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Cervical elastography using E-cervix for prediction of preterm birth in singleton pregnancies with threatened preterm labor

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ABSTRACT

Objective: E-Cervix™ (WS80A; Samsung, Seoul, Korea) elastography is a recent quantification tool to measure the stiffness of the cervix using strain elastography. The aim of this study was to evaluate the prediction performance of E-cervix for preterm birth in singleton gestation with threatened preterm labor (PTL).

Methods: This was a cohort study of singleton pregnancies without prior preterm birth presenting to obstetrics triage for threatened PTL between 23 0/7 and 33 6/7 week who received screening for PTL with transvaginal ultrasound cervical length (TVU CL) and cervical elastography with E-cervix at the time of triage. Cervical elastography parameters were examined and compared between women who delivered preterm and those who did not. The quantification of cervical strain was calculated by a data analysis system that directly analyses raw data from the region of interest (ROI) and described as hardness ratio (HR), mean strain level within 1 cm from internal os (IOS) and external os (EOS).

Results: Ninety-five singleton pregnancies without prior preterm birth and with threatened PTL between 23 0/7 and 33 6/7 week of gestation were included in the study. Forty-two (44.2%) had cervical length <25 mm, and were admitted for true PTL. Out of the 53 women with cervical length ≥25 mm, 40 (75.5%) were discharged, and 13 (24.5%) were admitted. Women with threatened PTL but without true PTL, had significantly higher HR compared to those with true PTL (49.0±20.9% versus 34.8±19.6%; $p < .01$), and significantly lower stiffness of cervical IOS and EOS. Women who delivered preterm had significantly lower HR compared to those who did not delivery preterm, in overall cohort, and in the subset of only women with true PTL. Incidences of HR < 50% and <35% were statistically significantly higher in women who delivered preterm compared to those who did not ($p < .01$).

Conclusions: Cervical elastography with E-cervix may be useful for the assessment of women presenting to obstetrics triage for threatened PTL. Women with low HR, especially with HR less than 50 or 35%, are at increased risk of PTB.

Condensation: Women who delivered preterm had significantly higher HR compared to those who did not delivery preterm and significantly lower IOS and EOS, in overall cohort, and in the subset of women with true PTL. Incidences of HR < 50% and <35% were statistically significantly higher in women who delivered preterm compared to those who did not ($p < .01$).

Key message: Cervical elastography with E-cervix may be useful for the assessment of women presenting to obstetrics triage for threatened PTL.

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Cerclage; cervical length; fetal fibronectin; pessary; progesterone

Introduction

Preterm birth is a major cause of perinatal morbidity and mortality [1–3]. Different strategies have been adopted for the prevention of preterm birth, including progesterone, cervical pessary, cervical cerclage, as well as lifestyle modification, and diet supplementation [4–39]. Most of the strategies have been studied in high-risk population, such as women with short cervical length. The evidence supports the use of vaginal

progesterone in singleton gestations with short transvaginal ultrasound cervical length (TVU CL) before 24 weeks [4]. Based on this evidence, universal TVU CL screening at around 16–23 6/7 week has been proposed for all singleton gestations at the time of the anatomy scan [35,36].

Transvaginal ultrasound cervical length has been assessed in several populations (e.g. asymptomatic women as well as women with symptoms of preterm

labor (PTL)) to evaluate the risk of preterm birth. A meta-analysis of randomized trials showed that there was a significant association between knowledge of cervical length and lower incidence of preterm birth and later gestational age at delivery in symptomatic singleton gestations with threatened PTL [39].

Recently, ultrasound elastography, which assesses the biochemical and mechanical properties of a tissue has emerged as a promising ancillary tool to conventional ultrasound, and additional of cervical elastography to conventional cervical length has been shown to increase preterm birth prediction performance in women with short cervix [38]. Limitations of cervical elastography include multiple pressure sources. As the elastographic image is made by an external pressure, the uniformed pressure is needed for the stable elastographic image [38]. E-Cervix™ (WS80A; Samsung, Seoul, Korea) elastography is a recent quantification tool to measure the stiffness of the cervix using strain elastography [38]. E-Cervix™ shows the strain ratio between the internal and external orifices of the uterus using the vibrations caused by the natural internal movements. This technology could increase reproducibility and reduce interobserver variance using the sum of 50 elastographic images acquired over 3.5 s.

Objective

The aim of this study was to evaluate the prediction performance of E-Cervix for preterm birth in singleton gestation with threatened PTL.

Materials and methods

Study design

This was a single-center retrospective cohort study. Data on singleton pregnancies without prior preterm birth presenting to obstetrics triage for threatened PTL between 23 0/7 and 33 6/7 week from January 2017 to January 2019 were collected. Multiple gestations and women with prior spontaneous preterm birth were excluded.

Study population

Women who presented to obstetric triage for threatened PTL were identified through labor and delivery (L&D) records, triage book, and medical records. Threatened PTL was defined as any symptoms of possible uterine contractions, including abdominal cramps, low back pain, pelvic pressure, or bloody show, for which the woman presented to our L&D

triage unit [35]. Women with threatened PTL were evaluated according to an approved clinical guideline [35,39]. PTL (true PTL) was defined as a threatened PTL with a short cervix <25 mm. Women with threatened PTL but without true PTL, and those with true PTL both received also cervical elastography with E-cervix at the time of triage.

Women with true PTL were recommended intervention, including admission, tocolysis, and steroids.

Cervical elastography parameters

Cervical elastography was obtained at the sagittal plane for cervical length measurement using E-Cervix™ (WS80A; Samsung, Seoul, Korea). The quantification of cervical strain was calculated by a data analysis system that directly analyses raw data from the region of interest (ROI) and described as hardness ratio (HR), mean strain level within 1 cm from internal os (IOS) and external os (EOS).

IOS was defined as standardized strain mean level in 1 cm circle of IOS (value range 0, hard; 1, soft). EOS was defined as standardized strain mean level in 1 cm circle of EOS (value range 0, hard; 1, soft). HR was defined as 30-percentile hardness area ratio within 1 cm from the cervical canal in ROI (value range 0 soft; 100% hard).

Outcomes

The primary outcomes were the cervical elastography parameters comparing women with PTL who delivered <37 weeks with those who did not. Distribution of all cervical elastography parameters was calculated. We also compared cervical elastography parameters between women with PTL and those with threatened PTL but without PTL.

Data on pregnancy outcomes were obtained from hospital maternity records. In case of preterm birth, records were examined to determine whether the delivery was medically indicated or spontaneous preterm birth. Spontaneous preterm birth included either spontaneous onset of PTL or preterm premature rupture of membranes (PPROM).

Data analysis

Data are shown as means \pm standard deviation (SD), or as number (percentage). Univariate comparisons of dichotomous data were performed with the use of the chi-square test with continuity correction. Comparisons between groups were performed with the use of the *t*-test to test group means by assuming

Table 1. Characteristics of the women included in study.

	Threatened PTL N = 53	True PTL N = 42
Age (years)	28.9 ± 6.1	28.4 ± 6.1
Smoking	8 (15.1%)	4 (9.5%)
TVU CL (mm)	32.6 ± 6.8	20.9 ± 5.2
TVU CL <15 mm	–	4 (9.5%)
TVU CL <10 mm	–	4 (9.5%)
TVU CL <5 mm	–	1 (2.4%)
Admitted for PTL	13 (24.5%)	42 (100%)
Steroids	7 (13.2%)	38 (90.5%)
Tocolysis	3 (5.7%)	15 (35.7%)
Progesterone	12 (22.6%)	15 (35.7%)
Cerclage	1 (1.9%)	0
Pessary	2 (3.8%)	2 (4.7%)
PTB <37 weeks	12 (22.6%)	30 (71.4%)

PTL: preterm labor; PTB True PTL: defined as women with threatened PTL and TVU CL ≤25 mm.

Data are shown as number (percentage) or as mean ± standard deviation.

equal within-group variances. Logistic regression, presented as unadjusted odds ratio (crude OR) or as mean difference (MD) with the 95% confidence interval (CI), was performed.

Sensitivity, specificity, positive and negative likelihood ratio (LR+ and LR–, respectively) were calculated for different HR cutoff point (50 and 35%).

Results

Characteristics of the study population

Overall, 235 singleton pregnancies without prior spontaneous preterm birth presented to obstetrics triage for threatened PTL between 23 0/7 and 33 6/7 week of gestation. Of them, 95 (40.4%) received TVU CL and cervical elastography with E-cervix at the time of triage and therefore were included in the study.

Characteristics of the women included in the study are shown in Table 1. Out of the 95 singleton pregnancies without prior preterm birth and with threatened PTL between 23 0/7 and 33 6/7 week of gestation, 42 (44.2%) had cervical length <25 mm, and therefore were admitted for true PLT. Out of the 53 women with cervical length ≥25 mm, 40 (75.5%) were discharged, and 13 (24.5%) were admitted for persistent contractions or for physicians' discretion. 90.5% of the women admitted for true PTL received steroids, while only 13.2% in the group of women with threatened PTL and cervical length ≥25 mm.

Pregnancy outcomes

Overall, 42/95 (44.2%) of the women presented in the obstetrics triage for threatened PTL delivered before 37 weeks. Thirty (71.4%) and 12 (22.6%) cases of preterm birth <37 weeks were recorded in the true PTL

Table 2. Cervical elastography parameters of the women included in study.

	Threatened PTL N = 53	True PTL N = 42	p Value
Threatened PTL versus True PTL			
HR (%)	49.0 ± 20.9	34.8 ± 19.6	<.01
IOS	0.27 ± 0.15	0.37 ± 0.22	<.01
EOS	0.29 ± 0.11	0.39 ± 0.21	<.01
PTB <37 weeks N = 42			
No PTB N = 53			
PTB versus no PTB			
HR (%)	28.9 ± 16.7	53.7 ± 18.2	<.01
IOS	0.45 ± 0.24	0.24 ± 0.14	<.01
EOS	0.44 ± 0.22	0.28 ± 0.12	<.01
PTB <37 weeks N = 30			
No PTB N = 12			
PTB versus no PTB (only true PTL)			
HR (%)	26.7 ± 13.8	55.1 ± 17.1	<.01
IOS	0.51 ± 0.25	0.37 ± 0.21	<.01
EOS	0.50 ± 0.22	0.35 ± 0.17	<.01

HR: hardness ratio; IOS: mean strain level within 1 cm from internal os; EOS: mean strain level within 1 cm from the external os; PTL: preterm labor; PTB: preterm birth.

Data are shown as mean ± standard deviation. Boldface data indicate statistical significance.

group and in the threatened PTL with cervical length ≥25 mm group, respectively.

Cervical elastography parameters

Cervical elastography parameters of the women included in the study are shown in Table 2. Women with threatened PTL but without true PTL (cervical length ≥25 mm) had significantly higher HR compared to those with true PTL (49.0 ± 20.9% versus 34.8 ± 19.6%; MD 14.20, 95% CI 6.03–22.37; $p < .01$), and significantly lower IOS ($p < .01$) and EOS ($p < .01$). Women who delivered preterm had significantly lower HR compared to those who did not delivery preterm and significantly higher IOS and EOS, in overall cohort, and in the subset of only women with true PTL.

Cervical elastography parameters compared to transvaginal ultrasound cervical length

Incidences of HR <50% and <35%, and of cervical length at less than 25 mm were statistically significantly higher in women who delivered preterm compared to those who did not ($p < .01$), while we did not find statistically significant differences in the incidence of cervical length at less than 15 mm. Sensitivity, specificity, LR+, and LR– for HR <50% and HR <35% are shown in Table 3.

Discussion

Main findings

This single-center study aimed to evaluate the prediction performance of E-cervix for preterm birth in

Table 3. Sensitivity and specificity for hardness ratio and transvaginal ultrasound cervical length with 95% confidence interval in prediction of preterm birth <37.

	No PTB N = 53	PTB <37 weeks N = 42	p Value	Sensitivity (95% CI)	Specificity (95% CI)	LR+	LR-
TVU CL < 25 mm	12 (22.6%)	30 (71.4%)	<.01	71% (55–84)	77% (64–88)	3.15	0.36
TVU CL < 15 mm	1 (1.9%)	3 (7.1%)	NS	7% (1–19)	98% (90–100)	3.78	0.94
HR < 50%	8 (15.1%)	32 (76.2%)	<.01	76% (61–88)	85% (72–93)	5.04	0.28
HR < 35%	17 (32.1%)	36 (85.7%)	<.01	86% (71–95)	68% (54–80)	2.67	0.21

HR: hardness ratio; TVU CL: transvaginal ultrasound cervical length; PTB: preterm birth; NS: nonsignificant; LR+: positive likelihood ratio; LR-: negative likelihood ratio.

Data are shown as mean \pm standard deviation. Boldface data indicate statistical significance.

singleton gestation with threatened PTL. We included 95 singleton pregnancies without prior spontaneous preterm birth presented to obstetrics triage for threatened PTL between 23 0/7 and 33 6/7 week of gestation. The overall rate of cervical length <25 mm was 44.2% and the rate of admission for inpatient monitoring was 57.9%, ranging from 24.5% from women with cervical length \geq 25 mm, to 100% for those with cervical length >25 mm. Our study showed that cervical elastography parameters were statistically significant differences between women with threatened PTL and those with true PLT, and more important between women who delivered preterm and those who did not, with IOS, and EOS being statistically higher, and HR statistically lower. Sensitivity and specificity of HR maybe also better than cervical length alone, with 76 and 85, and 86 and 68% being sensitivity and specificity for HR <50% and HR <35%, respectively. However, this was not the primary endpoint of the study, and therefore the study was not powered for this analysis.

This study has several limitations. First, findings from our study are limited by the small sample size, and by the retrospective single-center study design. Moreover, given the small sample size the cannot explore if E-cervix reading was affected by history of prior preterm birth.

Implication

Women presenting with signs and symptoms suggestive of PTL continue to represent a clinical challenge. The overall rate of preterm birth in our study was 44.2%, being more than half of women delivered at term. Prior study showed that, whether these women are treated or not, 90% will not deliver within seven days, and almost 75% deliver at term [40,41]. Standard methods for assessing the risk of preterm birth, include uterine contractions, manual cervical exam, TVU CL, and biochemical markers, such as fetal fibronectin. Uterine contractions and manual cervical exam have poor predictive values, especially in low-risk women. A meta-analysis of three randomized

trials, including 287 singleton gestations with threatened PTL, showed that there is a significant association between knowledge of TVU CL and lower incidence of preterm birth and later gestational age at delivery [39]. Berghella and Saccone showed that fetal fibronectin testing in singleton gestations with threatened PTL was not associated with the prevention of preterm birth or improvement in perinatal outcome but is associated with higher costs [42]. Esplin et al. for the nuMoM2b Network, recently found that among nulliparous women with singleton pregnancies, quantitative vaginal fetal fibronectin and serial TVU CL had low predictive accuracy for spontaneous preterm birth [37].

Ultrasound elastography, which assesses the biochemical and mechanical properties of a tissue, has emerged as a promising ancillary tool to conventional ultrasound. Strain elastography is based on the measurement of a tissue displacement under compression, with tissue-deforming impulse with probe movement [38]. E-CervixTM (WS80A; Samsung, Seoul, Korea) elastography is a recent quantification tool to measure the stiffness of the cervix using strain elastography. The main advantage is that the operator does not apply pressure to the cervix, and the patients are allowed to breathe normally. Therefore, the major strengths of the technique are the operator-independence and the reproducibility [43]. Our study showed that cervical elastography parameters were statistically significant differences between women with threatened PTL and those with true PLT, and more important between women who delivered preterm and those who did not, with IOS, and EOS being statistically higher, and HR statistically lower. Sensitivity and specificity of HR were particularly good for HR <50% and for HR <35%.

Conclusion

In summary, cervical elastography with E-cervix may be useful for the assessment of women presenting to obstetrics triage for threatened PTL. Women with low

HR are at increased risk of preterm birth, with <50% and <35% as clinical useful cutoffs.

Further study with a larger sample size is needed.

Disclosure statement

No potential conflict of interest was reported by the authors.

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