

Cervical Length Assessment: Who Needs Cervical Evaluation? And what does a short cervix mean?

By: Meiling Parker, MD, FACOG



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Objectives

- Background
- Examine the literature regarding mid-trimester cervical length assessment
 - Who should be screened?
 - How and when should screening occur?
- Discuss common pitfalls to cervical length assessment
- Review treatment options for ultrasound-detected short cervix
- Management of women with a prior spontaneous preterm birth

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Disclosures

- I have no financial conflicts of interest to disclose

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Background

- Preterm birth (PTB) is birth between 20 0/7 and 36 6/7 weeks
- #1 cause of neonatal mortality and the 2nd leading cause of all <5 childhood mortality in the US
- Definitions
 - Preterm labor – Uterine contractions and documented cervical change with intact membranes at 20-36 6/7 weeks (50% of PTB)
 - Cervical insufficiency – recurrent painless dilation leading to second trimester pregnancy loss (~1% of sPTB)
 - Premature preterm rupture of membranes (PPROM) – Rupture of membranes at <37 weeks (30% of PTB)
 - Iatrogenic preterm birth – Not spontaneous, includes medically indicated preterm deliveries (20%)

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Background

- Rate of PTB <37 weeks in the US was 9.9% in 2017 (marchofdimess.org)
 - Peaked at 12.8% (2006) and dropped to 9.6% in 2014 but has since risen 3 years in a row
 - High PTB rate due to ART, older and sicker mothers, improvements in ultrasound leading to earlier timing of births
 - Recent declines due to progesterone, reduced teen birth, lower rates of higher order multiples
- Over 1 million babies die of the consequences of PTB every year in the world, 1 every 30 seconds
 - RDS, BPD, IVH, NEC, sepsis, apnea, retinopathy of prematurity
 - Chronic lung disease, grade III/IV IVH, NEC, vision/hearing impairment, CP, etc

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Background

- Prediction and prevention of preterm birth
 - Screening test: beneficial only if an intervention reduces the outcome once the screening test is positive
 - 4 main risk factors for which there are effective interventions
 - Smoking
 - Short cervical length
 - Prior PTB
 - Asymptomatic bacteriuria

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Midtrimester Cervical Length Assessment

- Who is eligible for screening?
 - Asymptomatic, low risk women with a singleton gestation
 - Previously, screening was discouraged due to the absence of evidence based treatments
 - The publication of many RCTs has demonstrated the vaginal progesterone is effective in preventing preterm birth
- How and when should screening occur?
 - According to ACOG, it's up to us!
 - Problems due to lack of quality assurance
 - Lack of availability in all areas
 - Option #1: 2nd trimester TVUS only if TAUS is suspicious for abnormality
 - Option #2: Universal screening according to an already published protocol

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Midtrimester Cervical Length Assessment

- Short cervical length measured by transvaginal ultrasound has been associated with an increased risk of preterm birth
- Short cervix is commonly defined as < 20-25mm before 24 weeks gestation
- The shorter the cervical length, the greater the risk of preterm birth
- There is no cervical length threshold at which all women will delivery prematurely

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THE LENGTH OF THE CERVIX AND THE RISK OF SPONTANEOUS PREMATURE DELIVERY
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 RACHEL L. COPPER, M.S.N., C.R.N.P., FRANCES JOHANSON, R.N., B.S.N., JAMES M. ROBERTS, M.D.,
 AND THE NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT MATERNAL-FETAL
 MEDICINE UNIT NETWORK*

Abstract Background: The role of the cervix in the pathogenesis of spontaneous delivery is controversial. In a 24 weeks were compared with women with values above the 75th percentile; the relative risk of preterm delivery

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Midtrimester Cervical Length Assessment: TVUS vs TAUS

- TVUS is most reliable and reproducible
- TAUS is more susceptible to error
 - Maternal obesity
 - Position of the cervix
 - Shadowing from the fetal presenting part
- HOWEVER – using TAUS as the first step in a screening approach may be reasonable
 - Real world implementation of screening must take into account patient acceptance, ease of application, and utilization of resources
 - Use a higher TA cervical length cutoff (30-35mm)

Saul L. J *Ultrasound Med* 2008; 27:1305-11.
 Rhoades J. *Am J Perinatal* 2016; 33:473-9.

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Midtrimester Cervical Length Assessment: Proper technique

- Vaginal probe placed in anterior fornix of the vagina
 - Interobserver variation of only 5-10%
- Identify sagittal view
- Place calipers at internal and external os
- Take 3 measurements, record the shortest of the 3

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Internal Os External Os
 Endocervical Canal

AIUM.org

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Transvaginal Cervical Length: Proper technique

1. Flat internal os or triangle
2. Observe entire endocervical canal
3. Symmetric image of external os
4. Equal size and density of the anterior and posterior lips of the cervix

Burger M, et al. *Ultrasound Obstet Gynecol* 1997; 9:188-193

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Transvaginal Cervical Length: Proper technique

Radiologykey.com

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Midtrimester Cervical Length Assessment: Common pitfalls

- Excessive probe pressure – leads to falsely lengthened cervix
- Full bladder – leads to falsely lengthened cervix
- Unequal size and density of the anterior and posterior lips of the cervix
- Endocervical canal not well visualized

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Avoid Unequal size and density of anterior/posterior lips of cervix

Source: A. C. Fleischer, E. C. Toy, W. Lee, F. A. Manning, R. J. Romero: *Sonography in Obstetrics and Gynecology: Principles & Practice*, 7th Ed. www.accessmedicine.com Copyright © McGraw-Hill Education. All rights reserved.

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Avoid Poor Visualization of the Endocervical Canal

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Avoid a Full Bladder

Full bladder

Cervical length 35 mm


Empty bladder

Cervical length 17 mm

B = bladder
F = fetal head

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Measure the Portion of the Endocervical Canal That is Closed



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Radiopaedia.org

Treatment Options for Short Cervix: Vaginal Progesterone

Progesterone and the Risk of Preterm Birth among Women with a Short Cervix

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ABSTRACT

BACKGROUND
Previous randomized trials have shown that progesterone administration in women who previously delivered prematurely reduces the risk of recurrent premature delivery. Asymptomatic women found at midgestation to have a short cervix are at greatly increased risk for spontaneous early preterm delivery, and it is unknown whether

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Treatment Options for Short Cervix: Vaginal Progesterone

- 250 women with mostly (90%) singleton gestations and mostly no prior PTB (85%) with CL ≤15mm at 20-25 weeks
- Vaginal progesterone 200mg was administered nightly at 24 weeks until 34 weeks
- 44% reduction in PTB <34 weeks** (19% versus 34%, RR 0.56, 95% CI 0.36-0.86)
 - Subgroup analysis of only those without prior PTB confirmed benefit
- Incidence of CL ≤15mm was 1.7%, number needed to screen to prevent one PTB<34 weeks is 387
- Once CL ≤15mm is identified, NNT to prevent one PTB<34 weeks is 7

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Treatment Options for Short Cervix: Vaginal Progesterone

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Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial

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¹Perinatology Research Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development/National Institutes of Health/Department of Health and Human Services.

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Treatment Options for Short Cervix: Vaginal Progesterone

- 458 women, all with singleton gestations and mostly no prior PTB (84%) with CL 10-20mm at 19-23 6/7 weeks
- Vaginal progesterone 90mg daily started at 20-23 6/7 weeks until 36 6/7 weeks
- 45% reduction in PTB <33 weeks** (9% vs 16%, RR 0.55, 95% CI 0.33-0.92)
- 43% decrease in composite neonatal morbidity and mortality** (8% vs 14%, RR 0.57, 95% CI 0.33-0.99)
 - Subgroup analysis of only women without prior PTB confirmed benefit
- Incidence of CL 10-20mm was 2.3%, number needed to screen to prevent one PTB<33 weeks is 604
- Once CL 10-20mm is identified, NNT to prevent one PTB<33 weeks is 14

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Treatment Options for Short Cervix: Cerclage

- In women with singleton gestations, no prior PTB and CL<25mm before 24 weeks
 - Cerclage placement has no significant effect on reduction of PTB <35 weeks (RR 0.76, 95% CI 0.52-1.15)
- Physical exam indicated cerclage (PEIC) in singleton gestations with a cervix dilated to ≥1cm in the second trimester is associated with prevention of PTB and neonatal benefit
 - PEIC vs control results in ~4 week delay in delivery (30 vs 26 weeks)
 - 92% decrease in PTB <28 weeks compared to no cerclage
 - Antibiotics plus indomethacin preoperatively appears to be beneficial
 - Studies limited by mostly retrospective nature, small sample size, inclusion of twins, no control groups,

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Treatment Options for Short Cervix: What about 17-OHP?

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17-alpha hydroxyprogesterone caproate to prevent prematurity in nulliparas with cervical length

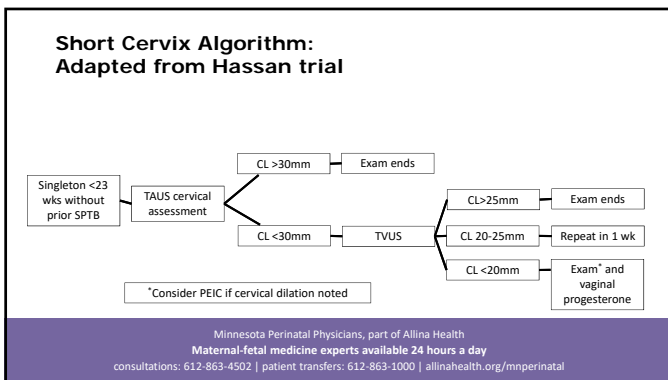
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Treatment Options for Short Cervix: What about 17OHP?

- Multicenter RCT showed no difference in PTB <37 weeks (25.1% vs 24.2%, RR 1.03, 95% CI 0.79-1.35)
- Other, smaller, studies have likewise shown no benefit to 17OHP
- **17OHP cannot be recommended for prevention of PTB in women with a short cervix and no prior history of PTB**

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What about women with prior spontaneous preterm birth

- Prior PTB or PPRM <37 weeks
- ACOG currently recommends weekly 17OHP from 16-36 wks **PLUS**
- Cervical length surveillance* from 16-22+5 weeks with ultrasound indicated cerclage placement if TVCL ≤25mm at <23 wks
- History indicated cerclage only if 3+ prior PTB

*Consider only for prior PTB <34 wks

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Prior sPTB

- Biologic plausibility to the use of progesterone in preterm birth prevention
 - Progesterone can inhibit myometrial contractions
 - Anti-progesterones are used as abortifacients

HOWEVER

- Progesterone levels exceed saturated receptor levels in pregnancy
- Administration of vaginal progesterone does not increase circulating concentrations

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Prior sPTB– the case for 17OHP

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Prior sPTB – the case for 17OHP

- N=310
- Significant reduction in PTB <37 weeks in 17OHP group versus placebo (36.3 vs 54.9%, $p<0.001$)
- Also significantly lower rates of NEC, IVH, and O₂ therapy in the newborns in 17OHP group

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Prior sPTB – the case for 17OHP

- Based on results from the 2003 Meis trial, FDA approved weekly IM administration of 250 mg 17OHP from 16-36 weeks in women with singleton pregnancy and a previous preterm birth

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Prior sPTB – the case against 17OHP

- Criticisms of the Meis trial
 - High rate of preterm birth (54.9%) in the placebo group compared to other studies
 - Frequency of preterm birth (36.6%) in the intervention group was similar to rates of preterm birth in placebo groups in other studies
 - A higher rate of miscarriage prior to 20 weeks noted in treatment group (1.6% vs 0%)

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Prior sPTB – the case against 17OHP

- PROLONG trial (2019)
 - N=1700
 - FDA-requested confirmatory study, initiated in 2009
 - Randomized, double-blinded, placebo-controlled trial evaluating Makena® in patients with a prior spontaneous singleton preterm delivery
- Difference in rate of PTB<35 weeks not statistically significant in treatment vs placebo group (11 vs 11.5%, $p=0.72$)
 - Rates of miscarriage and stillbirth were the same amongst the two groups

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Prior sPTB – the case against 17OHP

- 17OHP became standard of care in US during PROLONG trial
- Most enrollees were from European countries
 - Subgroup analyses of US patients to be done

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Prior sPTB – what about vaginal progesterone



Vaginal progesterone prophylaxis for preterm birth (the OPPTIMUM study): a multicentre, randomised, double-blind trial

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OA

Summary
Background Progesterone administration has been shown to reduce the risk of preterm birth and neonatal morbidity in women at high risk, but there is uncertainty about longer term effects on the child.
Methods We did a double-blind, randomised, placebo-controlled trial of vaginal progesterone, 200 mg daily taken from 22–24 to 34 weeks of gestation, on pregnancy and infant outcomes in women at risk of preterm birth (because of previous spontaneous birth at <24 weeks and 0 days of gestation, or a cervical length <25 mm, or because of a positive fetal fibronectin test combined with other clinical risk factors for preterm birth) in one of a history in a

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Prior sPTB – what about vaginal progesterone

- OPPTIMUM trial – long term effect of vaginal progesterone vs placebo in the prevention of preterm birth until age 2 yrs
- No benefit nor harm, nor significant prolongation of pregnancy

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Prior sPTB – what about vaginal progesterone

RESEARCH ARTICLE

Vaginal progesterone pessaries for pregnant women with a previous preterm birth to prevent neonatal respiratory distress syndrome (the PROGRESS Study): A multicentre, randomised, placebo-controlled trial



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Prior sPTB – what about vaginal progesterone

- Examined the effect of maternal vaginal progesterone on the risk of respiratory distress syndrome (RDS) in the neonate
- No difference in the rate of RDS or severe respiratory disease between the two groups

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Prior sPTB – what about vaginal progesterone

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Progesterone vaginal gel for the reduction of recurrent preterm birth: primary results from a randomized, double-blind, placebo-controlled trial

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Prior sPTB – what about vaginal progesterone

- Randomized, double-blind, placebo-controlled, multinational trial
- Examined rates of preterm birth ≤ 32 weeks in women randomized to vaginal progesterone gel versus placebo
- No difference in the primary outcome nor infant morbidity/mortality

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Prior sPTB – what about vaginal progesterone

- Criticisms of OPPTIMUM trial
 - Variable inclusion criteria: cervical shortening, positive FFN, prior PTB, prior PPROM
 - Low (60%) compliance rates
- Criticisms of PROGRESS trial
 - Inadequate characterization of "previous preterm birth"
 - Inclusion of twin pregnancies

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Prior sPTB – what about vaginal progesterone

Based on the 3 negative RCTs, SMFM recommends only 17OHP for prevention of recurrent preterm birth (2017)

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Prior sPTB – Add cerclage to the mix

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Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length

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Prior sPTB – Add cerclage to the mix

- TVCL from 16-23 weeks with randomization to cerclage vs expectant management if TVCL ≤ 25mm
 - Some participants also received 17OHP
 - No difference in primary outcome, PTB ≤ 35 weeks
 - Significant reduction in rates of PTB <24 weeks and <37 weeks, and perinatal death
 - Secondary analysis showed reduction in primary outcome if the TVCL < 15mm
- Subsequent meta-analyses have shown cerclage to be beneficial in women with prior sPTB <34 weeks and short cervix (<25mm)

BergHELLA et al. Cerclage for short cervix on ultrasonography: a Meta-analysis of trials using individual patient level data. *Obstet Gynecol* July 2005; Volume 106: 181-189.

BergHELLA et al. Cerclage for short cervix on ultrasonography in women with singleton gestations and previous preterm birth: a meta-analysis.

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Back to ACOG recommendations

- Prior PTB or PPROM <37 weeks
- ACOG currently recommends weekly 17OHP from 16-36 wks **PLUS**
- Cervical length surveillance* from 16-22+5 weeks with ultrasound indicated cerclage placement if TVCL ≤25mm at <23 wks

*Consider only for prior PTB <34 wks

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Referral process and programs

Easy referral/consultation process – provider referrals only

- Perinatologist consultation: 612-863-4502
- Referral/appointments: 612-863-4502 (for any clinic location – six throughout Mpls/St. Paul)
- Patient transfers available 24/7: 612-863-1000

How we support referring providers

- comprehensive multidisciplinary team
- consultations 24/7
- advanced technology ultrasound imaging
- genetic counseling and testing, including prenatal screening, CVS and amniocentesis
- coordinated case management

Unique partnerships & programs

- Neonatal care in conjunction with Children’s Minnesota
- Maternal Obstetric Medicine Surgical program
- Obstetric Intensive Care program
- Genetics program
- Morbidly Adherent Placenta program
- Fetal Echo and Early Fetal Echo programs

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Thank you!