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The role of routine cervical length screening in selected high- and low-risk women for preterm birth prevention

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The practice of medicine continues to evolve, and individual circumstances will vary. This publication reflects information available at the time of its submission for publication and is neither designed nor intended to establish an exclusive standard of perinatal care. This publication is not expected to reflect the opinions of all members of the Society for Maternal-Fetal Medicine.

Preterm birth remains a major cause of neonatal death and short and long-term disability in the US and across the world. The majority of preterm births are spontaneous and cervical length screening is one tool that can be utilized to identify women at increased risk who may be candidates for preventive interventions. The purpose of this document is to review the indications and rationale for cervical length screening to prevent preterm birth in various clinical scenarios. The Society for Maternal-Fetal Medicine recommends (1) routine transvaginal cervical length screening for women with singleton pregnancy and history of prior spontaneous preterm birth (GRADE 1A); (2) routine transvaginal cervical length screening not be performed for women with cervical cerclage, multiple gestation, preterm premature rupture of membranes, or placenta previa (GRADE 2B); (3) practitioners who decide to implement universal cervical length screening follow strict guidelines (GRADE 2B); (4) sonographers and/or practitioners receive specific training in the acquisition and interpretation of cervical imaging during pregnancy (GRADE 2B).

Key words: cervical insufficiency, cervical length, cervical length screening, preterm birth, short cervix, spontaneous preterm birth, transvaginal ultrasound

W orldwide, fifteen million babies are born too soon every year, causing 1.1 million deaths, as well as short- and long-term disability in countless survivors.¹ The majority (two thirds) of preterm births (PTB) are spontaneous, and recurrence risks are high; a history of a prior spontaneous PTB is historically the strongest risk factor for spontaneous PTB. Few prognostic tests are available to predict which pregnancies will deliver preterm; transvaginal cervical length (CL) measurement is an important clinical tool to identify women at high risk for PTB in order to allow for interventions to prevent, delay, or prepare for PTB. The purpose of this document is to review the currently accepted indications for CL length screening to prevent PTB in various common clinical scenarios.

What is the clinical significance of a sonographically short cervix?

Women with a history of a prior spontaneous PTB account for only 10% of all births < 34 weeks of gestation.^{2,3} Thus,

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researchers and clinicians have studied a variety of factors separate from past pregnancy history in order to further riskstratify women and attempt to identify those at highest risk for PTB. Currently, mid-trimester CL assessment by transvaginal ultrasound is the best clinical predictor of spontaneous PTB.⁴ Depending on the population studied and the gestational age of assessment, the threshold chosen in clinical practice as "short" ranges from 20 to 30 mm.

The risk of spontaneous PTB is inversely proportional to the length of the cervix; those with the shortest CL have the highest risk of prematurity. In one study of unselected pregnant women 22-24 weeks of gestation, only 1.7% had a CL <15mm, but they accounted for 86% of PTB <28 weeks of gestation and 58% of PTB less than 32 weeks of gestation.⁵ The specificity of a short CL is related to the cutoff used; in one study (including both high- risk and low-risk women), the specificity was 99.9% (95% CI 99.8-100.0%) for PTB < 34 weeks of gestation for a CL \leq 20mm; this decreased to 90.1% (95% CI 89.0-91.2%) for a CL \leq 30mm, and fell further to 65.5% (95% CI 63.8-67.3%) for CL \leq 35 mm.⁶ The finding of a short CL, irrespective of prior pregnancy history, has been consistently and reproducibly associated with an elevated risk of spontaneous PTB across

different gestational age cutoffs and multiple patient populations. In addition, women with a history of a prior spontaneous PTB *and* a short CL are at the highest risk.⁷

Should the cervical length be evaluated by transabdominal or transvaginal ultrasound?

Transvaginal ultrasound is considered the 'gold standard' measurement when assessing CL. In contrast to transabdominal ultrasound, transvaginal ultrasound measurements are highly reproducible, and measurements are unaffected by maternal obesity, cervical position, and shadowing from fetal parts.⁸⁻¹¹

Transvaginal ultrasound is also more sensitive than transabdominal ultrasound using CL cutoffs typically used to screen for a short cervix.¹² For example, the sensitivity using transabdominal ultrasound to identify a (confirmed by transvaginal ultrasound) short cervix <25 mm ranges from 44.7% (using a transabdominal cutoff of 25mm) to 96.1% (using a transabdominal cutoff of 36mm).^{12,13} Transvaginal ultrasound is safe, and when performed by trained operators results are reproducible with a relatively low inter-observer variation rate of 5-10%.^{14,15}

What steps should be performed to accurately evaluate the cervical length?

With the woman's bladder emptied, the vaginal transducer should be inserted into the anterior fornix of the vagina and positioned so that the endocervical canal is visualized. The ultrasound probe should be gradually withdrawn until the image is just visible to ensure there is not excessive pressure on the probe. A minimum of 3 CL measurements should be obtained by placing calipers at the internal and external os. The shortest, best measurement should be recorded.¹⁶⁻¹⁸ (Box 1)

Ideally, measurements should be obtained by sonographers and/or practitioners who have received specific training in the acquisition and interpretation of cervical imaging during pregnancy in order to avoid improper measurement. As part of a multicenter RCT involving CL measurement conducted by the Eunice Kennedy Shriver NICHD MFMU Network, a quality control study was performed. In this analysis, one in four CL ultrasound images initially submitted for certification by investigators at the participating centers did not meet published quality criteria.¹⁹ Improper measurement (caliper placement and/or failure to identify the shortest best image) and failure to obtain a satisfactory image (excessive compression, required landmark not visible, incorrect image size, brief examination and/or full maternal bladder) were the major reasons for deficient cervical images. Thus, similar to assessment of nuchal translucency with first trimester screening,²⁰ improper measurement of the cervix may lead to impaired performance of CL as a screening test.

Several training programs are available online, including the Cervical Length Education and Review (CLEAR) program (sponsored by SMFM and its Perinatal Quality

BOX 1

Steps for proper cervical length measurement

- (1) Ensure patient has emptied her bladder.
- $(2) \ \ {\mbox{Prepare the cleaned probe using a probe cover}.$
- (3) Gently insert the probe into the patient's vagina.
- (4) Guide the probe into the anterior fornix.
- (5) Obtain a sagittal, long-axis image of the entire cervix.
- (6) Remove the probe until the image blurs and then reinsert gently until the image clears (this ensures you are not using excessive pressure).
- (7) Enlarge the image so that the cervix occupies two thirds of the screen.
- (8) Ensure both the internal and external os are seen clearly.
- (9) Measure the cervical length along the endocervical canal between the internal and external os.
- (10) Repeat this process twice to obtain 3 sets of images/ measurements.
- (11) Use the shortest best measurement.

Cervical Length Education and Review (www.perinatalquality.org/CLEAR), a program of training and certification, is offered through the Perinatal Quality Foundation. SMFM. Role of routine cervical length screening for preterm birth prevention. Am J Obstet Gynecol 2016.

Foundation, available at https://clear.perinatalquality.org), and the Fetal Medicine Foundation's Certificate of Competence in cervical assessment (available at https:// fetalmedicine.org). We recommend sonographers and/or practitioners receive specific training in the acquisition and interpretation of cervical imaging during pregnancy. (GRADE 2B)

If the cervical length is assessed by ultrasound, when during pregnancy should it be evaluated?

If transvaginal CL screening is performed, the cervix should be assessed between 16 and 24 weeks gestation. It should not be routinely measured prior to 16 weeks of gestation.²¹ Prior to this time, the lower uterine segment is underdeveloped, making it challenging to distinguish this area from the endocervical canal. In fact studies evaluating first and early second trimester CL had not consistently shown adequate predictive value of CL measurement for preterm birth.²²⁻²⁵

Routine CL screening is also not advised beyond 24 weeks of gestation in asymptomatic women, because studies of interventions (e.g., cerclage, vaginal progesterone) have most often used 24 weeks of gestation as the upper gestational age limit for screening and initiation of therapies or interventions. CL screening after 24 weeks of gestation in asymptomatic women provides limited clinical value and there is absence of data to suggest it improves outcomes.

How should the approach to cervical length screening differ for women with and without a prior preterm birth?

The approach to CL screening varies based on patient characteristics and risk factors. Current SMFM and American College of Obstetricians and Gynecologists (ACOG) guidelines recommend women with a prior spontaneous PTB undergo CL screening with transvaginal ultrasound.^{10,11} Serial assessment of CL is usually performed (every 1-2 weeks as determined by the clinical situation) from 16 until 24 weeks of gestation. We recommend routine transvaginal CL screening for women with singleton pregnancy and history of prior spontaneous PTB. (GRADE 1A)

The issue of universal transvaginal ultrasound CL screening of singleton gestations without prior PTB for the prevention of PTB remains an object of debate.^{26,27} Current SMFM guidelines state CL screening in singleton gestations without prior PTB cannot yet be universally mandated. Nonetheless, implementation of such a screening strategy can be viewed as reasonable, and can be considered by individual practitioners. Given the impact on prenatal care and potential misuse of universal screening, stretching the criteria and management beyond those tested in RCTs should be prevented. **Practitioners who decide to implement universal CL screening should follow strict guidelines (GRADE 2B).**^{10,11}

Data regarding real-world implementation of CL screening programs are evolving.28-30 Ozechowski and colleagues published their experience with universal cervical length screening at a single institution.²⁸ Over an 18-month period, 1,569 women (72.3% of eligible) underwent transvaginal ultrasound screening and 1.1% of those without a prior spontaneous PTB has a cervix \leq 20 mm. Son and colleagues published their implementation experience comparing PTB rates before and after introduction of a formal program of universal cervical screening.²⁹ After implementation, of the 17,590 women (99.9% of eligible) 0.89% had CL \leq 25 mm. Introduction of the program was associated with a significant decrease in PTB < 37 wks (6.7% vs. 6.0%; adjusted OR 0.82 [95% CI 0.76-0.88]) and < 34 wks (1.9% vs. 1.7%; adjusted OR 0.74 [95% CI 0.64-0.85]). Finally, Temming and colleagues did CL screening for 10,871 women with a singleton pregnancy undergoing midtrimester anatomy survey (85% of eligible) and found 2% with cervix < 25 mm and 1.2% cervix < 20 mm.³⁰

Other special situations

Should women with a history of treatment for cervical dysplasia (in the absence of a prior preterm birth) undergo routine serial cervical length screening?

There is insufficient evidence to support additional screening for women with a previous electrosurgical procedure (loop electrical excision procedure, LEEP) or cold knife cone for cervical dysplasia.

A recent large retrospective cohort study, as well as a systematic review and meta- analysis, found that while average CL is shorter in women after a procedure, most nevertheless have a normal mid-trimester CL and more importantly, the increased risk of spontaneous PTB in this population appears related to the history of cervical dysplasia, not the procedure itself.³¹⁻³² Therefore, these otherwise low-risk women who have undergone treatment

for cervical dysplasia or have a history of dysplasia do not require additional evaluation beyond that which would routinely be offered to women without a history of a prior PTB.

Should women undergo routine cervical length screening after cerclage placement?

Several small studies evaluated this question in all types of cerclage (history-indicated, ultrasound-indicated, and physical exam-indicated).³³⁻⁴⁴ These results demonstrated that progressive cervical shortening after cerclage increases the risk of PTB,^{33-35,38} particularly if CL is <10mm,^{43,44} but neither overall CL nor length below the stitch correlate well with outcomes,^{35,36,39-41} and, importantly, there are currently no additional treatment options for a short cervix after cerclage (e.g. reinforcement suture does not improve outcomes).³⁴⁻³⁷ Although there may be theoretical psychological benefit to the patient and provider to visualize the stitch location post-procedure, there are insufficient data to suggest a clinical benefit of routine postcerclage CL measurement or surveillance.

Should women with multiple gestations undergo routine cervical length screening?

In women with multiple pregnancies, the cervix is shorter and associated with an increased risk of PTB.^{45,46} In the large, multicenter Preterm Prediction Study conducted by the MFMU Network, approximately 18% of twin gestations had a CL <25mm at 22-24 weeks of gestation (compared to 9% of singletons).⁴⁷ The risk of PTB with a CL <25mm was increased 8-fold in twins, compared to 6-fold in singletons.^{18,47}

Various interventions (e.g. progesterone, pessary) are currently being tested in RCT's for women with multiple gestation and shortened cervix, but at this time available data does not indicate adequate clinical benefit to justify routine screening of all women with multiple gestations.⁴⁸⁻⁵⁰ For this reason, routine CL screening in multiple pregnancies is not currently recommended by SMFM.¹¹

What is the role of cervical length screening to predict preterm birth for women in other clinical scenarios?

Threatened preterm labor

Transvaginal ultrasound CL measurement may serve as an adjunct to digital cervical examination in the assessment of women with symptoms of acute PTL.⁵¹⁻⁵³ Several observational studies have noted that the combination of CL and fetal fibronectin (FFN) assessment may improve prediction of PTB among women with symptoms of acute preterm labor.⁵⁴⁻⁵⁶ In triage units that combine CL screening and FFN testing in "symptomatic" patients, FFN does not add to PTB prediction in women with a very short (<20 mm) or long (>30 mm) CL. In these situations FFN may be discarded because the NPV of CL \geq 30 mm alone is high (96-100%) and women with CL <20 mm are at high enough risk that PTL treatment should be initiated based on CL alone.⁵⁴

	Recommendations	GRADE
1	We recommend routine transvaginal CL screening for women with singleton pregnancy and history of prior spontaneous PTB.	1A Strong recommendation, high-quality evidence
2	We recommend routine transvaginal CL screening not be performed for women with cervical cerclage, multiple gestation, PPROM, or placenta previa.	2B Weak recommendation, moderate-quality evidence
3	We recommend practitioners who decide to implement universal CL screening follow strict guidelines.	2B Weak recommendation, moderate-quality evidence
4	We recommend sonographers and/or practitioners receive specific training in the acquisition and interpretation of cervical imaging during pregnancy.	2B Weak recommendation, moderate-quality evidence

Summary of recommendations

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When used in combination with CL screening, FFN may be most useful in women with CL of 20-29 mm (e.g. the "grey zone"); in this situation a "negative test" ($\approx 80\%$ of cases) may allow for no treatment while a positive test would suggest the need for intervention (antenatal corticosteroids, transfer to tertiary center, etc).54-56 There remains some controversy with the routine use of FFN with or without CL screening to detect true PTL in symptomatic women. To date, only one interventional trial has shown that knowledge of CL and FFN improves outcomes. In 2007 Ness and colleagues published results of their single center RCT that involved 100 women who were being evaluated for threatened PTL. Knowledge of CL and FFN results was associated with a shorter duration of assessment in women with CL > 30 mm and overall a lower rate of SPTB (13% vs. 36.2%; p = 0.01).⁵⁵ However, a recent systematic review involving women being assessed for PTL utilizing FFN without CL screening did not show any clinical improvements.⁵⁷

Preterm premature rupture of membranes

Prospective studies incorporating nearly 500 women total with PPROM are conflicting; 4 studies found shorter CLs to be associated with shorter latencies,⁵⁸⁻⁶¹ but a fifth study did not.⁶² The latter study, however, was specifically powered to establish the safety of weekly CL measurements in the setting of PPROM, and found a similar incidence of chorioamnionitis among those in the no-probe and probe groups (28% versus 20%). The incidence of endometritis (6% versus 9%) and neonatal infection (17% versus 20%) were also similar between groups.⁶²

A prospective observational cohort of 105 women with PPROM between 23-33 weeks of gestation found that 40% of women had a transvaginal CL <2cm, and the positive predictive value of delivery within 7 days was 62%.⁶¹ Although CL measurement does not appear to cause

Clinical guidelines from professional societies that address CL screening or CL assessment to predict preterm birth

Organization	Title/Link	Year of publication
American College of Obstetricians and Gynecologists	Practice Bulletin #130: Prediction and prevention of preterm birth ¹⁰	2012 (Reaffirmed 2016)
International Society of Ultrasound in Obstetrics and Gynecology	ISUOG Practice Guidelines: Role of ultrasound in twin pregnancy ⁶⁶	2016
	ISUOG Practice Guidelines for performance of the routine mid-trimester fetal ultrasound scan ⁶⁷	2011
Royal Australian and New Zealand College of Obstetricians and Gynecologists	Cervical length in pregnancy, Measurement of (C-Obs 27) http://www.ranzcog.edu.au/ component/docman/doc_ view/1071-measurement-of- cervical-length-in-pregnancy- c-obs-27.html?ltemid=946	July 2012
Royal College of Obstetricians and Gynaecologists	Green-top guideline #60: Cervical cerclage https:// www.rcog.org.uk/en/ guidelines-research- services/guidelines/gtg60/	2011 (Last reviewed 2014)
Society for Maternal-Fetal Medicine	Progesterone and preterm birth prevention: translating clinical trials data into clinical practice ¹¹	2012 (Reaffirmed 2014)
Society of Obstetricians and Gynaecologists of Canada	#257: Ultrasonographic cervical length assessment in predicting preterm birth in singleton pregnancies ⁶⁸	2011
	#260: Ultrasound in twin pregnancies ⁶⁹	2011

The recommendations in this document reflect the national and international guidelines related to the cervical length screening for preterm birth prevention.

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harm with PPROM and a shortened cervix is associated with shorter latency, there are insufficient data to suggest a clinical benefit to CL measurement or surveillance.

Placenta previa

Three prospective studies, which included a total of approximately 185 women combined, evaluated the utility of CL *in the third trimester* as a predictor for emergency cesarean delivery and hemorrhage in women with previa.⁶³⁻⁶⁵ All studies used a CL cutoff of 30mm to define the cervix as 'short,' and reported that those with a short CL were more likely to have hemorrhage and emergent delivery. The largest study found that of 68 women with placenta previa, 29 had a transvaginal ultrasound CL <30mm; of

these, 79% delivered prematurely due to hemorrhage, compared to 28% of women with a CL \geq 30mm.⁶⁵

Whereas these three studies demonstrate that there may be an association between shortened CL and PTB in the setting of placenta previa, there are no prospective studies testing a management strategy based on CL, and there are insufficient data to suggest a proven clinical benefit of routine CL measurement or surveillance. We recommend routine transvaginal CL screening not be performed for women with cervical cerclage, multiple gestation, PPROM, or placenta previa. (GRADE 2B)

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