 weeks [17]. Large-scale studies of multiple pregnancies are required to address this discrepancy.

Cervical gland area

Cervical gland area (CGA) refers to the mucosal glands in the cervical canal, the absence of which can be a sign of preterm cervical maturity in the second trimester.

The detection rate of CGA remained constant until 31 weeks and significantly decreased thereafter in a prospective cohort study of singletons ($n=260$) [23]. Yamaguchi [24] confirmed this, demonstrating that the CGA/stroma mean grayscale level ratio increased with gestation (corresponding to “disappearance” of the CGA) and that this, combined with CL, could predict labor onset at term within one week.

CGA has also been used for PTB prediction in singletons. In the largest prospective cohort study ($n=3030$), Fukami [25] demonstrated that the absence of CGA in the mid-trimester showed a higher sensitivity and positive predictive value (PPV) for PTB <32 weeks than shortened CL (sensitivity 75% vs. 50%; PPV 54.5% vs. 8.3%). Two smaller cohort studies have determined sensitivities of 86% and 25% and 33% and 33% for delivery <34 and <35 weeks, respectively [26,27]. Two further prospective cohort studies also demonstrated a strong association between non-detection of CGA in the mid-trimester and PTB, although the gestation reported varied between 35 and 37 weeks [28,29]. Three cohort studies also demonstrated an association between the absence of CGA in symptomatic patients and PTB [30–32].

No studies have evaluated CGA in multiple pregnancies; however, given the consistent evidence in singletons, this warrants further investigation.

Cervical texture analysis

Ultrasound images of the cervix can be analyzed using a method based on comparison of speckle patterns surrounding each pixel of the image, in order to characterize the cervical microstructure. Two prospective cohort studies by the same group [33,34] analyzed sagittal cervical ultrasound images of patients with singleton pregnancies ($n=310$ and $n=633$) 19 + 0-

24 + 6 weeks using a learning algorithm. Both studies demonstrated that cervical texture assessment was significantly associated with PTB <37 weeks (AUROC 0.77/0.63), and a larger study also concluded that predictive potential could be improved by including CL [34]. Neither included multiple pregnancies.

Cervical sliding sign

The cervical sliding sign is the ultrasound observation of the anterior cervical lip “sliding” on the posterior lip when gentle pressure is applied. Volpe demonstrated that the presence of this sign is associated with reduced CL and is an independent predictor of delivery within 7 days (AUROC 0.69) in symptomatic singletons [35]. This was also demonstrated in a prospective study of singletons ($n=88$) with preterm premature rupture of membranes (AUROC 0.75) [36]. In a case-control study of an unselected population of singletons ($n=533$), the sliding sign was observed more often in those who delivered preterm [37]. There have been no studies on patients with multiple pregnancies.

Cervical stroma signal intensity

Using MRI, Chan [38] demonstrated that cervical stroma signal intensity increased with gestation in a prospective study ($n=91$) between 35–41 weeks, corresponding to increased water content. A higher signal intensity was associated with a shorter interval to delivery. This was confirmed in a second study ($n=57$) [39]. In contrast, Pates [40] demonstrated a reduction in single intensity with gestation in patients with a history of PTB, the reason for which was unclear. In 100 symptomatic patients, de Tejada [41] demonstrated that the risk of PTB is increased in patients with low cervical stromal differentiation on MRI. However, the sensitivity (23%) and negative predictive value (72%) were low and the authors concluded that there was no benefit over CL measurements. None of the studies included multiple pregnancies.

Biomechanical properties

Cervical elastography

Cervical elastography uses ultrasound to measure stiffness by detecting tissue response to deformation (strain). Strain can be applied mechanically using a transvaginal probe (strain elastography) or by using

acoustic waves to induce deformation (shear wave elastography).

A meta-analysis [42] included seven studies assessing cervical elastography for the prediction of PTB in singletons. Despite the heterogeneity of the patient population and elastography method, it demonstrated predictive potential with a sensitivity of 0.84, specificity of 0.82, and AUROC of 0.90. Since publication, further studies have demonstrated the role of cervical elastography in a range of populations, including an unselected pregnant population [37], patients with a short cervix (with and without progesterone) [43,44] and patients with previous cervical weakness [45]. However, not all studies have demonstrated a benefit [46,47].

Four studies evaluated cervical elastography in multiple pregnancies. Ono [48] demonstrated a significant negative correlation between cervical stiffness and gestation and a significant difference in stiffness between singleton and twin pregnancies ($n=280$). In contrast, whilst Diawtipsukon [49] demonstrated reduced stiffness with gestation, they did not find any significant differences between singletons and twins. The sample size was small ($n=36$) and did not show any difference in PTB rates between the groups, which may explain the differing findings. In a large prospective study ($n=138$), Sun [50] demonstrated that mean shear wave elastography (SWE) values decreased with gestation. The mean SWE value was lower in the preterm group at all gestations except for one. They concluded that the mean SWE value at 28–32 weeks of the inner anterior cervical lip is independently associated with PTB in DCDA twins and is superior to CL, with an AUROC of 0.677. In the largest study ($n=225$), Liu [51] demonstrated that the cervical hardness ratio decreased with gestation, while the internal and external os strains increased. This effect was greater in twin than in singleton pregnancies. Furthermore, the cervical hardness ratio was lower and the internal os strain was higher in those who delivered preterm.

Optical properties

Electrical impedance

Electrical flow through tissues is affected by the cellular structure (resistive and capacitive properties) and hydration. Measuring electrical impedance *in vivo* can act as a surrogate for detecting collagen cross-linking and hydration [53], and therefore, theoretically for predicting PTB.

A prospective singleton cohort study ($n=365$) demonstrated a lower mid-trimester cervical tissue transfer

impedance in those who deliver preterm. Cervical electrical impedance spectroscopy (EIS) predicted PTB <37 weeks with an AUROC of 0.76, which was better than that of CL and fFN [53]. A model including all three measures and a history of PTB improved the accuracy further (AUC 0.83 <37 weeks, 0.86 <32 weeks) and combining EIS with the QUIPP app is also beneficial [54].

There are no published studies evaluating EIS in multiple pregnancies.

Acoustic attenuation

Ultrasound attenuation is energy loss as an ultrasonic wave propagates through tissue and is related to tissue stiffness, collagen, and water concentration.

A prospective cohort study ($n = 40$) demonstrated that attenuation was an indicator of time to delivery but not of gestation or CL. This study was not powered to predict PTB [55]. More recently, McFarlin ($n = 67$) reported that cervical attenuation was lower at 17–21 weeks in patients who subsequently had a PTB, earlier than the reduced CL seen at 22–26 weeks [56].

Currently, there are no published studies evaluating ultrasound attenuation as a predictor of PTB or which include multiple pregnancies.

Backscattered power loss

Applying an ultrasound wave to a scatterer results in vibration, causing backscatter (echo), which varies according to the incident angle. Measuring the backscattered power loss as a function of the beam angle provides information about the organization of scatterers, such as collagen.

In a prospective cohort study ($n = 36$) [58], the mean backscattered power difference distinguished first- and third-trimester patients, with higher values in earlier pregnancy, corresponding to higher microstructural organization. There are currently no published studies that assess the prediction of PTB or which include multiple pregnancies.

Light induced fluorescence

Fluorescence describes the property whereby the absorption of light of a shorter wavelength results in the emission of light of a longer wavelength. Cross-linked collagen exhibits natural fluorescence, which is not observed in unlinked soluble collagen. Measurement of light-induced fluorescence (LIF) can

therefore act as a marker for cross-linked collagen concentration, the disruption of which is observed during cervical remodeling [58].

Maul reported that LIF correlated negatively with gestation and positively with time-to-delivery and was predictive of delivery within 24 h (AUROC 0.73) in a prospective study of singletons [58]. LIF measurements were also significantly lower in the patients with known cervical insufficiency [59]. The largest prospective cohort study ($n = 191$) confirmed that cervical LIF values progressively declined from the non-pregnant state to late gestation and reached their lowest levels during parturition before increasing postpartum [60]. None of these groups reported the detection of PTB or included patients with multiple pregnancies.

Near-infrared spectroscopy

Frequency domain near-infrared spectroscopy is a noninvasive technique that characterizes the absorption of light, which can be used to calculate the concentration of hemoglobin and water, and the scattering properties reflecting collagen organization.

Banos [61] used near-infrared spectroscopy to detect misoprostol-induced cervical changes in the first trimester of pregnancy in a prospective cohort study ($n = 10$). They demonstrated a reduction in total hemoglobin, oxyhemoglobin, and dexoyhaemoglobin, an increase in water content, and reduced scatter power. Hornung [62] demonstrated a reduction in oxygenated hemoglobin and total hemoglobin, and increased scatter power as a function of gestation, but no difference in deoxygenated hemoglobin and water content. Qu [63] demonstrated that the water content increased with advancing gestation in a prospective study ($n = 205$). These differing results may reflect the different sample sizes or differences between gestational cervical ripening and misoprostol-induced ripening.

No studies that assessed the prediction of PTB in either singleton or multiple pregnancies were identified.

Raman spectroscopy

Raman spectroscopy is a light-scattering method that produces a spectrum of peaks corresponding to the different vibrational modes of the scattered molecules. In this manner, the relative composition of the light scatterers (e.g. collagen) can be determined.

A prospective cohort study of 68 low-risk asymptomatic singletons demonstrated that Raman peaks

indicative of ECM proteins significantly decreased, whereas peaks corresponding to blood significantly increased throughout pregnancy. The sample included nine cases of late PTB (>35 weeks), and there was no significant difference in Raman spectra in this group, but the study was not powered for this and did not take into account baseline differences [64].

Masson [65] conducted a prospective cohort study of 30 singleton pregnancies undergoing either spontaneous or induced labor. During labor, there were significant decreases in Raman spectral features associated with collagen and other ECM proteins, and an increase in those associated with blood and lipid-based molecules.

Currently, no studies have evaluated the prediction of PTB or included multiple pregnancies.

Mueller matrix colposcopy

Mueller matrix colposcopy uses light polarization, which is sensitive to tissue structural changes, to provide information regarding collagen organization based on anisotropic and scattering properties.

However, studies using this technique have been limited. A small ($n=8$) prospective study demonstrated an increase in collagen disorganization between non-pregnant and third-trimester samples [66]. A further prospective study demonstrated a linear correlation between total depolarization and gestational age [67]. No studies have evaluated this technique for the prediction of PTB in either singleton or multiple pregnancies.

Discussion

As we transition from understanding cervical changes as the “cause” of PTB, to a model which identifies cervical remodeling as a common downstream pathway regardless of the initiating cause, we open up research avenues which focus on these cervical properties. These changes are as relevant to patients with multiple pregnancy as they are to singletons.

Only three techniques that evaluated the predictive accuracy of a technique in patients with multiple pregnancies were identified (Table 2): uterocervical angle, cervical consistency index, and cervical elastography. Of these, measurement of the uterocervical angle had the strongest evidence, with five cohort studies demonstrating at least acceptable predictive accuracy for more obtuse angles, with improved accuracy for earlier PTB gestations. Further large-scale

studies are required to better determine the optimal predictive cutoff and clinical utility.

As outlined in Table 1, several techniques have shown predictive potential in singleton pregnancies, but have not yet been studied in multiple pregnancies, which would be a logical expansion of research. Further techniques are at the early stages of investigation in pregnancy, demonstrating changes associated with gestation or iatrogenic cervical ripening, but have not yet been studied in the context of PTB. However, more techniques show theoretical potential (for example, optical coherence tomography and second harmonic generation microscopy), but as they have not yet reached *in vivo* studies, they were outside the scope of this manuscript.

Research on techniques with predictive utility for PTB in patients with multiple pregnancies is limited, and research in this group is challenging. The number of eligible patients is low, the potential for heterogeneity is greater, and the incidence of iatrogenic PTB may confound results. Additionally, the lack of effective preventative measures for patients with multiple pregnancy at risk of PTB may discourage researchers and participants alike. However, identifying effective prevention is likely to be negatively impacted by an inability to identify the most “high risk” patients and thus both research questions must be explored simultaneously.

In summary, uterocervical angle measurement and cervical elastography have the largest evidence base in the prediction of preterm birth in women with multiple pregnancies and would benefit from larger scale studies. Of the techniques which only have predictive accuracy studies in singleton pregnancies, cervical gland area evaluation and cervical electrical impedance have the strongest evidence and would warrant investigation in the context of multiple pregnancy.

Conclusion

PTB in multiple pregnancy is a research priority. Overall, the theory supports the investigation of cervical remodeling as a predictor of PTB, and there are numerous techniques in development that may have potential in this field.

Disclosure statement

The authors report no conflicts of interest.

Table 2. Studies which have reported predictive accuracies for techniques studied in women with a multiple pregnancy.

Author	Study design	Gestation	ample size	Area under Receiver Operating Characteristic curve (95% CI)	Optimal cut off	Discriminative performance
Uterocervical angle						
Benito Vielba (2021)	Retrospective cohort	19 + 0-22 + 0	424	<28 weeks: 0.902 (0.850–0.954) <32 weeks: 0.740 (0.627–0.854) <34 weeks: 0.676 (0.582–0.771)	120 degrees	<28 weeks: OR 39.17 (4.81–319.23), NPV 99.65%, PPV 12.3% <32 weeks: OR 4.23, NPV 96.84%, PPV 12.3% <34 weeks: OR 2.66, NPV 92.28%, PPV 18.4%
Benito Vielba (2022)	Retrospective cohort	19 + 0-21 + 6	177	<28 weeks: 0.840 (0.77–0.99) <32 weeks: 0.706 (0.55–0.80) <34 weeks: 0.674 (0.56–0.79)	117 degrees	<28 weeks: OR 15.394 (1.664–142.379), NPV 99.2%, PPV 10.81% <32 weeks: OR 3.844 (1.048–14.092), NPV 96.1%, PPV 13.5% <34 weeks: OR 3.107 (1.192–8.097), NPV 90.6%, PPV 24.3%
Knight (2018)	Retrospective cohort	16 + 0-22 + 6	259	<28 weeks: 0.882 (NR) <32 weeks: 0.887 (NR)	<28 weeks: 114 degrees < 32 weeks: 110 degrees	<28 weeks: OR 24.3 (6.7–88.5), Sens 80%, Spec 84% <32 weeks: OR 15.7 (7.2–34.4), Sens 80%, Spec 82%
Lynch (2020)	Retrospective cohort	15 + 0-24 + 6	137	<37 weeks: 0.66 (0.56–0.76)	110 degrees	<32 weeks: OR 2.87 (0.75–11.00) <34 weeks: OR 2.63 (0.79–8.75) <37 weeks: OR 3.6 (1.2–10.5), PPV 53.2%, NPV 80%
Van der Merwe (2020)	Prospective cohort	18 + 0-22 + 6	63	<34 weeks: 0.72 (0.57–0.87) <37 weeks: 0.76 (0.65–0.88)	<34 weeks: 103 degrees < 37 weeks: 105 degrees	<34 weeks: OR 6.2 (NR), Sens 68.8%, Spec 73.8% <37 weeks: OR 10.2 (NR), Sens 65.4%, Spec 84.4%
Cervical consistency index						
Rosen (2020)	Prospective cohort	18 + 0-22 + 6	80	<34 weeks = 0.490 (0.297–0.683) <37 weeks = 0.488 (0.358–0.619)	N/A	
Van der Merwe (2020)	Prospective cohort	18 + 0-22 + 6	63	<34 weeks: 0.82 (0.72–0.92) <37 weeks: 0.82 (0.72–0.92)	N/A	
Cervical elastography						
Sun	Prospective cohort	20-23 + 6, 24-27 + 6, 28-32	92	<37 weeks = 0.677 (0.571–0.771)	7.94 kPa	<37 weeks: Sens 83.3%, Spec 57.9%

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Data availability statement

Data sharing is not applicable to this manuscript as no new data were created or analyzed in this study.

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