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Predictive value of cervical length by ultrasound and cervical strain elastography in labor induction at term

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Abstract

Objective: This study aimed to examine whether addition of cervical elastographic parameters measured by ElastoScan for the cervix (E-cervix) improves the predictive value of cervical length (CL) in induction of labor at term by dinoprostone.

Methods: We conducted a prospective, observational study between January 2020 and June 2020 in term primiparous women (n = 73) who were scheduled for labor induction by a 10-mg dinoprostone vaginal insert. The time intervals from the start of labor induction to regular uterine contractions and to vaginal delivery were calculated as the primary outcomes. We divided subjects into two groups using a threshold of 24 hours. Ultrasound measurements were compared between the two groups and the area under the curve (AUC) of the prediction model was calculated.

Results: Women who delivered vaginally within 24 hours had a shorter CL and softer cervix than those who delivered after 24 hours. The combination of CL and elastographic parameters increased the AUC to 0.672 compared with CL alone (AUC = 0.637).

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Conclusions: Measurement by E-cervix is relatively reproducible. Addition of cervical strain elastography slightly improves the predictive performance of CL in vaginal delivery within 24 hours. This technique is a promising ancillary tool for use with ultrasound.

Keywords

Transvaginal ultrasound, cervix, strain elastography, labor induction, cervical length, vaginal delivery

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Introduction

Induction of labor (IOL), which is artificial stimulation of labor before its spontaneous onset, is a common practice in modern obstetrics. Nearly one quarter of all births require IOL.[1] When the risks of continuing the pregnancy outweigh the risks associated with IOL and delivery, promptly terminating the pregnancy via IOL to reduce maternal and neonatal morbidity and mortality is essential. In some cases, IOL might result in a prolonged, and even an ineffective, labor process. This ultimately leads to an increased risk of a cesarean section and other postpartum and neonatal complications.[2,3] These risks add psychological and economic burden to patients.

Pre-induction cervical status is the most important predictor of a successful induction, and initiation of labor is an extremely complex physiological process.[4] Therefore, various technologies for assessing the cervical condition are used. The Bishop score system has been adopted worldwide to classify the cervix as "favorable" or "unfavorable" and to decide on management of IOL.[5,6] However, some issues of the Bishop score limit its reproducibility, diagnostic accuracy and patients' acceptance. These inherent disadvantages require new techniques to overcome these limitations.

Transvaginal sonography technology is more objective and less operator-dependent, and may provide an alternative or complementary method to digital palpation. Ultrasound cervical length (CL) measurement is associated with success of IOL, preterm delivery, and even the outcome of delivery after IOL.[7–9] Sonography can be used to measure stiffness of the target tissue, including strain elastography and shear wave elastography. [10,11] Carlson et al.[12] conducted a longitudinal study to quantifiably describe the softness of the cervix by measuring shear wave speed in pregnant women and considered this technology promising. Agarwal et al.[13,14] conducted clinical studies, which showed that cervical shear wave elastography was useful for assessing the risk of preterm birth. However, some problems remain in application of this new tool because of cervical anatomy and microstructure.[15] Cervical strain elastography has been introduced to evaluate cervical softness to predict spontaneous preterm delivery[16,17] and successful IOL.[18–22] Despite these positive results, cervical strain elastography is still controversial because of a paucity of standardized measures. Because the pregnant cervix is not completely homogeneous, regions of interest (ROIs) selected subjectively in previous studies cannot reflect the whole cervix.

To address the disadvantages that limit the clinical practicability and comparability of cervical strain elastography, ElastoScan for the cervix (E-cervix), which is a semi-automatic program for performing strain elastography in the cervix, was created. This tool obtains multiple parameters related to cervical stiffness based on tissue displacement induced by physiological arterial pulsations. E-cervix also semi-automatically evaluates the whole cervix as an ROI and analyzes the heterogeneity of the entire cervix. This novel technology has been studied to predict cervical insufficiency[23] and spontaneous preterm delivery in several studies,[16,24,25] in which the results were all positive.

This study aimed to assess the reproducibility of E-cervix. We also aimed to examine whether addition of cervical elastographic parameters measured by E-cervix can improve the predictive value of CL in IOL at term by dinoprostone.

Methods

Patients

We performed a prospective, observational study between January 2020 and June 2020 in Women's Hospital, Zhejiang University School of Medicine, China. Patients who were included in the study met the following criteria: 1) singleton pregnancy, 2) $\geq$37 gestational weeks, 3) a live fetus with cephalic presentation, 4) indications of induced labor, 5) a cervical Bishop score <6, and 6) intact amniotic membranes. Exclusion criteria were as follows: 1) an abnormal fetus or clear contraindications of vaginal delivery and 2) a history of cervical insufficiency or cervical surgery. Informed consent for performing cervical strain elastography was signed by all patients. Approval for the study protocol was obtained from the institutional review board of Women's Hospital, Zhejiang University School of Medicine (IRB-20200276-R).

Acquisition of clinical data

Maternal weight and height were measured when patients were admitted to hospital, and maternal characteristics and obstetric history were recorded in the database of the hospital medical system. Bishop score data were acquired by clinical obstetricians. Digital palpation was performed twice by two obstetricians who had more than 5 years of experience in the obstetric field. The Bishop score was recorded only when the two obstetricians scored the same. If this was not the case, another senior obstetrician assessed the cervix again and determined the final score.

Cervical elastography

Assessment of pre-induction cervical ultrasound was performed transvaginally by one of two sonographers who had more than 15 years of experience in obstetric and gynecologic ultrasound and had received related training on the new program. A Samsung ultrasound machine (WS80A; Samsung Medison, Seoul, South Korea) equipped with a V5-9 transvaginal transducer (frequency range: 5–9 MHz) and an ElastoScan (Samsung Medison) option was used. The patients were required to empty their bladders and were placed in the dorsal lithotomy position. The transducer was gently inserted and placed in the anterior fornix of the vagina. CL was measured from the internal os to the external os in the midsagittal plane with the entire cervical canal visible on a grayscale ultrasound image as described by Iams et al.[26] The operator then started the ElastoScan to perform cervical strain elastography with dual images, with a grayscale image on the left and an elastogram on the right side (Figure 1). During the

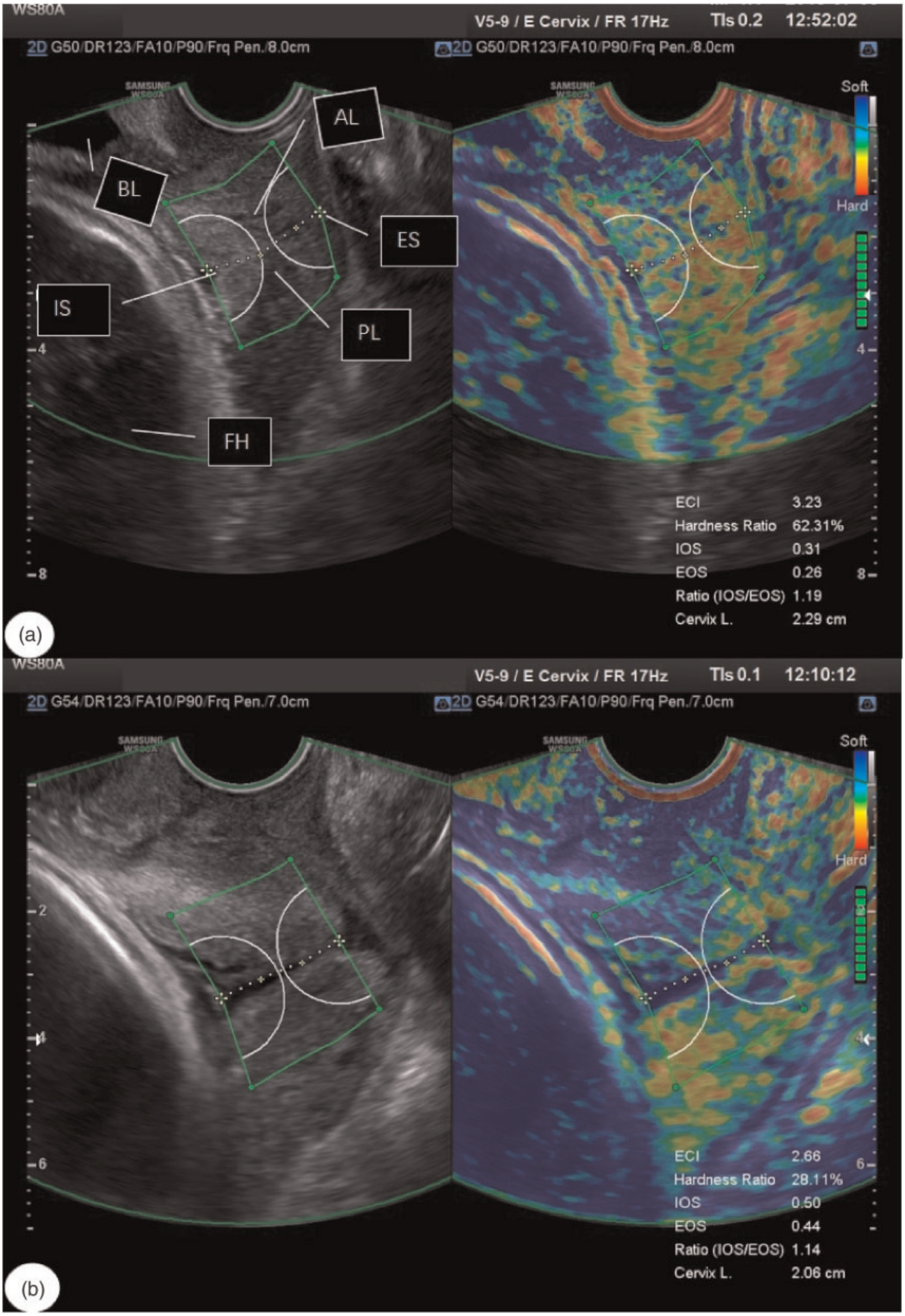

Figure 1. Transvaginal cervical elastographic images obtained by ElastoScan software on a Samsung WS80A system in two pregnant women with a singleton term pregnancy. (a) Image of an unfavorable cervix. (b) Image of a favorable cervix.

BL, bladder; AL, anterior lip of the cervix; PL, posterior lip of the cervix; IS, internal os; ES, external os; FH, fetal head.

examination, no additional pressure was applied to the cervix by the operator and the patient was asked to breathe normally. The motion bars on the right side of the screen monitored the steadiness of the transducer. All motion bars turned green and strain images were generated only when the force provided by the operator on the cervix or fetal movements were within the predetermined range. The image was displayed in a spectrum of colors from blue (soft) to red (hard) and the sonographers were blind to the Bishop scores of the subjects.

After the elastogram was displayed, all elastographic parameters were calculated by the E-cervix system. First, the operator drew the cervical canal by selecting four points between the internal and external os of the cervix (Figure 1). Once the cervical canal was defined, the ROI automatically appeared, and it included the entire cervical area. The operator could adjust green points to redefine the ROI. Simultaneously, two fan-shaped ROIs with a radius of 1 cm that were automatically generated around the internal os and the external os were defined. Finally, the following multiple parameters were calculated by E-cervix and displayed in the bottom right corner of the screen. 1) The elasticity contrast index (ECI) is an average contrast index of the pixels within the ROI, and it represents how heterogeneous or homogeneous the object is within the ROI box. The range of the ECI is from 0 (homogeneous) to 81 (heterogeneous). 2) The hardness ratio (HR) is the percentage of the upper 30% of the red (hard) pixel area within the ROI and represents how much area is occupied by hard pixels in the ROI, with a range from 0% to 100%. 3) The mean average strain value of the internal os (IOS) and external os (EOS) ranged from 0 (hard) to 1 (soft). 4) The IOS was divided by the EOS to obtain the ratio.

Reproducibility of cervical elastography

To evaluate the reproducibility of cervical strain elastography of E-cervix, we performed pre-induction ultrasound elastography three times in the first 60 participants. Operator A (Yimin Zhou) performed the elastography twice consecutively for the intraobserver test, while operator B (Lulu Zhou) performed elastography once for the interobserver test. For the data of these 60 patients for final analysis, we included the shortest CL and the average of elastographic parameters of three measurements.

IOL

IOL was performed in all patients by Propess® (10-mg dinoprostone vaginal insert; Controlled Therapeutics FERRING, East Kilbride, Scotland, UK). Propess was placed transversely in the posterior fornix of the vagina. External cardiotocography was performed to monitor the fetal status and uterine contractions. Regular contractions, one of the signals of labor, were defined as those that occurred every 5 to 6 minutes, and each one lasted at least 20 to 30 s. The Propess was removed once spontaneous delivery occurred. If there were no signs of reaching labor (with irregular contractions or no contractions) in 24 hours, the cervix was assessed again and another Propess was inserted if required.

The time intervals from IOL to regular uterine contractions and to vaginal delivery were the main outcomes in our study. For women in whom another Propess was applied, the time interval was calculated from the time point of when the first Propess was inserted to the endpoints. Other pregnant outcomes were recorded and analyzed, such as neonatal birthweight. Patients who never reached regular contractions and ultimately underwent cesarean section were excluded from further analysis.

Statistical analysis

Clinical characteristics of the patients are shown as median (interquartile range) and number (%). Intraobserver and interobserver reproducibility of these parameters are expressed by intraclass correlation coefficients (ICCs) and the 95% confidence interval (CI).[27,28] The Bland–Altman plot of the average against the difference between the two measurements was produced. Subjects were grouped by time intervals using a threshold of 24 hours (≤24 hours and >24 hours). Comparisons of maternal demographic characteristics, and pregnancy and neonatal outcomes between the two groups were performed using the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables. The area under the curve (AUC) of the prediction model was calculated by a receiver operating characteristic (ROC) curve. The sensitivity and specificity were calculated at the optimal cutoff determined by the Youden index. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) and a two-tailed $P<0.05$ was considered statistically significant.

Results

Figure 2 shows a flowchart of the study. A total of 106 women were originally included in this study after having cervical elastography performed. Nine patients were excluded in whom cesarean section was performed because of fetal distress before regular uterine contractions were achieved. Of the 97 participants, 60 reached regular uterine contractions within 24 hours. Seventy-three women achieved successful vaginal delivery after IOL and the remaining women were excluded from further analysis for delivery by cesarean section (15 for relative cephalopelvic disproportion, 7 for fetal distress, 1 for placental abruption, and 1 for uterine infection).

The ICCs for operator A ranged from 0.723 (95% CI, 0.536–0.834) to 0.905 (95% CI, 0.840–0.943) for elastographic parameters and the ICC was 0.966 (95% CI, 0.944–0.980) for CL (Table 1). This finding indicated that repeatability of measurements by the same operator was good to excellent based on common criteria.[29] The interoperator reproducibility was excellent, with the ICCs ranging from 0.772 (95% CI, 0.618–0.864) to 0.938 (95% CI, 0.896–0.963) for elastographic parameters and 0.964 (95% CI, 0.940–0.979) for CL. Bland–Altman plots show the degree of concordance between pairs of parameters generated by the same observer and by two observers (Figures 3 and 4). Up to 10% (6/60) of the points were outside the 95% limit of agreement in the Bland–Altman plots of intraobserver agreement and there was up to 8% (5/60) for interobserver agreement.

Maternal demographic characteristics, ultrasound cervical assessments, and pregnancy outcomes were compared between the two groups of the time interval of induction to regular contractions (Table 2). Maternal age, gestational weeks at examination, pre-pregnancy body mass index (BMI), and outcomes of pregnancy were not significantly different between the two groups. However, BMI was significantly higher in the longer time interval group (>24 hours) compared with the shorter time interval group (≤24 hours) ($P=0.045$). In the ≤24 hours group, the median CL was significantly shorter ($P=0.005$) and the Bishop score was higher ($P=0.025$) than those in the >24 hours group. Among all elastographic parameters, although the HR of participants in the ≤24 hours group was lower and the IOS, EOS, and IOS/EOS ratio were higher than those in the >24 hours group, this was not significant. ROC curves were created to show the predictive efficiency of each individual parameter, and the results are shown

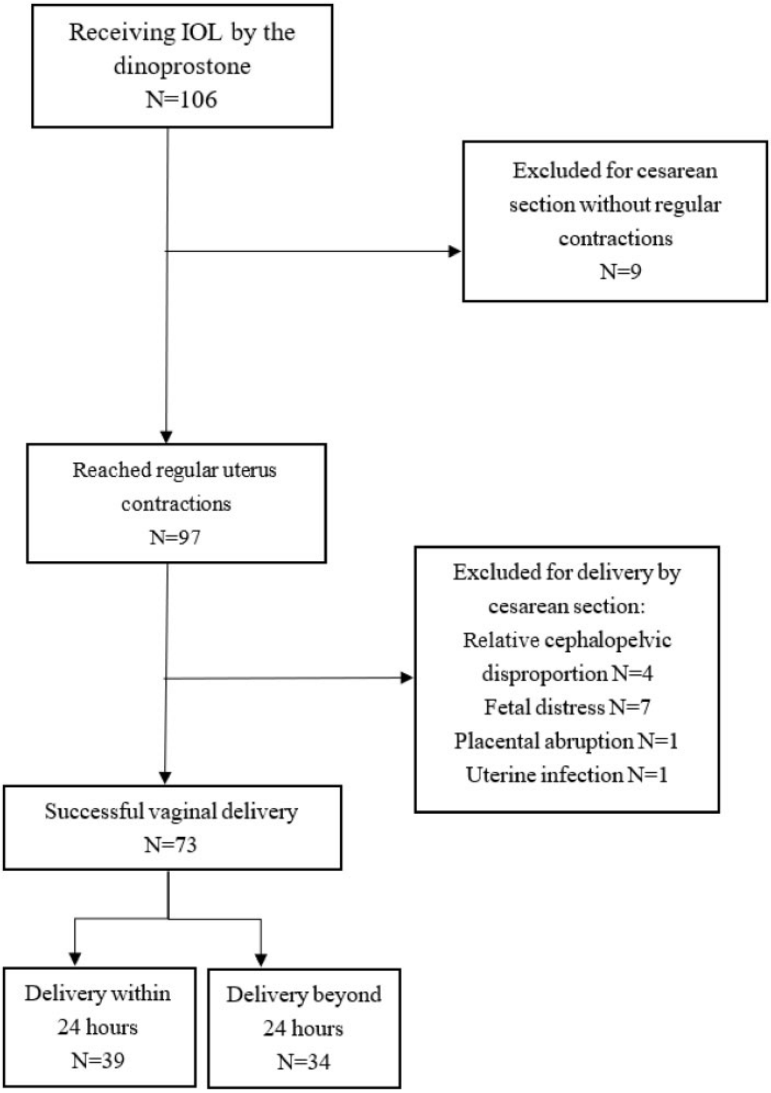

Figure 2. Flowchart showing participation and exclusion in the study.
IOL, induction of labor.

in Table 3 and Figure 5. The AUC of CL (0.670, 95% CI 0.543–0.797) was higher than that of the Bishop score (0.631, 95% CI: 0.516–0.745) for predicting an interval >24 hours.

When parameters were grouped by vaginal delivery within 24 hours, BMI was still significantly different between the two groups (P=0.017) (Table 4). CL was significantly shorter (P=0.044) and the Bishop score was higher (P=0.031) in the ≤24 hours group than in the >24 hours group, which indicated a more favorable cervical status. For elastographic parameters, the median HR was significantly lower (P = 0.02) and the IOS was higher

Table 1. Intraobserver and interobserver reproducibility for CL and all elastographic parameters.

Parameters	Intraobserver reproducibility ICC (95% CI)	Interobserver reproducibility ICC (95% CI)
CL	0.966 (0.944–0.980)	0.964 (0.940–0.979)
ECI	0.733 (0.553–0.841)	0.801 (0.666–0.881)
HR	0.905 (0.840–0.943)	0.938 (0.896–0.963)
IOS	0.838 (0.729–0.903)	0.904 (0.839–0.942)
EOS	0.777 (0.626–0.867)	0.829 (0.713–0.898)
Ratio	0.723 (0.536–0.834)	0.772 (0.618–0.864)

ICC, interclass correlation coefficient; CI, confidence interval; CL, cervical length; ECI, elasticity contrast index; HR, hardness ratio; IOS, mean strain level of the internal os; EOS, mean strain level of the external os; ratio, IOS/EOS.

($P = 0.033$) in the ≤24 hours group than in the >24 hours group. To show the predictive efficiency of cervical parameters on vaginal delivery within 24 hours, we constructed ROC curves (Table 3, Figure 6) and found that the AUCs of CL, the HR, the IOS, and the Bishop score were similar, and the combination of CL and elastographic parameters resulted in a larger AUC value. The optimal cutoff of CL was 2.27 cm, with a sensitivity of 85.3% and specificity of 48.7%. For the HR and IOS, the sensitivity was 55.9% and 52.9%, and the specificity was 79.5% and 74.4%, respectively, when using a cutoff of 57.95% for the HR and 0.33 for the IOS, which maximized these data.

Discussion

In our study, we investigated the predictive value of CL and parameters of strain elastography as measured by E-cervix at two time intervals from the start of IOL to regular uterine contractions and to vaginal delivery. We found the following findings in term primiparous women with a singleton pregnancy who underwent IOL by dinoprostone. 1) Transvaginal CL measurement and elastography by E-cervix were fairly reproducible. 2) There were significant differences in CL and the Bishop score between women who reached regular uterine contractions within 24 hours and those who did not. 3) There were significant differences in CL, the HR, and the IOS between women who achieved vaginal delivery within 24 hours and those who did not. 4) Addition of the HR and IOS mildly improved the predictive performance of vaginal delivery within 24 hours by CL.

The reproducibility of elastographic parameter measurements by E-cervix has been previously evaluated with varying results. Excellent intra- and interobserver agreement (ICC: 0.947–0.991 and 0.855–0.989, respectively) were acquired by Du et al.[30] ($n = 60$) who found that multiple parameters provided by E-cervix were repeatable. Kwak et al.[31] showed that the reproducibility of elastographic parameters could be improved in terms of intraobserver and interobserver variance (ICC: 0.639–0.725 and 0.538–0.718, respectively) in 90 singleton pregnant women at 16 weeks and 32 weeks of gestation. Our study showed fairly good reproducibility of ultrasound elastography in 60 term singleton women with an intraobserver ICC of 0.723–0.905 and interobserver ICC of 0.772–0.938. We used the same technique that Swiatkowska-Freund et al.[18] and Hwang et al.[19] used, and cervical elastographic parameters were calculated on the basis of tissue displacement caused by physiological arterial pulsations and the patient's respiration. The motion bars on the screen guaranteed the force that the

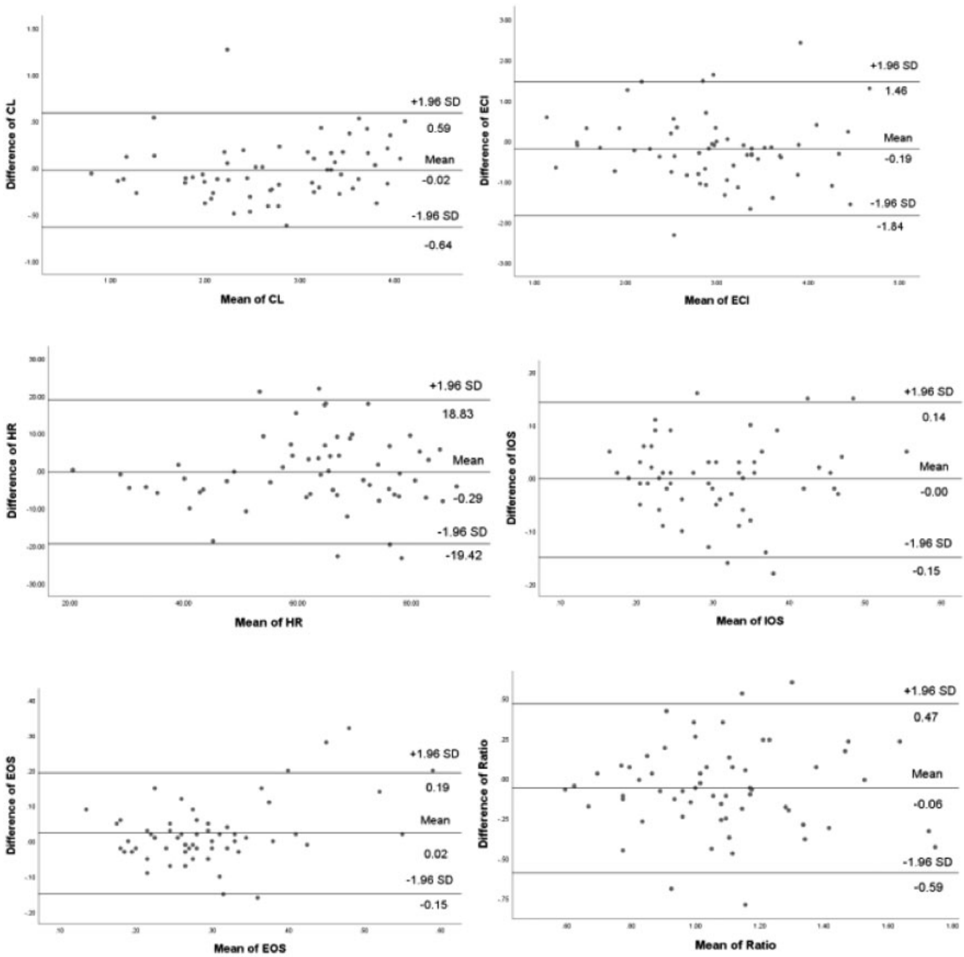

Figure 3. Bland–Altman plots of intraobserver agreement of parameters of ElastoScan for the cervix obtained by operator A. The central line represents the mean difference, and the upper and lower lines represent the mean $\pm$ 1.96 $\times$ standard deviation.
CL, cervical length; ECI, elasticity contrast index; HR, hardness ratio, IOS, EOS, mean strain level of the internal/external os; Ratio, IOS/EOS.

operators applied on the cervix or that fetal movement was within the predetermined range. Manual compression applied by operators is highly dependent on the operator and a different degree of compression is possible among operators. Therefore, our new technology, E-cervix, could considerably reduce such errors caused by the manual compression, thus possessing better reproducibility. CL measurement showed better repeatability with an intraobserver ICC of 0.966 (0.944–0.980) and an interobserver ICC of 0.964 (0.940–0.979) compared with elastographic parameters. Because measuring CL is easy to perform and CL data are accurately obtained when a clear image of the whole cervix is displayed, this explains why ultrasound measurement of CL is more repeatable than the other parameters.

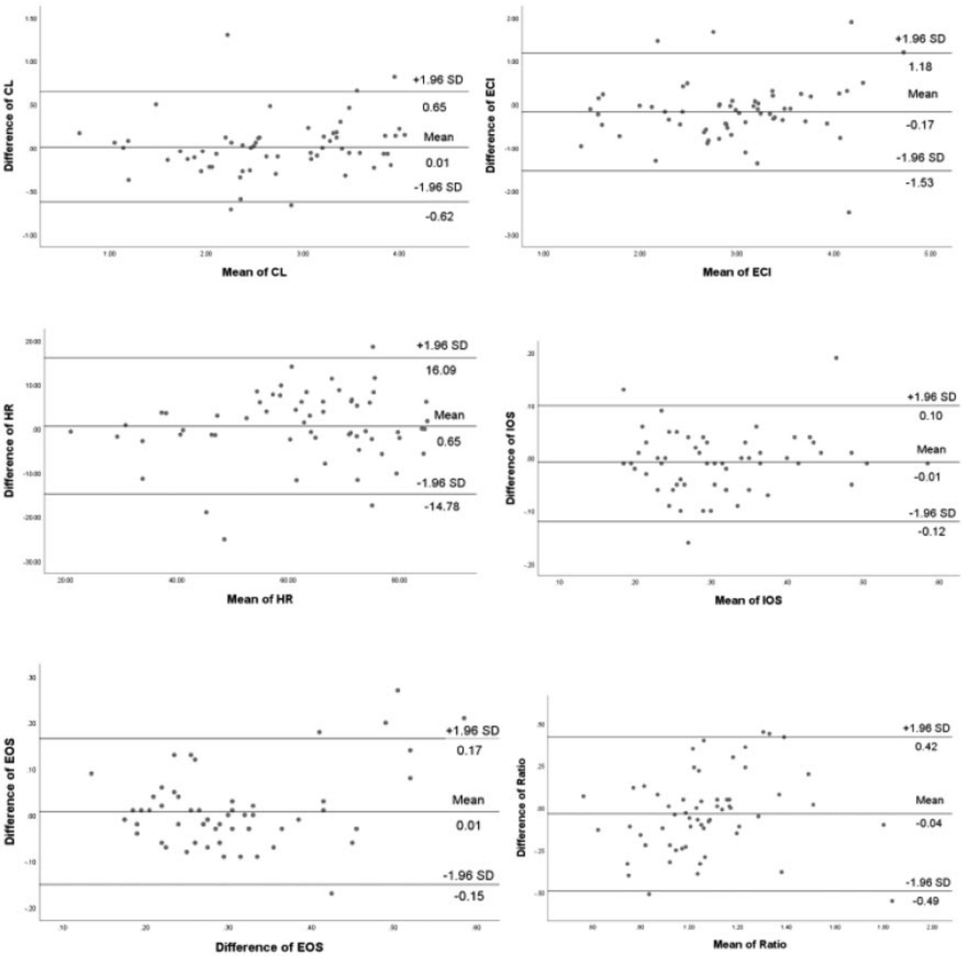

Figure 4. Bland–Altman plots of the interobserver agreement of parameters of ElastoScan for the cervix obtained by operators A and B. The central line represents the mean difference, and the upper and lower lines represent the mean $\pm$ 1.96 $\times$ standard deviation.
CL, cervical length; ECI, elasticity contrast index; HR, hardness ratio, IOS, EOS, mean strain level of the internal/external os; Ratio, IOS/EOS.

IOL has become an indispensable part of contemporary clinical practice. On account of potential risks of IOL, such as prolongation of the labor process and chorioamionitis,[32] the effect of medical management applied and subsequent outcomes need to be predicted. Recent articles on cervical strain elastography have indicated the potential of this modality to predict successful IOL.[18–21] Swiatkowska-Freund et al.[18] first investigated the usefulness of cervical strain elastography in assessing cervical status in pregnancy and reported a promising result. Hwang et al.[19] showed that this new tool predicted successful IOL in nulliparous patients when using imaging analysis, and the combination of elastographic features with CL had more predictive value than each technique alone. Hee et al.[20] found that this semi-quantitative

Table 2. Maternal and neonatal characteristics of the two groups categorized by the time interval of induction to regular contractions.

	Total (n = 97)	≤24 hours group (n = 60)	>24 hours group (n = 37)	P value
Maternal age (years)	29 (26.5–32)	29 (26–32)	30 (27–33)	0.579
GA at examination (weeks)	38 (38–40)	39 (38–40)	40 (39–40)	0.271
Gravidity	1 (1–2)	1 (1–2)	2 (1–2)	0.069
Weight gained (kg)	14.0 (11.3–16.0)	13.0 (11.1–16.0)	15.0 (11.0–16.5)	0.241
Pre-pregnancy BMI (kg/m^2)	20.70 (19.48–23.02)	20.26 (19.25–22.86)	21.23 (19.78–23.24)	0.133
BMI	26.38 (24.97–28.35)	25.83 (24.26–28.26)	27.24 (25.53–29.13)	0.045
Indications of IOL				
Prolonged pregnancy	35 (36.08)	19 (31.67)	16 (43.24)	0.249
GDM	11 (11.34)	6 (10.00)	5 (13.51)	0.744
Hypertensive disorder	8 (8.25)	5 (8.33)	3 (8.11)	1.000
Abnormal cardiotocography	8 (8.25)	7 (11.67)	1 (2.70)	0.150
Oligohydramnios	8 (8.25)	5 (8.33)	3 (8.11)	1.000
Thrombophilia	13 (13.40)	5 (8.33)	8 (21.62)	0.073
Others	14 (14.43)	13 (21.67)	1 (2.70)	0.010
Cervical length (cm)	2.76 (2.00–3.22)	2.49 (1.81–3.03)	2.99 (2.43–3.38)	0.005
ECI	3.75 (2.86–4.49)	3.90 (2.85–4.76)	3.48 (2.78–4.12)	0.147
HR	53.75 (39.13–65.12)	51.42 (38.99–62.63)	59.76 (41.47–71.81)	0.117
IOS	0.33 (0.29–0.42)	0.34 (0.30–0.44)	0.31 (0.25–0.40)	0.070
EOS	0.33 (0.28–0.43)	0.34 (0.28–0.43)	0.31 (0.26–0.44)	0.329
Ratio	1.02 (0.84–1.18)	1.03 (0.84–1.20)	1.00 (0.82–1.14)	0.293
Bishop score	3 (2–4)	3 (3–4)	3 (2–4)	0.025
GA at delivery	40 (39–40)	40 (39–40)	40 (39–40)	0.288
Neonatal birth weight (g)	3310 (3075–3600)	3260 (3028–3593)	3440 (3160–3615)	0.318
Neonatal sex				
Male	51 (52.58)	29 (48.33)	22 (59.46)	0.286
Female	46 (47.42)	31 (51.67)	15 (40.54)	
Hemorrhage of delivery (mL)	250 (200–350)	250 (150–350)	200 (200–300)	0.982

Data are expressed as median (interquartile range) and number (%).
GA, gestational age; BMI, body mass index; IOL, induction of labor; GDM, gestational diabetes mellitus; ECI, elasticity contrast index; HR, hardness ratio; IOS, mean strain level of the internal os; EOS, mean strain level of the external os; ratio, IOS/EOS.

Table 3. Predictive performance of significant individual parameters and combined parameters for prediction of contractions and vaginal delivery.

	Parameter	AUC (95% CI)	Cutoff	Sensitivity (%)	Specificity (%)
Regular contractions within 24 hours	CL	0.670 (0.543–0.797)	2.34 cm	90.9	45.1
	Bishop score	0.631 (0.516–0.745)	2.5	43.2	81.7
Vaginal delivery within 24 hours	CL	0.637 (0.509–0.765)	2.27 cm	85.3	48.7
	HR	0.659 (0.530–0.788)	57.95%	55.9	79.5
	IOS	0.645 (0.516–0.774)	0.33	52.9	74.4
	Bishop score	0.643 (0.516–0.770)	4.5	94.1	28.2
	CL+HR+IOS	0.672 (0.553–0.791)	–	87.2	43.6

AUC, area under the curve; CI, confidence interval; CL, cervical length; HR, hardness ratio; IOS, mean strain level of the internal os.

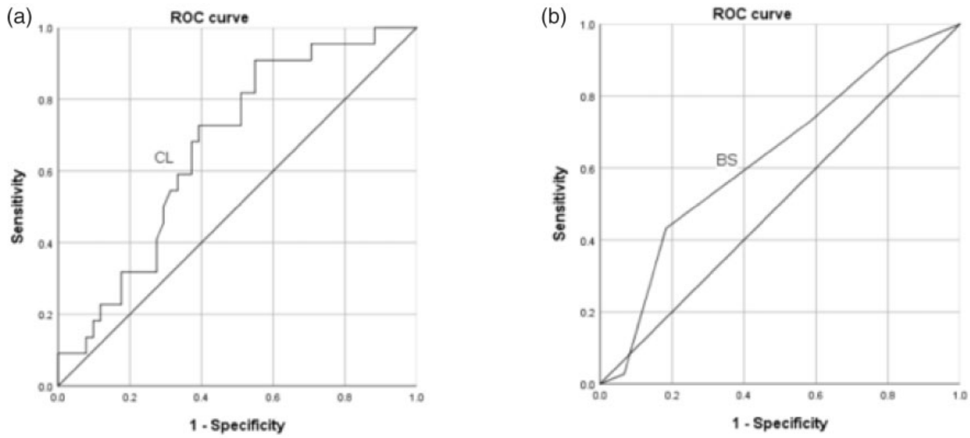

Figure 5. Receiver operating characteristic curves of CL and the BS for predicting a time interval of ≤24 hours for induction to regular uterine contractions
CL, cervical length; BS, Bishop score.

elastography was better for predicting the time of prolonged cervical dilation during labor than the Bishop score and CL. A recent meta-analysis investigated the diagnostic accuracy of different methods for evaluating cervical status during pregnancy in predicting successful IOL and vaginal delivery.[21] This meta-analysis showed that cervical strain elastography was as reliable as CL, and their performance was better than the Bishop score.

The definition of successful IOL varies and there is no general consensus. Therefore, we chose two time intervals to assess the effect of IOL instead of redefined successful IOL. Achieving regular uterine contractions and vaginal delivery were our two endpoints. Most studies regarded vaginal delivery as successful IOL.[33,34] This remains questionable because a large number of patients undergo emergency cesarean section for fetal distress or worsening of maternal diseases, and have a satisfactory process of labor. To exclude such confounders that might interfere in the process of labor, especially in the first and second stages of labor, we considered that the time interval of induction to regular contractions could reflect the efficiency of IOL more directly. Additionally, the decision on whether to induce labor mostly depends on the requirement of delivery in a short time. Predicting vaginal delivery within a specific time is necessary when an immediate delivery is required in women with some complications of pregnancy.

We found that CL was significantly shorter in women who reached regular contractions within 24 hours than in those who did not. This finding indicates that a shorter cervical canal has better performance of induction. Additionally, the Bishop score was significantly higher in women who reached regular contractions within 24 hours than in those who did not. These results are in line with clinical experience and previous studies.[8,9] We also found that CL measurement had a higher AUC value than that of the Bishop score, which was more dependent on an obstetrician's experience. Among the elastographic parameters, the HR appeared to be lower and the ECI, IOS, EOS, and IOS/EOS ratio were higher in the <24 hours group than those in the ≥24 hours group, but this was not significant. We speculate that

Table 4. Maternal and neonatal characteristics of the two groups categorized by the time interval from induction to vaginal delivery.

	Total (n=73)	≤24 hours group (n=39)	>24 hours group (n=34)	P value
Maternal age (years)	29 (27–32)	29 (26–32)	30 (27–32)	0.735
GA at examination (weeks)	39 (38–40)	39 (38–40)	39 (38–40)	0.789
Gravidity	1 (1–2)	1 (1–2)	2 (1–2)	0.110
Weight gained (kg)	14.0 (11.3–16.0)	12.5 (11.0–16.0)	14.3 (11.5–16.3)	0.597
Pre-pregnancy BMI (kg/m^2)	20.52 (19.37–22.86)	20.19 (18.83–21.48)	21.02 (19.74–23.24)	0.040*
BMI	26.05 (24.44–28.22)	25.71 (24.01–27.24)	26.88 (25.31–29.92)	0.017*
Indications of IOL				
Prolonged pregnancy	24 (32.88)	13 (33.33)	11 (32.35)	0.929
GDM	9 (12.33)	3 (7.69)	6 (17.65)	0.288
Hypertensive disorder	6 (8.22)	3 (7.69)	3 (8.82)	1.000
Abnormal cardiotocography	6 (8.22)	5 (12.82)	1 (2.94)	0.206
Oligohydramnios	6 (8.22)	3 (7.69)	3 (8.82)	1.000
Thrombophilia	10 (13.70)	3 (7.69)	7 (20.59)	0.172
Others	12 (16.44)	9 (23.08)	3 (8.82)	0.124
Cervical length (cm)	2.64 (1.99–3.03)	2.53 (1.78–3.03)	2.82 (2.41–3.23)	0.044
ECI	3.82 (2.86–4.49)	3.97 (2.81–4.63)	3.67 (2.91–4.42)	0.615
HR	52.46 (38.98–64.29)	48.49 (34.24–57.84)	60.82 (44.02–67.00)	0.020
IOS	0.34 (0.29–0.42)	0.38 (0.32–0.46)	0.32 (0.25–0.39)	0.033
EOS	0.34 (0.28–0.43)	0.36 (0.29–0.44)	0.31 (0.27–0.40)	0.150
Ratio	1.02 (0.83–1.18)	1.03 (0.90–1.18)	0.98 (0.79–1.18)	0.246
Bishop score	3 (2–4)	4 (3–5)	3 (2–4)	0.031
GA at delivery	40 (39–40)	40 (39–40)	40 (39–40)	0.841
Neonatal birth weight (g)	3210 (3040–3530)	3170 (2950–3440)	3295 (3155–3543)	0.137
Neonatal sex				
Male	38 (52.05)	20 (51.28)	18 (52.94)	0.887
Female	35 (47.95)	19 (48.72)	16 (47.06)	
Hemorrhage of delivery (mL)	200 (150–350)	200 (150–350)	250 (200–363)	0.301

GA, gestational age; BMI, body mass index; IOL, induction of labor; GDM, gestational diabetes mellitus; ECI, elasticity contrast index; HR, hardness ratio; IOS, mean strain level of the internal os; EOS, mean strain level of the external os; ratio, IOS/EOS.

mainly the small sample size contributed to this insignificant difference.

For predicting vaginal delivery within 24 hours, we compared multiple elastographic parameters between the two groups. Among these parameters, the HR and IOS were significantly different. The HR represents the stiffness of the whole ROI and the IOS represents the mean strain value of the internal os. Our study showed that the cervix was significantly softer and the IOS was softer in the ≤24 hours group than in the >24 hours group with vaginal delivery. Although CL and the Bishop score also showed significant differences between the groups, ROC curve analysis showed that the AUC of the HR was the largest, with a sensitivity of 55.9% and specificity of 79.5%. The AUCs of the IOS and Bishop score were the most similar and that of CL was the lowest. Additionally, the combination of the HR, the IOS, and CL increased the AUC value to 0.672.

Our study is the first to investigate the usefulness of elastographic parameters generated by E-cervix in predicting the time interval of induction to regular contractions and vaginal delivery within 24 hours in singleton pregnant women at term who were induced by dinoprostone. A strength of our

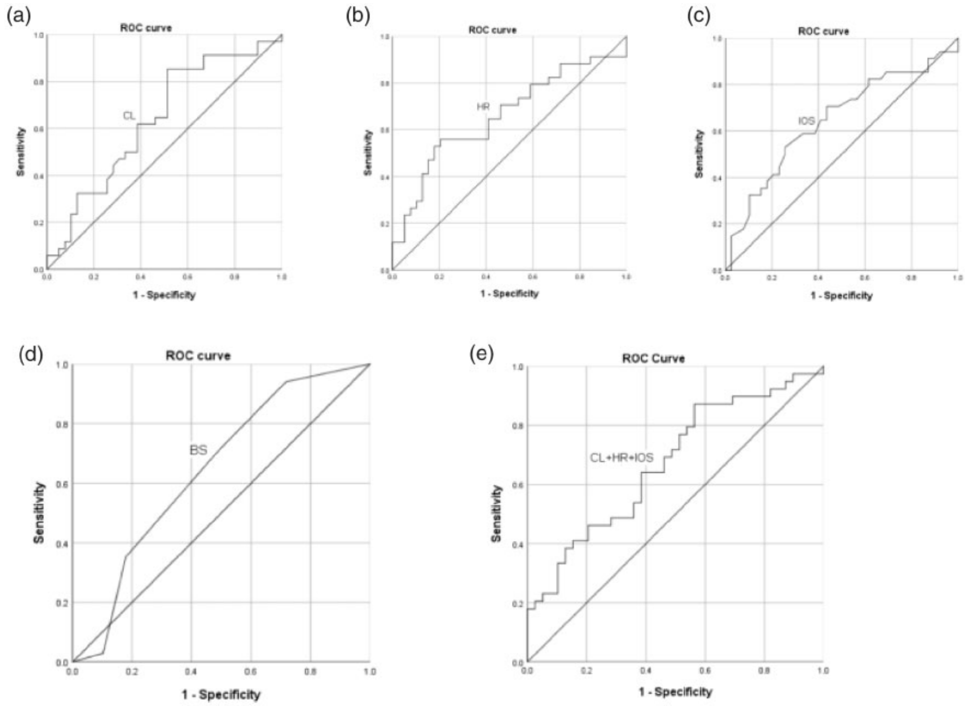

Figure 6. Receiver operating characteristic curves of CL, the HR, IOS, and BS and CL+HR+IOS for predicting vaginal delivery within 24 hours.
CL, cervical length; HR, hardness ratio; IOS, mean strain level of the internal os; BS, Bishop score.

study is that this new technique regards the whole cervix as the ROI and acquires multiple parameters to comprehensively assess the stiffness of the cervix. Another strength of our study is that it was a prospective, observational study in nulliparous women. Parous women have a more rapid labor, which may affect the predictive efficiency of these parameters.

The main limitation of our study is the small sample size. Additionally, BMI was significantly different between the two groups when the time interval of induction to regular uterine contractions was analyzed. Because BMI might affect the induction process of labor, a larger sample size is required to balance this factor.

From a clinical point of view, cervical strain elastography provides an objective assessment of ultrasound besides CL to evaluate cervical status before IOL, and it has the potential to be an ancillary tool for use with conventional ultrasound. Measurement of ultrasound is less operator dependent compared with the subjective Bishop score as assessed by digital palpation. Additionally, E-cervix is a semiautomatic tool that evaluates the cervix (both CL and stiffness) on the basis of intrinsic compression. Therefore, this tool enables standardization of measurements and generalization to different grades of hospitals. However, strain elastography has an inherent problem. Unlike shear wave elastography, strain elastography shows the relative stiffness of different parts in target tissue and it is not considered as a quantitative measurement. To address this problem, Hee et al.[20] applied a cap made of a material with a well-defined stiffness to the end of the ultrasound transducer. However, this method led to another problem that the reference cap reduced the quality of image, sometimes making differentiation of cervical anatomy difficult. Therefore, elastic parameters measured by E-cervix are semi-quantitative.

Our study shows that E-cervix is a repeatable tool for measuring stiffness of the cervix. Elastographic parameters measured by E-cervix can provide an equivalent predictive value to CL in achieving vaginal delivery within 24 hours. Although the addition of elastographic parameters does not result in a large increase in predictive performance in vaginal delivery within 24 hours, this technique is a promising ancillary tool to be used with ultrasound with improvement of the imaging process. Future studies with a larger sample size and a more homogenous population will help further determine the usefulness of E-cervix.

Author contributions

Conception and design of the study: BHZ, HFH, and QL. Acquisition of data: YMZ ML, YC, FFX, and MMY. Analysis of data: NJ, ML, and YJ. Interpretation of data: NJ, QQC, and YJ. Drafting the article: NJ and YMZ. Critically revising the article for important intellectual content: QL and HFH. All authors read and approved the final manuscript.

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding authors on reasonable request.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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