Prediction of preterm birth using the cervical consistency index

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KEYWORDS: cervical consistency; preterm birth; transvaginal ultrasound

ABSTRACT

Objectives To assess the diagnostic power of a new cervical consistency index (CCI) obtained using transvaginal sonography for the prediction of spontaneous preterm birth (PTB) and to establish reference ranges for this new variable.

Methods Included in this prospective cross-sectional study were 1115 singleton pregnancies at 5–36 weeks of gestation. Anteroposterior cervical diameter was measured before (AP) and after (AP′) application of pressure on the cervix using the transvaginal probe. The index was calculated using the formula: CCI = (AP/AP′) × 100. Cervical length was also measured. The outcomes evaluated were spontaneous PTB before 32, 34 and 37 weeks. Logistic regression and analysis of receiver-operating characteristics (ROC) curves were performed to evaluate the diagnostic power of CCI and cervical length (adjusted for gestational age). Intraclass correlation coefficients (ICCs) and Bland–Altman analysis were used to evaluate intra- and interobserver variability.

Results In the 1031 women with follow-up, the rate of spontaneous PTB before 32 weeks was 0.87%, before 34 weeks was 2.13% and before 37 weeks was 7.76% (n = 80). There 31 (3.01%) iatrogenic PTBs before 37 weeks. An inverse linear correlation between gestational age and CCI was observed, with regression equation: CCI (in %) = 89.8 – 1.35 × (GA in weeks); \( r^2 = 0.66, P < 0.001 \). Cervical length showed an inverse quadratic relationship with gestational age: CL (in mm) = 31.084 − 0.0278 × (GA in weeks)² + 1.0772 × (GA in weeks); \( r^2 = 0.076, P < 0.14 \). The intra- and interobserver ICCs for CCI were 0.99 (95% CI, 0.988–0.994) and 0.98 (95% CI, 0.973–0.987), respectively. The area under the ROC curve for CCI in the prediction of spontaneous PTB before 32 weeks was 0.947, for spontaneous PTB before 34 weeks it was 0.943 and for spontaneous PTB before 37 weeks it was 0.907. For a 5% screen-positive rate, CCI had a sensitivity of 67%, 64% and 45% for prediction of spontaneous PTB before 32, 34 and 37 weeks, respectively, with equivalent values of 11%, 9% and 11% for cervical length.

Conclusions CCI shows a clear inverse linear relationship with GA. Assessment of CCI is reproducible and is effective in the prediction of spontaneous PTB. This new variable appears to provide better prediction of spontaneous PTB than does cervical length. Copyright © 2011 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Preterm birth (PTB) is one of the greatest causes of perinatal mortality and also leads to long-term morbidity and increased healthcare costs1–5. It is responsible for more than half of all neonatal deaths as well as neurological sequelae3. Recent evidence suggests that the measurement of cervical length by transvaginal sonography (TVS) is effective in screening patients at high risk for PTB. Shortening of the cervix as evaluated by cervical length measurement has been shown to be one of the best predictors of PTB6,7.

The cervical changes evaluated by the measurement of cervical length using TVS have been the subject of numerous publications in the last 30 years, with more than 600 studies published8–12. However the cut-off points to be used and the poor positive predictive value for PTB remain controversial, especially in populations at low risk13. Despite the widespread use of cervical length...
measurement in screening for PTB in recent years, its rate has not been decreased. To the best of our knowledge, consistency of the cervix has not yet been evaluated using ultrasound. The aims of this study were to define and standardize a new TVS technique for determining cervical consistency (cervical consistency index (CCI)), to establish reference ranges for this new variable, to determine whether it is correlated with cervical length and to assess the potential value its assessment in the prediction of spontaneous PTB before 32, 34 and 37 weeks in asymptomatic pregnant women.

METHODS

Study population

This was a prospective cross-sectional study conducted from April 2009 to March 2010. It included 1115 consecutive pregnant women attending our ultrasound clinic for routine growth scans at 5–36 weeks’ gestation. Each woman underwent a TVS examination of the cervix once during pregnancy, at which cervical length and the CCI were evaluated. No longitudinal assessments of CCI were conducted. We included pregnant women without a history of conization, cerclage, cervical incompetence and Mullerian malformations. Patients with multiple pregnancies and preterm labor at the time of the examination were excluded. Gestational age was confirmed by first-trimester ultrasound in all cases. The study was approved by the institutional ethics committee and informed consent was obtained from all participants.

Ultrasound examination

Sonographic assessment of the cervix was performed by one of four physicians, each with more than 5 years of experience in prenatal ultrasound, using a Voluson E8, 730 Expert or 730 Pro (GE Healthcare Ultrasound, Milwaukee, WI, USA) ultrasound machine, equipped with a multifrequency volumetric transvaginal 6–9-MHz probe. The following variables were recorded: CCI, cervical length, gestational age and maternal weight, height, body mass index (BMI), parity and age. The endocervical funnel was not included in the measurement of cervical length. Images were collected and saved in Digital Imaging and Communications in Medicine (DICOM) format.

TVS assessment of cervical consistency index

To determine the CCI, the following five steps were performed. (1) Cervical length was measured using the standard technique, as described previously, avoiding excess pressure to the anterior lip of the cervix (Figure 1a, Videoclip S1). (2) Once the calipers had been placed, the screen was divided into two, and the image showing the cervical length measurement was fixed on the left side. With the right side of the screen displaying real-time images, pressure was applied softly and progressively on the cervix until no further shortening of the anteroposterior diameter could be observed. To determine accurately the point at which there was greatest shortening of the anteroposterior diameter, the cineloop function was used. The cervical length was then measured on the right side of the screen, with the traced line on each side of the screen then being moved to align with the longitudinal axis of the cervix if it did not already do so (Figure 1a). (3) The mid-point of the line running along the longitudinal axis of the cervix was calculated (C2) on each side of the screen (Figure 1a, Videoclip S1). (4) The anteroposterior diameter was measured on each side of the screen, perpendicular to the longitudinal axis of the cervix and through the point C2, from the most anterior to the most posterior lip of the cervix (Figure 1b, Videoclip S1). On the left side of the screen, this diameter was termed AP, and on the right side of the screen it was termed AP’. (5) Diameter AP’ was divided by diameter AP and this ratio multiplied by 100 to obtain the CCI: CCI = (AP’/AP) × 100. In the example illustrated in Figure 1, AP = 46 mm, AP’ = 24 mm and so CCI = (24 mm/46 mm) × 100 = 52%.

The duration of the examinations was 5–9 min. All ultrasound measurements to obtain the CCI were repeated twice and the lowest of the two measurements was used for statistical analysis.

Data on pregnancy outcome were collected from patients’ medical records. The obstetric records of all patients who delivered before 37 weeks were examined to determine whether the PTB was iatrogenic or spontaneous. The latter included those with spontaneous onset of labor and those with preterm prelabor rupture of membranes. Women who underwent active intervention with progesterone were excluded from the analysis.

Statistical analysis

Data were analyzed using SPSS v.18 (SPSS Inc., Chicago, IL, USA). We performed univariate analysis using measures of central tendency and dispersion, as well as simple linear and multiple regression. Pearson’s correlation coefficient was used to assess the relationship between quantitative variables. The CCI and cervical length were analyzed primarily in relation to gestational age, but maternal BMI, parity and age were also considered in multiple regression models. Multivariable logistic regression analysis was used to identify variables that provided a significant independent contribution in explaining the rate of spontaneous PTB before 32, 34 and 37 weeks. Receiver–operating characteristics (ROC) curves were generated for each diagnostic test (percentiles of cervical length and CCI according to gestational age) to evaluate their diagnostic ability to predict spontaneous PTB. The areas under the ROC curves (AUCs) and the 95% CIs of these areas were calculated.

The ROC curves were also used to determine the mathematically best cut-off value for each diagnostic test, this value being defined as that corresponding to the point on the ROC curve situated furthest away from
Ultrasound images with annotation illustrating the assessment of the cervical consistency index (CCI). (a) First step: the cervical length is measured (in mm). Second step: a line showing the cervical length is drawn on both sides of the screen (yellow lines), which is then shifted to align with the longitudinal axis of the cervix (red lines). Third step: the mid-point of the cervical length is calculated (CM/2) on both sides of the screen. (b) Fourth step: the anteroposterior diameter is measured on each side of the screen perpendicular to the longitudinal axis of the cervix and through point CM/2, from the most anterior to the most posterior lip of the cervix (white bracket). On the left side of the screen this diameter is termed AP and on the right side it is termed AP’. Fifth step: diameter AP’ is divided by diameter AP and this ratio is multiplied by 100 to obtain the CCI.
the reference line. The sensitivity, specificity, positive and negative predictive values and positive likelihood ratios of the mathematically best cut-off values with regard to the prediction of spontaneous PTB before 32, 34 and 37 weeks were also calculated. Women examined at >32 weeks or >34 weeks were excluded from the analysis of the prediction of spontaneous PTB ≤32 weeks or ≤34 weeks, respectively.

Repeatable of measurements
To evaluate intraobserver variability, additional measurements were obtained in 102 patients. These patients were evaluated twice by the same observer, the second measurement being made approximately 30 min after this first, with the observer blinded to the previous measurement. Thus, two measurements were obtained (A1, A2). To evaluate interobserver variability, 98 patients were evaluated by a second examiner, with a single measurement being obtained by each examiner (A, B).

For each measurement, the observer obtained a new image, using the technique described to measure the cervical length and to calculate the CCI. The investigators were not present during each other’s examinations and were blinded to each other’s results until the study had been completed. Intraclass correlation coefficient (ICC), with variance components estimated by analysis of variance of replicate measurements. In addition, the repeatability coefficient was calculated as described by Bland and Altman, defining the range within which the difference between two measurements by the same observer will fall for 95% of subjects. Interobserver repeatability was evaluated using Bland–Altman plots to assess the systematic bias between the two observers and to assess the relationship between the differences and the magnitude of their measured values. Bias between the two observers was also assessed by calculating the 95% CI for the mean difference between them; if zero lay inside this interval, it was assumed that there was no bias. Limits of agreement, defining the range within which 95% of the differences between the two observers were likely to fall, were calculated as described by Bland and Altman.

To determine how precise our estimates of the limits of agreement were, we calculated the 95% CI of their lower and upper limits. Interobserver agreement was also evaluated using the ICC, with variance components estimated by analysis of variance of replicate measurements.

RESULTS
• Of the 1115 women undergoing routine growth scans, 298 were evaluated in the first trimester of pregnancy (5 + 0 to 13 + 6 weeks), 402 in the second trimester (14 + 0 to 26 + 6 weeks) and 415 in the third trimester (27 + 0 to 36 + 6 weeks). Complete outcome data were available for 1031 (92.5%) of the 1115 included pregnancies; the 84 without outcome data (including six (0.58%) cases of intrauterine demise and four (0.39%) women treated with vaginal progesterone) were excluded from analysis. Among the 1031 pregnancies with follow-up, there were 80 (7.76%) spontaneous PTBs before 37 weeks, 22 (2.13%) before 34 weeks and nine (0.87%) before 32 weeks. Iatrogenic PTB occurred in 31 (3.01%) cases before 37 weeks and in 17 (1.65%) cases before 34 weeks.

The demographic characteristics of the 1031 patients are shown in Table 1. Tolerance of the CCI assessment procedure was satisfactory, and it was possible in 99.9% of the women evaluated. Only six patients (0.5%) showed some discomfort, although the whole examination could be performed and both ultrasound variables were evaluated in these cases.

We found an inverse linear correlation between CCI and gestational age (GA), with the following equation: $\text{CCI (in %)} = 89.2 - 1.35 \times \text{(GA in weeks)}; \ r^2 = 0.66, \ P < 0.001$ (Figure S1). There were significant differences in CCI between the three trimesters ($P < 0.0001$), with an average CCI of 76.3% for the first trimester, 59.4% for the second trimester and 45.6% for the third trimester. Percentiles of CCI according to gestational age are shown in Figure S2 and Table S1. When other obstetric parameters (maternal age, parity and BMI) were also included in a multiple regression analysis, we found that the coefficient for gestational age was not modified substantially. Therefore, the most important factor in estimating the expected CCI was gestational age.

We observed a progressive increase in cervical length until week 22 followed by a gradual decrease, with the following second-order polynomial regression equation: cervical length (in mm) = 31.084 - 0.0278 \times (GA in weeks)^2 + 1.0772 \times (GA in weeks); \ r^2 = 0.076, \ P < 0.14$ (Figure S3). The average cervical length was 39 mm for the first trimester, 41 mm for the second trimester and 35 mm for the third trimester.

Table 1: Demographic characteristics of the study participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR) or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28 (20–35)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>17 (1.5)</td>
</tr>
<tr>
<td>Black</td>
<td>56 (5)</td>
</tr>
<tr>
<td>Mixed</td>
<td>1042 (93.5)</td>
</tr>
<tr>
<td>Body-mass index (BMI) (kg/m^2)</td>
<td>26.1 (22.0–28.2)</td>
</tr>
<tr>
<td>quad BMI &lt; 18.5</td>
<td>9 (0.81)</td>
</tr>
<tr>
<td>BMI 18.5–24.9</td>
<td>480 (43.3)</td>
</tr>
<tr>
<td>BMI 25.0–29.9</td>
<td>425 (38.1)</td>
</tr>
<tr>
<td>BMI &gt; 30.0</td>
<td>201 (18)</td>
</tr>
<tr>
<td>Cigarette smoking during pregnancy</td>
<td>15 (1.3)</td>
</tr>
<tr>
<td>Obstetric history</td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>523</td>
</tr>
<tr>
<td>Primiparous</td>
<td>407</td>
</tr>
<tr>
<td>Multiparous</td>
<td>185</td>
</tr>
<tr>
<td>Previous history of preterm birth (PTB)</td>
<td></td>
</tr>
<tr>
<td>One previous PTB</td>
<td>79 (7.1)</td>
</tr>
<tr>
<td>Two previous PTBs</td>
<td>18 (1.6)</td>
</tr>
<tr>
<td>&gt; Three previous PTBs</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>

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38.07 mm for the third trimester, but the differences between these were not statistically significant ($P = 0.11$).

Percentiles of cervical length according to gestational age are shown in Figure S4 and Table S2.

### Relationship between cervical consistency index (CCI) and cervical length

There was an inverse quadratic relationship between CCI and cervical length (Figure S5). However, this was accounted for relatively little of the variance observed ($r^2 = 0.10$ (95% CI, 0.07–0.14), $P < 0.001$). Stronger correlation was observed for values of cervical length ≤ 28 mm ($r^2 = 0.13$ (95% CI, 0.02–0.56), $P = 0.004$), while for cervical length measurements ≥ 29 mm the relationship was not statistically significant ($r^2 = 0.02$ (95% CI, 0.01–0.04), $P = 0.58$).

### CCI and cervical length to predict spontaneous preterm birth

The estimated detection rates of spontaneous PTB before 32, 34 and 37 weeks by cervical length were 33% (3/9), 27% (6/22) and 26% (21/80), respectively, for a 5% screen-positive rate. The AUC (95% CI) for cervical length in the prediction of spontaneous PTB was 0.6305 (0.4762–0.7845), 0.6453 (0.5356–0.7550) and 0.6432 (0.5863–0.7001), respectively (Figure 2).

### Table 2

<table>
<thead>
<tr>
<th>SPTB ≤ 32 weeks</th>
<th>CCI</th>
<th>Cervical length</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Detection rate (% (95% CI)) for fixed screen-positive rates of:</td>
<td>5%</td>
</tr>
<tr>
<td>SPTB ≤ 32 weeks</td>
<td>Sensitivity</td>
<td>66.7 (30.3–100)</td>
</tr>
<tr>
<td>Specifity</td>
<td>97.1 (96.1–98.2)</td>
<td>88.2 (86.2–90.3)</td>
</tr>
<tr>
<td>PPV</td>
<td>17.1 (32–31.1)</td>
<td>7 (2.2–11.9)</td>
</tr>
<tr>
<td>NPV</td>
<td>99.7 (99–100)</td>
<td>100 (99.9–100)</td>
</tr>
<tr>
<td>LR+</td>
<td>23.3 (12.9–41.8)</td>
<td>8.1 (7.2–10.1)</td>
</tr>
</tbody>
</table>

| SPTB ≤ 37 weeks | Sensitivity | 63.6 (41.3–86.0) | 90.9 (76.6–100) | 95.4 (84.5–100) | 9.1 (0–23.4) | 27.3 (6.4–48.2) | 40.9 (18.1–63.7) |
| Specifity       | 98.4 (97.6–99.2) | 89.4 (87.4–91.4) | 78.2 (75.6–80.8) | 97.9 (96.9–98.8) | 94.9 (93.6–96.4) | 86.7 (84.5–88.8) |
| PPV             | 46.7 (27.2–66.2) | 15.9 (9.1–22.7) | 8.8 (4.9–12.6) | 8.7 (0–22.4) | 10.7 (1.7–19.7) | 6.3 (1.9–10.7) |
| NPV             | 99.2 (98.6–99.8) | 99.8 (99.4–100) | 99.9 (99.6–100) | 98.1 (97.1–98.9) | 98.3 (97.5–99.2) | 98.5 (97.7–99.9) |
| PPV             | 39.7 (22.2–70.9) | 8.6 (6.9–20.7) | 4.4 (3.8–5.1) | 4.32 (1.1–17.3) | 2.2 (1.2–31) | 3.1 (1–5.8) |

| SPTB ≤ 37 weeks | Sensitivity | 45 (33.5–56.5) | 78.8 (64.2–88.6) | 87.5 (79.7–95.4) | 11.3 (3.7–18.8) | 26.3 (15.9–36.5) | 38.8 (27.4–50.1) |
| Specifity       | 99.8 (99.4–100) | 94.9 (93.4–96.4) | 81.9 (79.4–84.4) | 98.5 (97.7–99.3) | 96.3 (95.0–97.5) | 88.2 (86.1–90.3) |
| PPV             | 94.7 (86.3–100) | 56.8 (47.1–66.4) | 29.2 (23.2–25.3) | 39.1 (17.0–61.3) | 37.5 (23.9–51.1) | 21.8 (14.7–28.9) |
| NPV             | 95.5 (94.2–96.9) | 98.1 (97.2–99.1) | 98.7 (97.9–99.6) | 92.9 (91.2–94.5) | 93.9 (92.3–95.4) | 94.4 (92.8–96.0) |
| LR+             | 211.7 (51.9–863.3) | 15.44 (11.5–20.8) | 4.84 (4.13–5.7) | 7.6 (6.1–9.5) | 7.1 (4.3–11.5) | 3.3 (2.4–4.6) |

The sensitivity, specificity, positive and negative predictive values (PPV and NPV) and positive likelihood ratio (LR+) are shown in Figure S4 and Table S2.

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Figure 3 Receiver-operating characteristics curves for percentiles of cervical length according to gestational age in the prediction of spontaneous preterm birth before before 32 (– – –), 34 (– – –) and 37 (– – –) weeks. The area under the curve (95% CI) for delivery \( \leq 32 \) weeks was 0.6305 (0.4762–0.7845), for delivery \( \leq 34 \) weeks was 0.6453 (0.5356–0.7550) and for delivery \( \leq 37 \) weeks was 0.6432 (0.5863–0.7001).

Figure 4 Plot of cervical consistency index (CCI) against gestational age, according to gestational age at delivery (O, term > 37 weeks; ▲, preterm ≤ 37 weeks).

Figure 5 Plot of cervical length against gestational age, according to gestational age at delivery (O, term > 37 weeks; ▲, preterm ≤ 37 weeks).

The relationship between mean CCI and both intra- and interobserver differences is shown in Tables S3 and S4 and Figures S6 and S7. The SD of differences between repeat readings by the same observer was 1.99% and the SD of interobserver differences was 2.86%. Consequently, on 95% of occasions, the difference between two measurements by the same observer would not differ by more than 4%, and the corresponding value for two observers would be 5.72%. The intraobserver ICC was 0.9919 (95% CI, 0.9881–0.9945) and the interobserver ICC was 0.9817 (95% CI, 0.9729–0.9877) for the evaluation of CCI.

The relationship between mean cervical length and both intra- and interobserver differences is shown in Figures S8 and S9.

**DISCUSSION**

To the best of our knowledge this is the first study to assess cervical consistency in pregnant women using TVS. We found the CCI to show a clear linear relationship with gestational age, and also found that it was lower in pregnancies that went on to deliver preterm. CCI had a high sensitivity for the prediction of spontaneous PTB and could be determined easily, showing a high level of intra- and interobserver repeatability.

According to our observations, the cervix softens before it shortens. This is an important finding because changes in cervical length may be a late feature, reflecting changes that occur in the cervical microstructure and water concentration during the ripening process. These changes occur without symptoms and are not detected by early cervical length screening in the first trimester, as reported previously. It is therefore reasonable to consider the use of CCI to detect early changes in cervical consistency (even before 10 weeks' gestation), because early identification of the group at high risk of subsequent early PTB would improve pregnancy outcome through early intervention.

There was a statistically significant relationship between CCI and cervical length, but with a low \( r^2 \) value of 0.1008 (95% CI, 0.069–0.144) \( (P < 0.001) \). This association was stronger for cervical lengths ≤ 28 mm \( (r^2 = 0.13 \text{ (95\% CI, 0.02–0.315)}, \ P < 0.004) \), but was not statistically significant for cervical lengths > 29 mm \( (r^2 = 0.018 \text{ (95\% CI, 0.005–0.038), P = 0.58}) \). Thus, the well-described association between short cervical length and spontaneous PTB may be mediated through changes in cervical consistency that are apparent as a low CCI as early as the first trimester of pregnancy.

PTB is a syndrome caused by multiple etiologies. However, the common pathway, in accordance with our results, may be an early softening of the cervix (perhaps caused by edema and inflammation) that causes early shortening and subsequent PTB. The cervical length becomes shorter during late pregnancy in a pattern that differs from that which we observed for the CCI. There may be a continuous decrease in cervical length, an increased shortening rate starting at around 30 gestational weeks, or a sudden decrease in cervical length at birth. In patients with the latter two patterns of shortening, PTB will not be predicted by cervical length measurement.
Cervical consistency index and PTB

Cervical length is relatively constant until 30 weeks of pregnancy, with most studies recording physiological shortening after this gestational age. However, in our study, cervical length showed an unusual distribution, progressively increasing in length until week 22 and thereafter progressively shortening until 36 weeks. A similar trend has been described previously by Kushnir et al., who measured by TVS the cervical length in normal gravid patients between 8 and 37 weeks and found that the maximum length was at 20–25 weeks. This may be because they measured cervical length in a straight line from the inner cervical os to the external cervical os, and in the first trimester the cervix is more curved, resulting in underestimation of the cervical length. In the second trimester the uterus leaves the pelvis and the cervix tends to be straighter with an apparent increase in length.

The $r^2$ for cervical length in relation to gestational age was low in our group ($r^2 = 0.076$), consistent with the findings reported recently by Valadares et al. in a study of 1061 pregnant women between 20 and 34 weeks ($r^2 = 0.079$). In contrast, Gramellini et al. reported a strong or moderate negative correlation between cervical length and gestational age ($r^2 = 0.85$). These discrepant results may be explained by differences in measurement technique, study design, period of gestation studied, statistical methods used and/or interpretation of results.

For example, in the presence of cervical curvature, Gramellini et al. measured cervical length in two or more segments; using this technique, cervical length is on average, 2.9 (range, 0.4–13.4) mm longer than it is when measured in a straight line.

In most published studies, the dispersion of measurements increases with gestational age, which is in accordance with our present results. For example, we found ranges of 30–34 mm and 11–50 mm for the 5th–95th percentiles at 16 and 36 weeks, respectively, similar the findings of Salomon et al. in a study of 6614 patients between 16 and 36 weeks; they reported ranges of 32–53 mm and 15–48 mm for the 5th–95th percentiles at 16 and 36 weeks, respectively.

Changes in cervical ripening as observed by ultrasonic attenuation have been studied recently. An interesting finding was that attenuation was a predictor of the interval between ultrasound examination to delivery, however, the observed $r^2$-value was low ($r^2 = 0.055$). The evaluation of attenuation assumes homogeneous tissue, but in clinical practice the echogenicity of the cervix may be influenced by the endocervical canal, cystic areas and vessels, as well as by the cervical anatomy and variety of positions themselves. All of these technical limitations must be overcome in future studies.

A potential limitation is that, although with adequate training in our standardized technique, reproducible measurement of CCI was possible in this single-center study, its reproducibility requires confirmation in other centers.

Further prospective randomized studies are needed to evaluate the effect of prophylactic use of progesterone in patients with CCI below the 10th percentile, considering that 91% of patients with PTB before 34 weeks in our group had CCI below this percentile, and it is this group which had the highest morbidity and mortality rate.

ACKNOWLEDGMENTS

We are very grateful to Dr. Israel Díaz-Yunez, research study coordinator of CEDIUL (Barranquilla, Colombia), and the medical staff of the Department of Gynecology and Radiology, for their contribution to this work.

Declaration of interests

The authors declare do not have conflict of interests. The authors are the only responsible in the content and the wording of article.

REFERENCES


Figure S6 Intraobserver Bland–Altman plot for cervical consistency index (CCI).

Figure S7 Interobserver Bland–Altman plot for cervical consistency index (CCI).

Figure S8 Intraobserver Bland–Altman plot for cervical length.

Figure S9 Interobserver Bland–Altman plot for cervical length.

Videoclip S1 Video demonstrating assessment of the cervical consistency index.
Please check that all affiliations are correct and complete. If you want to add the quadratic equation, please could you supply it?

Repeated by whom – the same observer? Was this repetition of measurement done within the 5–9 minute duration?

Dr Parra, I’ve inserted the line space because the data on pregnancy outcome etc does not fall under the heading ‘TVS assessment of cervical consistency index’.

Looking at your description in the methods, there’s something missing from here: Here it sounds like both sides of the screen are the same – we need to clarify here the difference between left and right sides – the left is without and the right is with pressure from the probe, is that right or is more detail needed?

< changed to ≤ here and elsewhere – is this correct?

Is this rewording correct: “the second measurement being made approximately 30 min after this first, with the observer blinded to the previous measurement. Thus, …”?

Is this rewording correct: “For each measurement, the observer obtained a new image”?

‘Of the 1115 women undergoing routine growth scans, 298 were evaluated in the first trimester of pregnancy (5 + 0 to 13 + 6 weeks), 402 in the second trimester (14 + 0 to 26 + 6 weeks) and 415 in the third trimester (27 + 0 to 36 + 6 weeks).’ added – OK? However, wouldn’t it be better to have these numbers for the 1031 included in the study?

Please clarify. Were these 84 excluded from everything? Table 1, and your totals for the number of fetuses at each gestational week and in each trimester (sentence above) total 1115 not 1031 – so in these the 84 are included. Please could you clarify this – it affects several of the numbers and the percentage calculations.

‘There were six (0.58%) cases of intrauterine demise and four (0.39%) women were treated with vaginal progesterone; these pregnancies were excluded from the final analysis’ has been removed from the end of this paragraph and the following has been added here – please check very carefully that this is correct: ‘the 84 without outcome data (including six (0.58%) cases of intrauterine demise and four (0.39%) women treated with vaginal progesterone) were excluded from analysis’ HOWEVER, should these percentages not be 0.54 and 0.34 (with 1115 as the denominator)? Or have I misunderstood?

‘3.01%’ added

You had n (%) here for BMI – I’ve changed it to kg/m²

“The demographic characteristics of the 1031 patients are shown in Table 1”, This table seems to include 1115 not 1031 cases. Are there incorrect values in the table?

Should this be 89.8 as in the Abstract? Which is correct?

Do we need to state here and elsewhere that these are completed gestational weeks?

I’ve rounded to 2 decimal places. If you want to keep the detail please supply to four decimal places in all cases.

< changed to ≤ in Figs 4 and 5 – is this correct?

Should “CCI” here, be ‘CCI percentiles according to gestational age’? (OS)

‘The cervical length becomes shorter during late pregnancy in a pattern that differs’ - is this in PTB or is this the normal prelabor situation??

Also, is this sentence repeating the information above about shortening starting around 30 weeks, or is this a different situation (see query above)?

Is this rewording ok: “they measured” (ie. Kushnir measured)?

Is ‘dispersion’ the right word here?

Can I just double check this is correct: ‘and’ changed to ‘−’, i.e. lowest was 30 at 5th centile and highest was 54 at 95th centile at 16 weeks – is that right?

Are there other limitations that should be mentioned?

Do we need to state here and elsewhere that these are completed gestational weeks?

I’ve added the website here – is this correct? When did you last access this document in the writing of this paper?

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