CERVICAL LENGTH IN PRETERM LABOR PREDICTION

INTRODUCTION
Prematurity causes 70% of fetal/neonatal deaths, with 11.4% of births occurring at < 37 weeks' gestation. The rate of prematurity increases with the number of fetuses - singletons 10%; twins 54.9%; and triplets 93.6%.

Methods to assess cervical lengths have gradually evolved over the past decade. The expansion of the bladder that is required with the transabdominal approach results in cervical lengthening (Fig. 1), and the translabial or transperineal technique (Fig. 2) is not always successful because of reduced visualization secondary to bowel gas. Therefore, the transvaginal approach is the most accurate method to assess the cervical length.

Figure 1. Transabdominal ultrasound of the membranes hourglassing through the cervix (x cursors) into the vagina (+ cursors).

Click for larger image
Cervical length is inversely related to the risk of preterm labor\(^3\). In this important study, a cervical length of 25 mm corresponded to the 10th percentile and was identified as a clinically appropriate threshold of identifying preterm delivery risk. A cervical length increases the preterm delivery risk by approximately six-fold. Uterine contractions and the inherent tensile strength of the cervix undoubtedly play a role. Epidemiologic studies have established a link between bacterial vaginosis and an increased risk of preterm delivery. Hence, the cervix may also act as a barrier between the vagina and amniotic cavity\(^4\).

**MANUAL CERVICAL EXAMINATION**

The manual assessment of cervical length is subjective and has poor intraobserver variability\(^5\). The cervix starts to shorten and dilate at the internal cervical os. This process cannot be appreciated on a digital examination.

In women with a diagnosis of preterm labor, the transvaginal examination of the cervix has been found to be superior to a digital exam in predicting preterm delivery\(^6\).

Rozenberg et al\(^7\) have stopped utilizing digital exams in their unit on patients with symptoms of preterm labor. A cervical length < 26 mm with at least 2 contractions in 10 minutes before 34 weeks' gestation are used as criteria for admission and treatment.

**GUIDELINES FOR TRANSVGINAL CERVICAL LENGTH ASSESSMENT**

Proper technique is critical for accurate and reproducible cervical length measurements. Therefore, the Perinatal Quality Foundation developed the cervical length education and review (CLEAR) program composed of online continuing medical education lectures and voluntary image review (https://clear.perinatalquality.org/). The patient's bladder should be emptied prior to the exam. A small amount of gel is placed on the previously sterilized transducer and then it is covered with a condom. The patient is asked to insert the transducer. If she is unable or unwilling, the sonographer can slowly insert the probe. He/she should stop if there is too much resistance or patient discomfort. A sagittal image of the cervix is obtained. The transducer is slowly removed until the image begins to blur. The transducer is
then reinserted until the image is clear. The cervix should occupy at 75% of the screen. The cervix is measured from the internal to the external cervical os (Fig. 3). The cervical glands (Fig. 4) can help determine the length of the endocervical canal. According to the CLEAR guidelines, using the trace tool is not recommended. The cervical canal should be equidistant from the anterior and posterior cervical walls (Fig. 1). Three-measurements should be obtained and the shortest and best should be used.
A dynamically changing cervix has been associated with uterine contractions. In term women in labor, the cervix shortens approximately 50% during a contraction. The presence of induced cervical shortening has been found in some studies to increase the positive predictive value of the cervical measurement in diagnosing preterm labor. Other authors have not found this to be the case.

CLEAR guidelines include application of mild suprapubic or fundal pressure for 15 seconds to watch for dynamic changes (i.e. funneling). Transvaginal probe pressure should be reduced during this assessment.

The total examination time should be 3-5 minutes.

A dynamically changing cervix, either spontaneously, or after fundal pressure, improves the predictive accuracy of cervical length in predicting preterm delivery. Focal myometrial contractions may obscure the internal cervical os and result in a longer measurement (Fig. 5).

![Figure 5. Lower uterine segment contractions (c) resulting in an erroneously longer cervical length.](Click for larger image)

In most studies the addition of cervical funneling does not improve the predictive accuracy of cervical length in preterm labor prediction (Fig. 6). This may, in part, be due to the wide variations noted in funnel measurement. Rust et al. have found that as a categorical variable (present or absent), a funnel is a significant risk factor for preterm labor. However, the latter study had a small sample size and was retrospective in nature. Additional prospective studies will be required to determine if the presence of a funnel adds to the predictive accuracy of cervical length in predicting preterm delivery.
Cervical length is a continuous variable, with a mean of 35 mm to 40 mm. A cervical length of 25 mm has generally been found to be at the 10th percentile\textsuperscript{3,14}.

WHEN SHOULD CERVICAL LENGTH BE MEASURED?
Most patients who deliver preterm will have a cervical length < 25 mm between 16 and 22 weeks' gestation\textsuperscript{15}. A cervical length < 25 mm rarely occurs before 14 weeks' gestation. Since the lower uterine segment may not have developed, a short cervix is difficult to identify at < 14 weeks' gestation. The bladder reflection has generally been considered the boundary between the lower uterine segment and cervix. There is a gradually progressive shortening of cervical length after 30 weeks' gestation\textsuperscript{16}.

For patients at highest risk for preterm delivery (prior 24 week delivery, 2nd trimester losses), an initial examination at 15 to 16 weeks should be considered. For patients at a lower risk (cone biopsy, uterine malformations), a first exam could be obtained during the 18 to 20 weeks anatomy scan.

FETAL FIBRONECTIN
Fibronectin is a glycoprotein present in amniotic membranes and decidua. It is released by inflammatory mediated damage to the placenta or membranes\textsuperscript{17}. Fetal fibronectin in cervical secretions after 20 weeks' gestation is associated with preterm labor\textsuperscript{18}.

Cervical length and fetal fibronectin may identify different patients at risk for preterm labor. The predictive accuracy of either test is based on the pretest probability of preterm labor in the population under investigation\textsuperscript{19}.

Honest et al\textsuperscript{17} conducted a meta-analysis of 40 studies in women with symptoms of preterm labor and of 28 studies of women without symptoms of labor. In the asymptomatic and symptomatic groups a positive fibronectin had a likelihood ratio (LR) of 4.01 and 5.42, respectively. The LR of a negative fibronectin was 0.78 and 0.25 for the asymptomatic and symptomatic women, respectively. Fetal fibronectin is most accurate in predicting preterm labor within 7 to 10 days among women with symptoms of preterm labor.
CERVICAL LENGTH IN HIGH-RISK PATIENTS

In low-risk women, there is an increased risk of preterm labor as cervical length decreases. However, only 25% of low-risk women with a short cervix deliver early\(^3\). In a high-risk population, 75% with a cervical length \(\leq 25\) mm at 16-18 weeks' will deliver prematurely\(^1\). 532 pregnancies from 3 studies presented with preterm labor at 24-36 weeks' gestation. If the cervical length was < 15 mm, delivery occurred within 3 days\(^2\).

As a patient's number of preterm births increases and the gestational age at preterm delivery decreases, the likelihood of another preterm delivery rises by 3 to 4-fold. Yost and co-workers\(^2\) found that these historical variables did not affect the predictive accuracy of a cervical length < 25 mm between 16 and 19 weeks' gestation. However, because of the small sample size, the power of the study to detect a clinically significant difference was low. Until additional studies are reported, prior preterm delivery should be considered a categorical variable that increases the risk of preterm labor.

A cervical length \(\leq 25\) mm has a 13-fold risk for preterm delivery in women with uterine anomalies. In one study of 64 pregnant women with uterine anomalies, the sensitivity, specificity, positive and negative predictive values of a cervical length \(\leq 25\) mm for preterm delivery were 71%, 91%, 50%, and 96%, respectively\(^2\). The positive predictive value is higher if an abnormally shortened cervix was detected at 14 to 18 weeks in contrast to 18 to 22 weeks\(^3\). In a blinded study of patients with a history of preterm deliveries, a shortened cervical length had a sensitivity and positive predictive value of 69% and 55%, respectively in predicting preterm labor\(^1\). Hence, patients at highest risk may be evaluated between 14 and 18 weeks' gestation, while those at slightly lower risk need not be evaluated until 18 to 22 weeks\(^4\).

Faster rates of cervical shortening between 16 and 24 weeks' gestation is an additional independent factor associated with an increased prevalence of preterm labor\(^5\). The rate of cervical shortening in cases of incompetent cervix diagnosed between 15 and 19 weeks' gestation is ~ 0.52 cm/week. Between 15 and 24 weeks' gestation the length of a competent cervix is essentially unchanged\(^5\).

Chorioamniotic membrane visualization at the internal cervical os indicates disruption of the decidua-membrane interface and is an independent risk factor for preterm delivery (Fig. 7). Finally, minimal (1-4 mm) endocervical canal dilatation has been associated with an increased risk of preterm labor (Fig. 8)\(^6\).
Figure 7. Cervical funnel extends to the external cervical os. Separation of decidua membrane interface (arrow). Contractions (c) narrowed cervical canal. Blood (b) present within lower aspect of amniotic sac. Click for larger image.

Figure 8. Minimal endocervical canal dilatation that has been associated with an increased risk of preterm labor. Click for larger image.

SHORT CERVIX AND INTRAUTERINE INFECTION
Patients with a cervical length < 15 mm have a higher rate of positive amniotic fluid cultures than patients with a cervical length > 15 mm (26.3% versus 3.8%)\textsuperscript{27}. The earlier the gestational age and the
shorter the cervix, the higher the likelihood of intra-amniotic infection. This relationship may be due to: 1) intra-amniotic infection resulting in contractions and a shortened cervix; or 2) a short cervix may predispose to ascending infection.

TWINS

Cervical length ≤25 mm in twin pregnancies at 27 weeks' gestation predicts delivery before 34 weeks (sensitivity 77%, specificity 86%, positive predictive value 34%) better than a digital examination. Cervical length ≤ 25 mm at 18 weeks (likelihood ratio =9.7, sensitivity 14.3%) and < 22 mm at 24 weeks (likelihood ratio = 9.6, sensitivity 28.6%) were found to be the best predictors of preterm labor in twins. The poor sensitivity of cervical length as a predictor of preterm labor in twins makes it unsuitable as a single test.

The negative predictive value of a long cervix has also been evaluated. It has been suggested that cervical length > 35 mm at 24-26 weeks' gestation predicts that a twin pregnancy will deliver at term (negative predictive value 86% - 97%). However, the likelihood ratio of 0.54 to 0.80 indicates that this is not a valuable predictor of delivery ≥ 35 weeks.

3D CERVICAL ASSESSMENT

The measurement of cervical length with 3D sonography (Fig. 9a, b) is longer than with the 2-dimensional approach. Bega et al. found a > 5 mm difference between the 2 measurements. The longer the cervix, the greater the difference between the 2D and the 3D approach.

Figure 9a. Multiplanar display of the cervix. The image was acquired in a sagittal plane (a); b=transverse; c=coronal.

Click for larger image
Severi et al\textsuperscript{34} also found a significant difference (p < 0.001) between cervical length measured with 2D ultrasound (37.6 mm) and 3D ultrasound (39.8 mm). A correct, mid-sagittal plane was more accurately determined with 3D in contrast to 2D ultrasound\textsuperscript{34}. Whether the difference in cervical length between the 2 measurement techniques is clinically significant remains to be determined.

**CERCLAGE FOR A SHORT CERVIX ON TRANSVAGINAL ULTRASOUND**

Berghella et al\textsuperscript{35} performed a meta-analysis of 4 properly conducted trials that included a total of 305 cerclage patients and 302 controls. A cervical cerclage did not prevent preterm birth in all women with a shortened cervical length. In twins the placement of a cerclage was associated with an increased incidence of preterm birth. In a sub-group of patients with a history of a prior preterm birth, cerclage may reduce the preterm birth rate.

Cervical length generally increases after a cerclage. The lengthening of the cervix after cerclage is associated with a higher likelihood of a term delivery\textsuperscript{36,37}. A cervical length < 25 mm or a cervical length of < 10 mm above the suture have been found to be predictive of preterm labor (Fig. 10)\textsuperscript{38}. 

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**Figure 9b.** Reconstructed image of the cervix provides a reliable measurement of length. *Click for larger image.*
CONCLUSIONS

Preterm labor is a heterogeneous process. The presence of multiple interactive continuous variables explains the relatively low predictive value of any one variable. A transvaginal assessment of cervical length is one of the best tests for predicting preterm birth. A cervical length < 25 mm (10th percentile) between 15 and 24 weeks’ gestation is generally agreed upon as increasing the risk of preterm labor. The shorter the cervical length, the greater the likelihood of preterm labor. The positive predictive value of a 25 mm cervix for preterm labor is dependent upon the patient’s pretest probability (i.e. high-risk or low-risk for preterm labor).

Universal cervical length screening, typically performed during the fetal anatomical survey has gained some acceptance among maternal-fetal medicine specialists. In comparison to a risk-based approach, universal cervical length screening in singleton pregnancies (without a history of a prior spontaneous preterm birth) resulted in 913 fewer PTBs <35 weeks 63 fewer neonatal deaths. Prior spontaneous preterm birth, fetal fibronectin, cervical length, and bacterial vaginosis are associated with early preterm birth, with some of these effects additive. These associations indicate that there is more than one pathway resulting in preterm delivery. In the future, a multifactorial assessment of patients at risk for preterm delivery should improve the positive predictive value of our testing schema. Specific therapeutic regimens depending upon the etiology or etiologies of preterm labor will be required and should improve our current limited successfully inhibition of preterm labor.

REFERENCES


34. Severi FM, Bocchi C, Florio P, Picciolini E, D’Aniello G et al. Comparison of two-dimensional and three-


