Diagnosis and Management of Short Cervix in Singleton Pregnancies

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ABSTRACT
Prevention of preterm labor will reduce perinatal mortality. Screening of cervical length by ultrasound should begin at 16 weeks by transvaginal ultrasound. If the cervical length is more than 35 mm, the exam should be repeated every 2 to 3 weeks till 32 weeks. If the cervical length is between 25 and 35 mm the ultrasound screening should be done weekly or biweekly. Fetal fibronectin estimation should provide supplemental information. If the cervical length is less than 25 mm cervical cerclage should be performed if gestational age is less than 22 weeks. Progesterone therapy is preferred if the gestational age is more than 22 completed weeks.

Keywords: Preterm labor, PPROM, Ultrasound cervical length, Cervical cerclage, Progesterone therapy.

INTRODUCTION
Preterm delivery (PTD) is the leading cause of infant mortality. One in 10 pregnant women in the US will deliver prematurely, of whom 2% will deliver prior to completed 32 weeks of gestation. Between 60 and 80% of all nonanomalous infant deaths are attributed to PTD, and as many as 30% of infants born prior to the 31st gestational week and 60% of infants born prior to the 26th gestational week will suffer some form of disability. Recent reports described an increase in the incidence of preterm births, resulting in growing pressure on health services and healthcare providers. The major causes of PTD are preterm labor (PTL), preterm rupture of membranes (PTROM), and multiple gestation pregnancies, accounting for as many as 80% of all cases. The causes for the other ~20% PTD cases include maternal and fetal conditions, such as cervical incompetence, hypertension, infection, bleeding, and fetal growth restriction. PTD is also associated with socioeconomic and occupational factors, such as low socioeconomic status, pregnancy at early age, single women, depression, and deleterious working conditions. Despite the awareness of these associations, maternal risk scoring fails to detect up to 70% of infants who are delivered spontaneously before term.

Cervical incompetence accounts for 8 to 9% of preterm deliveries. The diagnosis of incompetent cervix is based upon historical, clinical and sonographical findings. Clinical findings of premature cervical effacement or painless dilation of the cervix, soft cervix on digital examination, or fetal membrane bulging are suggestive of incompetent cervix. Other clues of incompetent cervix include previous second trimester loss, preterm delivery, precipitated labors as well as cervical dilation before the onset of labor. Sonographic signs of cervical incompetence often present prior to clinical signs and include shortening of cervical length and funneling.

MEASUREMENT OF CERVICAL LENGTH BY ULTRASOUND
Cervical length can be assessed manually or by ultrasound (US) examination. Manual examination of cervical length has high intraobserver variation (~50%), is inaccurate when compared with US measurement, and has limited value in assessing the internal os. Unlike a digital examination, sonographic evaluation of the cervix allows the inspection of the internal os and proximal cervix. Adherence to the basic rules for cervical length measurement is essential. The maternal bladder should be emptied prior to the examination, which should be performed transvaginally. The vaginal probe should be inserted into the vaginal fornix and then withdrawn gently until no pressure is being applied to the cervix. The cervix should be observed for a few minutes after which pressure should be applied to the uterine fundus. Measurements should be made between the external os to the internal os along the cervical canal. If there is funneling, the measurement should be made until the point of funneling (Fig. 1).

CAN WE PREDICT PRETERM DELIVERY?
Predicting PTD delivery has proven to be elusive. PTD can occur in nulligravid women without any apparent risk factors
as well as in asymptomatic women. Indeed, uterine contractions are a normal part of pregnancy, and they do not necessarily precede delivery. In fact, the condition resolves spontaneously in 50% of symptomatic gravid women hospitalized for preterm contractions and they go on to deliver at term.6

Currently employed methods for the prediction of PTD are fetal fibronectin and cervical length. Discovered in 1991, fibronectin was found to have a high sensitivity (93%) and negative predictive value (99%) for predicting PTD in symptomatic patients. However, fibronectin has low positive predictive value (30% in most populations) and does not change the clinical management in most cases.7 It is reliable only when measured after 22 weeks of gestation. In addition, it may produce false results in the presence of semen, lubricants and other substances in the vagina. Furthermore, fibronectin is not accurate in predicting PTD in asymptomatic women. Nevertheless, it was found to increase the sensitivity of cervical length measurement when the cervix is less than 30 mm long.8 It has been suggested that fibronectin be measured simultaneously with ultrasonic cervical length in borderline situations (i.e. when the cervix is 20-30 mm long).9

Cervical length changes during pregnancy. The median is 35 to 40 mm at 24 to 28 weeks of gestation and 30 to 35 mm at 32 weeks’ gestation. Between 22 to 30 weeks of gestation, the 10th percentile of cervical length is 25 mm. Overall, a cervix shorter than 25 mm in length is abnormal. In a prospective multicenter study involving over 2500 women, Iams et al10 showed a correlation between cervical length measured at 24 weeks’ gestation and PTD prior to 35 weeks’ gestation. Those authors showed that the risk of PTD increases as cervical length shortens. Others have reported the same correlation.5,11,12 The specificity of US is higher than fibronectin for measuring cervical length (40% vs 18% respectively), while the sensitivity, negative and positive predictive values are similar. Heath et al13 reported that a cervix less than 15 mm in length is a strong predictor of PTD, and concluded that measurement of cervical length provides accurate prediction of risk for early PTD.

**Low-risk versus High-risk and Symptomatic versus Nonsymptomatic Women**

There is a general consensus that cervical length should not be applied as a screening tool in low-risk patients.14 Leitich et al15 reviewed 13 studies on the efficacy of US in predicting PTL in both symptomatic and asymptomatic women, and found US not to be efficacious for the latter. In their study on low-risk primigravid women, Iams and Goldenberg16 did not find cervical length at 22 to 24 weeks’ gestation to be predictive of PTL in this population. The literature does, however, support the use of US for measuring the cervix in high-risk and symptomatic women.14 In a systematic review of the literature, Crane et al17 concluded that cervical length measured by transvaginal US in asymptomatic high-risk women can predict spontaneous PTL at less than 35 weeks.17 Owen et al18 showed that cervical length of less than 25 mm is predictive of PTD before 35 weeks’ gestation in a group of women with singleton pregnancy and prior PTD (RR 3.3, 95% CI 2.1-5.0). Tsoi et al19 examined 216 women at 24 to 36 weeks’ gestation with a singleton pregnancy and painful contractions. After excluding women in active labor or ruptured membranes, over one-third (37%) of the study women whose cervix was less than 15 mm long delivered within 7 days regardless of therapy. Only one out of 173 women whose cervix was 15 mm or more in length delivered within 7 days. Those authors concluded that sonographic measurement of cervical length helps distinguish between true and false labor in women with threatened PTD. In their review of the literature, Grimes-Dennis and Berghella concluded that cervical length is a predictor of PTD in all groups studied, symptomatic or not. They reported that using cervical length as a screening tool for prediction and prevention of PTL can significantly improve the health outcomes of pregnant patients and their babies.5

The issue of funneling (dilation of the internal cervical os and canal) is less clear. Several reports claimed that funneling of less than 25% of the closed cervix is not associated with PTD, while funneling of more than 25% predicts a higher risk for PTD.20 21 Moreover, the combination of funneling and a short cervix is a more powerful predictor of PTD compared with a short cervix alone.20 It is unclear whether funneling in a
cervix of normal length (more than 25 mm) could serve as a predictor of PTD.\textsuperscript{22}

Cervical length is the best currently available method for predicting PTD. The method of measuring is safe, reliable, well accepted and considered as being valid in all populations studied. A cervix less than 25 mm in length at 16 to 24 weeks' gestation is a reliable indicator of increased risk for PTD.

**HOW SHOULD WE MANAGE A SHORT CERVIX?**

Many measures have been proposed for the prevention of PTD, and they are mostly unsubstantiated. Cerclage for early intervention and progesterone for later intervention are the most prominent among them. Althuisius et al.\textsuperscript{23} studied cerclage outcome in women with risk factors for PTD and/or symptoms of cervical incompetence, and a cervix less than 25 mm in length before 27 weeks of gestation. They found that therapeutic cerclage with bed rest reduces PTD before 34 weeks of gestation and reduces neonatal morbidity. Other investigators, however, did not observe those results.\textsuperscript{24,25} In their 2003 Cochrane review, Darkeley et al.\textsuperscript{26} did not find cerclage to be useful in preventing second trimester loss or preterm birth (before 34 weeks) whether or not a short cervix had been diagnosed prior to the procedure. Cerclage has been associated with pyrexia, tocolysis use and hospital admissions. Berghella et al.\textsuperscript{27} performed a meta-analysis of four randomized trials that examined whether cerclage, as opposed to bed rest, prevented PTD in women with a short cervix discovered by US during second trimester screening. Cerclage was associated with significantly fewer PTDS at less than 37 weeks (RR 0.84; CI 0.71-0.99), fewer PTDS at less than 35 weeks for women with previous second trimester PTD (RR 0.75; CI 0.58-0.97), and fewer PTDS for women with a cervix less than 25 mm in length. Screening for cervical length in women with prior second trimester PTD may alert the clinician to the women who are more likely to benefit from cerclage.

Recent years have witnessed a growing interest in progesterone as a promising agent in the management of imminent PTD. Progesterone was shown to block the activity of oxytocin on the myometrium, inhibit gap junction formation between muscle cells and inhibit smooth muscle contraction.\textsuperscript{28} In clinical studies, progesterone was found to be effective in preventing PTD and its complications in high-risk women, especially those who experienced PTD in the past.\textsuperscript{29,30} In 2006 Cochrane review, Dodd et al.\textsuperscript{31} showed that women at risk for PTD who received intramuscular progesterone were less likely to deliver at less than 37 weeks. Their infants were less likely to be born at a birth weight of less than 2500 gm and less likely to deliver at less than 37 weeks. They found that therapeutic cerclage with bed rest reduces PTD before 34 weeks of gestation and reduces neonatal morbidity. Other investigators, however, did not observe those results.\textsuperscript{24,25} In their 2003 Cochrane review, Darkeley et al.\textsuperscript{26} did not find cerclage to be useful in preventing second trimester loss or preterm birth (before 34 weeks) whether or not a short cervix had been diagnosed prior to the procedure. Cerclage has been associated with pyrexia, tocolysis use and hospital admissions. Berghella et al.\textsuperscript{27} performed a meta-analysis of four randomized trials that examined whether cerclage, as opposed to bed rest, prevented PTD in women with a short cervix discovered by US during second trimester screening. Cerclage was associated with significantly fewer PTDS at less than 37 weeks (RR 0.84; CI 0.71-0.99), fewer PTDS at less than 35 weeks for women with previous second trimester PTD (RR 0.75; CI 0.58-0.97), and fewer PTDS for women with a cervix less than 25 mm in length. Screening for cervical length in women with prior second trimester PTD may alert the clinician to the women who are more likely to benefit from cerclage.

In examinations performed after 22 weeks' gestation.

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progesterone or bed rest. The women who received progesterone had significantly fewer deliveries at less than 34 weeks and did not suffer any significant side effects from the medication.

**CONCLUSIONS**

PTD is a serious condition with considerable impact on fetal mortality and morbidity. Managing the complications of PTD puts a major financial burden on community resources. Our recommendations for the management of PTD are as follows:

1. Women at high risk for PTD might benefit from screening of the cervical length between 16 and 24 weeks. If it measures more than 35 mm, the exam should be repeated every 2 to 3 weeks until 32 weeks’ gestation.
2. A cervical length of 35 to 25 mm should be managed with weekly or biweekly follow-up to monitor the length of the cervix over time.
3. Fibronectin testing can be given to provide supplemental information when cervical length is between 20 to 30 mm in examinations performed after 22 weeks’ gestation.
4. If the cervical length is less than 25 mm, the choice of therapy will depend on gestational age: Cerclage should be performed following exclusion of infection and PTROM at less than 22 completed weeks. If the cervical length is less than 25 mm at more than 22 completed weeks, intramuscular progesterone is the preferred therapy.

**REFERENCES**

10. Iams JD, Goldenberg RL, Meis PJ, Mercer BM, Moawad A, Das A, et al. The length of the cervix and the risk of spontaneous


