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Title: The Maternal Cervix: Why, When and How? Revised

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Abstract

Introduction The incidence of preterm birth has continued to rise in most countries in the world during the last decade. There are many clinical risk factors that increase the risk of preterm birth. It has been shown that a sonographically shortened cervical length is a strong indicator of subsequent preterm birth in pregnancy.

Background It has been established that women at an increased risk of preterm birth should have the cervical length recorded using a transvaginal approach. The sensitivity of a shortened cervical length to predict preterm birth is higher in women with a previous preterm birth, with reduced sensitivity in low risk women. The maternal cervix may be assessed using transabdominal, transperineal and transvaginal ultrasound approaches. This article discusses the available research into the use of these differing techniques and current guidelines for measuring maternal cervical length.

Summary Measuring the maternal cervical length has become an important part of the mid trimester morphology examination. The appropriate technique to screen the cervical length in women at low risk of preterm birth is still debatable throughout the wider obstetric and ultrasound communities.

Keywords: Preterm Birth, Cervix, Ultrasound, Pregnancy

Why?

Risk Factors

Preterm birth rates have continued to rise worldwide in the last decade.^{1,2}

In Australia in 2011 preterm birth occurred in 7.5% of all gestations. A small proportion of mothers gave birth at 20 to 27 weeks gestation (0.9%), with 0.8% at 28-31 weeks, while 6.6% gave birth at 32-36 weeks.¹ The rate of mortality for the 32-36 week infants was five times higher than that of term born babies in Australia in 2009 at 4.7 per 1000 births. The mortality rate was 410 per 100 for babies born before 28 weeks and 30 per 1000 for babies born from 28-31 weeks.^{2,3} Preterm Birth is now the leading cause of neonatal death, and in children up to 5 years of age, the second largest cause of death.⁴

There are many clinical risk factors that can contribute to an increased risk of preterm birth (PTB) during pregnancy, though many women who deliver preterm do not have any known risk factors. The greatest risk factor for PTB is a PTB in a previous pregnancy.⁵ Women with a uterine anomaly or history of previous cervical cone biopsy/large loop excision of the transformation zone, fibroidectomy and multiple cervical dilatations are also at an increased risk of PTB.^{6,7} It has been shown that women with a prior PTB have a 2.5 fold increase risk of subsequent PTB. However this fact is not helpful in nulliparous women, who make up nearly half of all patients experiencing PTB.⁵ Whilst a previous full term birth has been shown to decrease the risk of PTB in subsequent pregnancies.⁸

Currently, using ultrasound, the length of the cervix is the feature that we can assess to indicate the strength of the cervix.⁹ A shortened cervical length (CL) as seen on transvaginal ultrasound (TVU) is a strong indicator that a baby will be born preterm in

singleton and multiple gestations.¹⁰ The shorter the cervical length the greater the risk of spontaneous PTB.¹⁰ Even so, it is important to note that 75% of women with a shortened cervix do not deliver preterm.⁶ It has been shown that a shortened cervical length on TVU has a sensitivity of over 50% for subsequent PTB in women presenting with a clinically increased risk of PTB. In women with no risk factors the sensitivity is reduced to 37%.^{6,11}

In a high risk population the risk of PTB at 20weeks with a cervical length of 25mm is 26%, this increases to 32% at 20mm with an increase to 56% and 64% at 5mm and 0mm respectively.¹²⁻¹⁴ Ultrasound can also recognise intra-amniotic sludge and choriodecidual separation. Intra-amniotic sludge in isolation has no increased risk of PTB but in conjunction with a shortened CL as seen in figure 1, results in a higher risk of PTB than a short cervix alone.¹⁵ Detachment of fetal membranes from the decidua at the level of the internal os as seen in figure 2, is also associated with an increased risk for PTB.¹⁵

INSERT FIGURE 1 & 2 HERE

There have been nomograms constructed which demonstrate expected cervical length throughout pregnancy.¹⁶⁻¹⁸ At 20 weeks gestation the mean cervical length in singleton pregnancies has been shown to be 42mm.¹⁹ Medical intervention is not usually considered until CL is less than 25mm.¹⁹⁻²¹ In women with a cervical length of <15mm there are higher rates of intra-amniotic infection than those with a cervical length >15mm. This may be due to an intra-amniotic infection resulting in

contractions and a shortened cervix or a short cervix predisposing the patient to ascending infection.²²

Interventions

There have been some trials testing the effectiveness of medical interventions in cases of shortened cervical length. Cervical cerclage has been widely used as a surgical method to prevent recurrent mid-trimester pregnancy loss in women at risk.²³ A suture or tape is placed around the cervix to attempt to prevent dilatation resulting in subsequent PTB.⁴ It has been found that cerclage can significantly reduce PTB rates in high risk women (prior PTB) who present with a shortened TVU CL prior to 24 weeks gestation.¹⁵ However cerclage is associated with increased rates of vaginal bleeding and discharge and fever with a significant increase in caesarean section deliveries also.⁴ In cases of twin pregnancy, cerclage has been associated with a higher incidence of PTB and is contraindicated.¹⁵

A trial involving over 32 000 high and low risk asymptomatic women²⁴ and the use of vaginal progesterone on the maternal cervix resulted in a reduction of spontaneous preterm delivery before 34 weeks gestation. In these women, 733 were identified with a cervical length of between 10-20mm. The participants' were randomized into a placebo and progesterone group comprising 229 and 236 women respectively (268 women declined to participate). The PTB rate in the placebo group was 2.1%, with a reduction to 1.85% in the progesterone group.²⁴ Studies to date have shown progesterone treatment to be ineffective in preventing PTB in multiple gestations or women presenting in preterm labor.⁴

The cervical pessary is a silicone device traditionally used for treatment of genital prolapse that has been shown to have a significant reduction in spontaneous delivery before 34 weeks with no serious adverse effects. A small pilot study has found a significant reduction in PTB rates in multiple gestations.¹⁵ Clinical protocols for this device are still in the development stage.⁴

Standard management paradigms recommend that low risk women presenting with a cervical length of 20 to 25mm undergo a repeat CL in 1 to 2 weeks.⁷

In women with a CL of 10 to 20mm it is recommended that daily vaginal progesterone is administered until 36 or 37 weeks gestation^{7,25}, and women with a sonographic cervical length of <10mm should receive cervical cerclage.²⁵ In high risk women there have been recommendations of history indicated cerclage placement at 12-14 weeks gestation with removal at ≥ 36 weeks gestation, or cervical surveillance from 16 weeks gestation and vaginal progesterone between 16 and 36 or 37 weeks gestation.^{7,25}

When?

Screening of the CL has been shown to be not very effective when performed before 14 weeks.²⁰ This is because the endocervical canal is continuous with the lower uterine segment, which is falsely 'counted' in the cervical length.²⁰ In the first trimester the lower segment of the uterus is undeveloped due to the smooth muscle in the isthmic portion of the uterus undergoing marked hypertrophy in early pregnancy, the gestational sac is also usually located fundally and therefore exerts very little pressure on the lower uterine segment.⁹ It has been shown that due to these factors cervical insufficiency does not generally develop until the second trimester, and nearly all women, including those at high risk of PTB will have a normal cervical length prior to 14 weeks gestation.^{6,15,20}

For the prediction of likelihood of PTB due to shortened CL, it has been shown that the optimal time to register the CL is between 16 and 24 weeks gestation.^{25,26}

Measurements later in pregnancy have a decreasing predictive value for PTB, and it is recommended measurements should not be performed after 28 weeks gestation.²⁵ The Australasian Society for Ultrasound in Medicine (ASUM) guidelines recommend that cervical length can be registered until 35 weeks gestation,²⁶ and the 3 Centres Collaboration in Victoria defines a short cervix as a cervical length of less than 20mm at 18 to 22 weeks gestation.⁷

It has also been shown that cervical length measurements in late pregnancy may be a useful not to screen for PTB, but to aid in the prediction of successful induction of labour.²⁸ It is also important to note that the earlier in pregnancy that a cervix is found to be short, the greater the risk is of PTB.^{7,25}

How?

Cervical length

The length of the cervix is measured as the distance between the junction of the endocervical mucosa and the lower uterine segment (internal os) and the junction of the ectocervix and endocervical mucosa (external os). The closed length of the cervical mucosa is measured. This usually has a hyperechoic appearance and is surrounded by hypoechoic glandular tissue in many patients. The Fetal Medicine Foundation²⁹ recommends a straight line measurement be utilised. The straight line measurement has been shown to have better reproducibility between operators.^{29,30} Some authors suggest a two straight line approach or a tracing of the canal in curved cervixes.³¹ Research by To et al³² recommend being mindful of the effect of a highly curved cervical canal on patient management if a straight line technique is utilised, whilst concluding that a curved cervix is considered to be normal and a short cervix will become straight.

It has been established that high risk patients should be offered TV cervical length. The TV approach is considered to be the gold standard for accurate measurement of cervical length.¹¹ There is continuing debate as to the best way to measure the cervical length in women who are considered to be at a low risk of PTB.³³

The American congress of Obstetricians and Gynaecologists in conjunction with the American College of Radiology and the American institute of Ultrasound in medicine recommend that 'the cervix be examined sonographically when feasible'. They recommend that 'TV or transperineal (TP) ultrasound may be considered if the cervix appears shortened or cannot be adequately visualized during the transabdominal examination'.³⁴

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) guidelines on measurement of cervical length for prediction of PTB state that 'accurately measured ultrasound cervical length has an inverse relationship with the risk of PTB. It also states that 'cervical length is most accurately measured by TVU' and 'there is a growing body of evidence suggesting that interventions, such as progesterone and/ or cervical cerclage may be of benefit for women otherwise considered low risk of PTB found to have a short cervix in the mid-trimester'.³⁵

The SCOG recommends that 'because of poor positive predictive values and sensitivities and lack of proven interventions, routine TV CL is not recommended in women at low risk of PTB.²⁶ The International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) guidelines for the second trimester obstetric examination

conclude that ‘Currently there is insufficient evidence to recommend routine cervical length measurements at the mid trimester in an unselected population’.³⁶ ASUM guidelines for the second trimester examination state that the ‘cervix should be examined’.²⁷

Each ultrasound approach that can be utilised has technical considerations. It is important that the correct landmarks be acquired for the appropriate ultrasound approach that is utilised in your department.

Ultrasound approaches

Transabdominal approach

There have been numerous studies comparing the transabdominal cervical length using a full maternal bladder to the transvaginal (TV) approach. These studies found that the cervical length was measurable in 100% of cases. Hernandez-Andrade et al³⁷, Marren et al²¹ and O’Hara et al³⁸ found that a cervical length obtained with a full bladder overestimated the TV cervical length by 8mm, 6.1mm and 14mm respectively. The TA full bladder cervical length can also be problematic in that the cervical canal may be compressed by the bladder and ‘mask’ the appearance of funnelling of the cervical canal due to premature rupture of membranes.³⁹

Some authors have compared TA cervical length with to TV cervical length with an empty maternal bladder (TABE). Saul et al⁴⁰ were able to measure the TABE cervical length in 100% of cases as were. Studies by Marren et al²¹, Friedman et al⁴¹, To et al³² and O’Hara et al³⁸ were able to register measurements for TABE

cervical length in 82.8%,82.1%,50% and 98% of patients respectively, with the research by To et al performed in 2001.

The studies by To et al³² and Friedman et al⁴¹ also found that the mean TABE cervical length was shorter than TV cervical length by -2.5 and -2.6mm different respectively. The recent studies by Marren et al²¹ and O'Hara et al³⁸ found a mean difference of 0.6mm and -0.6mm between TA empty bladder and TV cervical length respectively.

It has also been proposed that there is a need to establish a TA cervical length over which we can be confident that the TV cervical length will be greater than 25mm. Friedman et al⁴¹ concluded that a TA cervical length of 35mm or greater would need to be obtained to be confident that the TV cervical length would be greater than 25mm, this study included TA cervical length measurements acquired with a full bladder. Marren et al²¹ concluded that a policy of routinely assessing the cervix by TABE measurement and proceeding to TV if the TABE cervical length is less than 25mm would miss 67% of cases with a shortened cervical length. Saul et al⁴⁰ found that a TABE cervical length cut off of 30mm or less showed 100% sensitivity for identifying cervixes with lengths of 25mm or less on TVU, whilst O'Hara et al³⁸ and Stone et al⁴³ found that all TABE cervical lengths greater than 30mm registered a TV cervical length greater than 25mm.

Transabdominal cervical length measurement technique

The maternal bladder should be empty to only partially full due to overestimation of cervical length with a full maternal bladder. It has been recommended that the

bladder should not exceed a one vertical height measurement of 5cm.^{40,44} The TABE approach utilizes the amniotic fluid as the acoustic window. The transducer placement is slightly cephalid with a caudal tilt to visualise the cervical mucosa. The transducer is manipulated with oblique and parasagittal movements to delineate the full length of the cervical mucosa and internal and external os. The image should be magnified to aid visualization of the cervix. The internal os should have a flattened T- shape appearance. Amnion may be visible especially in cases of a prominent mucus plug. The external os often appears as a very slight indentation. The posterior wall of the cervix should also be used as a guide when placing the caliper delineating the external os.^{39,40,44} An advantage of the TABE CL is that the cervix may be interrogated multiple times throughout the fetal morphology scan.

Figure 3 is an example of the full maternal bladder causing elongation of the cervical canal due to compression of the lower uterine segment. The same cervix imaged post void can be seen at figure 4 with figure 5 the TV cervical length.

Figure 6 is a further image of TACL post void.

INSERT FIGURES 3,4,5,6

Transvaginal Cervical Length

In 2006 Kagan et al³⁰ concluded that the best approach for measurement of cervical length is by TVU. TVU is highly reproducible, and in 95% of occasions, the difference between two measurements by the same observer and by two observers is 3.5mm or less and 4.2mm or less, respectively.³⁰ On TVU the most important technical pitfall is elongation of the endocervical canal caused by distortion of the cervix by the transducer.⁴⁵ This approach can utilise a high frequency endovaginal transducer to allow greater detail of the sonographic landmarks of the cervical canal.²¹ In all previously mentioned studies comparing other ultrasound approaches to the TV approach, the TV cervical length was registered in 100% of cases.

In patients with a premature rupture of membranes with amniotic fluid loss or bleeding in cases of placenta praevia TV approach will be contraindicated.⁴⁶ Consent can also be problematic with the TV approach. Recently authors researching the implementation of a TV cervical length screening program for low risk and high risk women in the American population found that 18% and 21% of women respectively declined to undergo the TV approach. With further problems encountered with women not able to have the TV approach due to language barriers.^{47,48}

Transvaginal Cervical length measurement technique

The patient should be in an elevated lithotomy position. The transducer should be advanced into the vagina until the cervical mucosa and internal and external os are identified. The transducer is then withdrawn until the image is just out of focus and then readvanced just enough to again identify the landmarks for the cervix. This is to

overcome artifactual lengthening of the cervical canal which can occur with too much probe pressure on the anterior fornix of the cervix.^{29,31,39} The cervical canal should be equidistant from the anterior and posterior cervical walls as seen in figure 7, with unequal distances being a sign of too much probe pressure as seen in figure 8.

The cervix should be magnified to fill 75% of the image. The internal os may appear as a typical V-shaped notch or as a flattened T-shape appearance, and the external os is seen with a triangular notch as seen in figure 7. The amnion may be seen at the internal os, figure 9 is an example of cervical measurement in a case of a prominent mucous plug with caliper placement for the internal os at the amnion. Three measurements should be taken over a 3 to 5 minute period. Dynamic changes should be noted during this time. The shortest accurate length obtained is registered as the cervical length.^{29,31,39}

INSERT FIGURES 7,8,9

Transperineal cervical length

There have been some authors who have compared the transperineal (TP) approach to the TV. A study by Cicero et al⁴⁹ looked at the cervix using the TP approach in the mid trimester (22-24 weeks). They showed a mean difference in CL of 0.2mm between TV and TP CL, though were only successful in 80% of patients. Yaziki et al⁴⁵ showed a mean CL difference of 1mm between TP and TV approaches and were successful in measuring the TP CL in 89% of patients. O'Hara et al³⁸ showed a mean difference of -0.16mm between TP and TV CL and were successful in 90% of cases.

The main technical issues with the TP approach are rectal gas overlying the external os⁵⁰ and the lower transducer frequency required to image the cervix.

Transperineal cervical length measurement technique

The patient should be in the elevated lithotomy position. The elevated position has been shown to help alleviate rectal gas over the external os.⁵⁰

A low frequency curved abdominal transducer is needed to enable adequate penetration to the internal os. The transducer is placed on the labia majora or perineum. Oblique or parasagittal movements are used to delineate the full length of the cervical canal. The caliper placement for the internal os should be adjacent to the cervical mucosa at the point where the opposing sides of the cervix come together and form a flattened T- shape appearance. The caliper placement for the external os should be adjacent to the cervical mucosa at the point where the cervix meets the vagina. A small hypoechoic ‘notch’ may be seen on some patients. The posterior wall of the cervix should also be used as a guide when placing the caliper delineating the external os.^{31,39,49,51} Figure 10 is an example of transperineal cervical length.

INSERT FIGURE 10

Further examples of cervical length imaging

Undeveloped Lower Uterine Segment

In some patients the lower uterine segment remains undeveloped or ‘immature’ into the early second trimester. The cervix can appear quite curved and have a

‘horizontal’ orientation in relation to the maternal vagina. All ultrasound approaches can be technically difficult. This appears to occur more frequently in patients in their first gestation. The external os is difficult to appreciate, and using the TVU approach the transducer needs to be withdrawn to delineate the appropriate landmarks. Often a lower frequency is needed to be able to also image the full cervical mucosa to the internal os. Figures 11 and 12 are examples of cervical length measurement in cases of an undeveloped lower uterine segment.

INSERT FIGURES 11&12

Lower Uterine Contractions

In cases of lower uterine contractions the measurement of the true cervical canal can be technically difficult in all ultrasound approaches. Ideally the cervix will be measured following relaxation of the contraction. The prominence of the cervical glandular tissue or cervical mucosa in the cervical canal is used to delineate the internal os from the lower uterine segment. Figure 13 is an example of TVU cervical length measurement with the presence of a lower uterine contraction.

INSERT FIGURE 13

Cervical Length measurement with cervical funnelling

Recent research has found that in cases of cervical funnelling or PROM measurement of the funnel length or width are unnecessary for prediction of PTB. The most important measurement to be registered is the length of the remaining cervical canal or functional length¹⁵, as demonstrated in figure 14. The distance from the inferior edge of the placenta to the internal edge of the remaining canal should also be documented, and the width and length of the funnel may also be documented as in figure 2 to aid in the planning of treatment.

INSERT FIGURE 14

Summary

Measuring the maternal cervical length has become an important part of the mid trimester morphology examination due to its strong relationship with a subsequent preterm birth. As yet there is no formal consensus on the best method to register cervical length in low risk women. Cervical length should be ideally registered between 16 and 24 weeks gestation. In high risk women cervical length should be acquired using a transvaginal approach due to the increased sensitivity of a shortened cervical length for PTB. A cervical length of less than 25mm is considered clinically significant and it has been found that a transabdominal cervical length of 30mm or greater acquired with an empty maternal bladder has a 100% sensitivity for a transvaginal cervical length of greater than 25mm. Transabdominal cervical length acquired with an empty bladder will not be successful at registering the appropriate landmarks in some cases and a transvaginal approach should then be used.

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Figure Legends

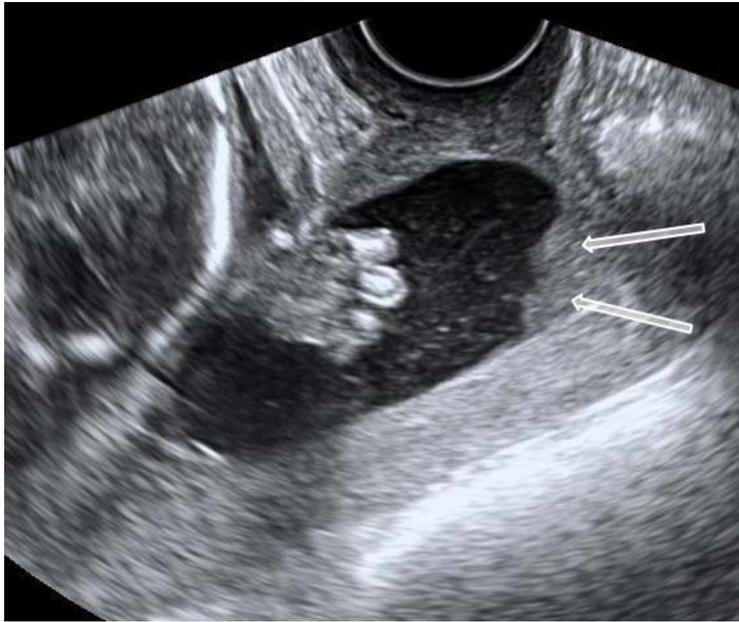


Figure 1. Transvaginal ultrasound of a shortened cervix with arrows pointing to intra-amniotic sludge

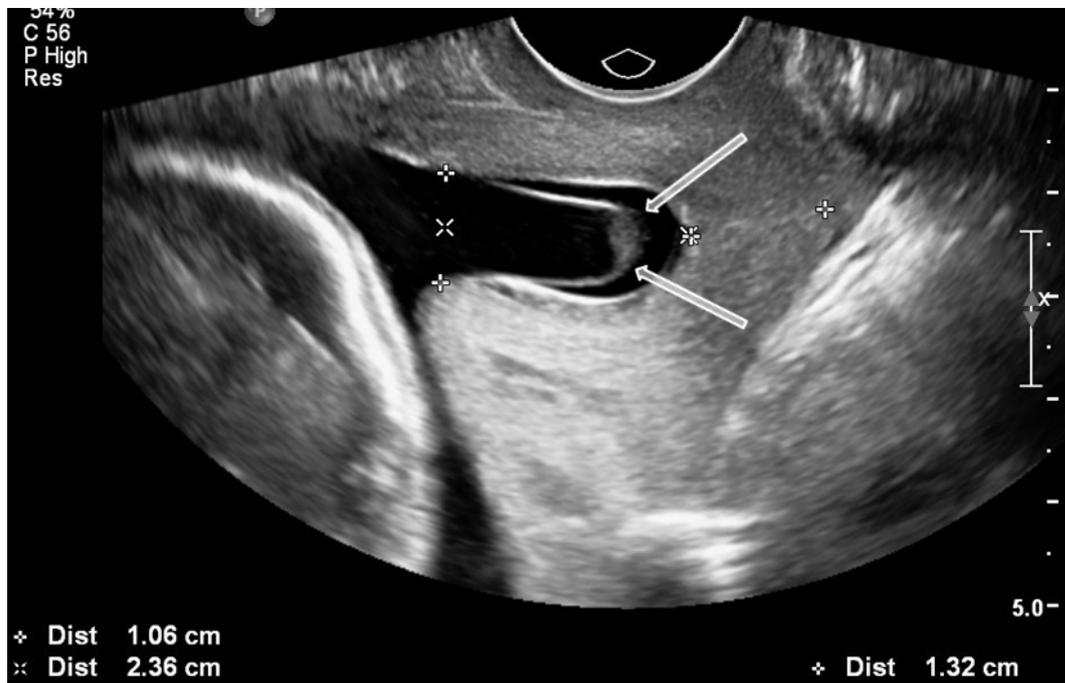


Figure 2. Transvaginal ultrasound of a shortened cervix with arrows pointing to detachment of fetal membranes

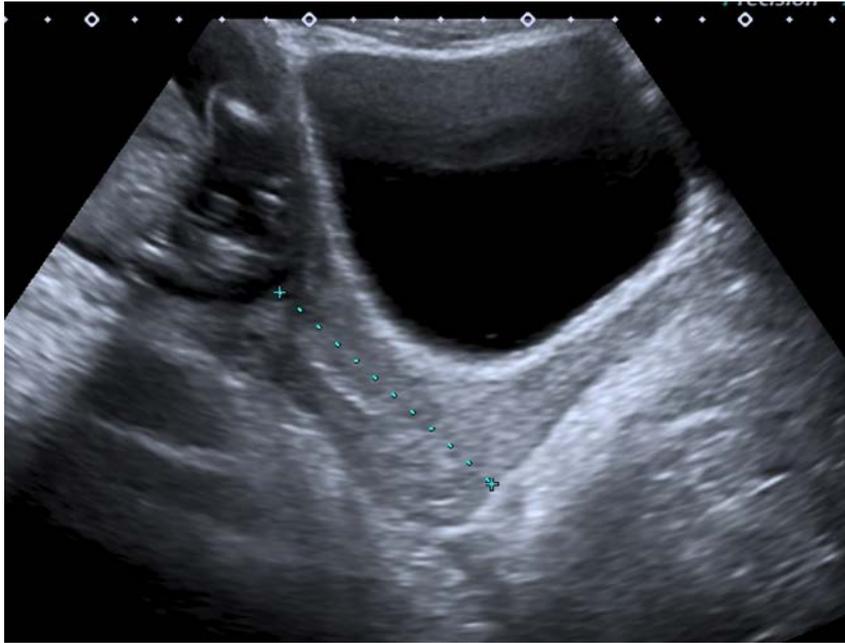


Figure 3. Transabdominal ultrasound full bladder cervical length of 57.8mm



Figure 4. Transabdominal ultrasound empty bladder cervical length of 34.7mm



Figure 5. Transvaginal ultrasound cervical length of 34.2mm

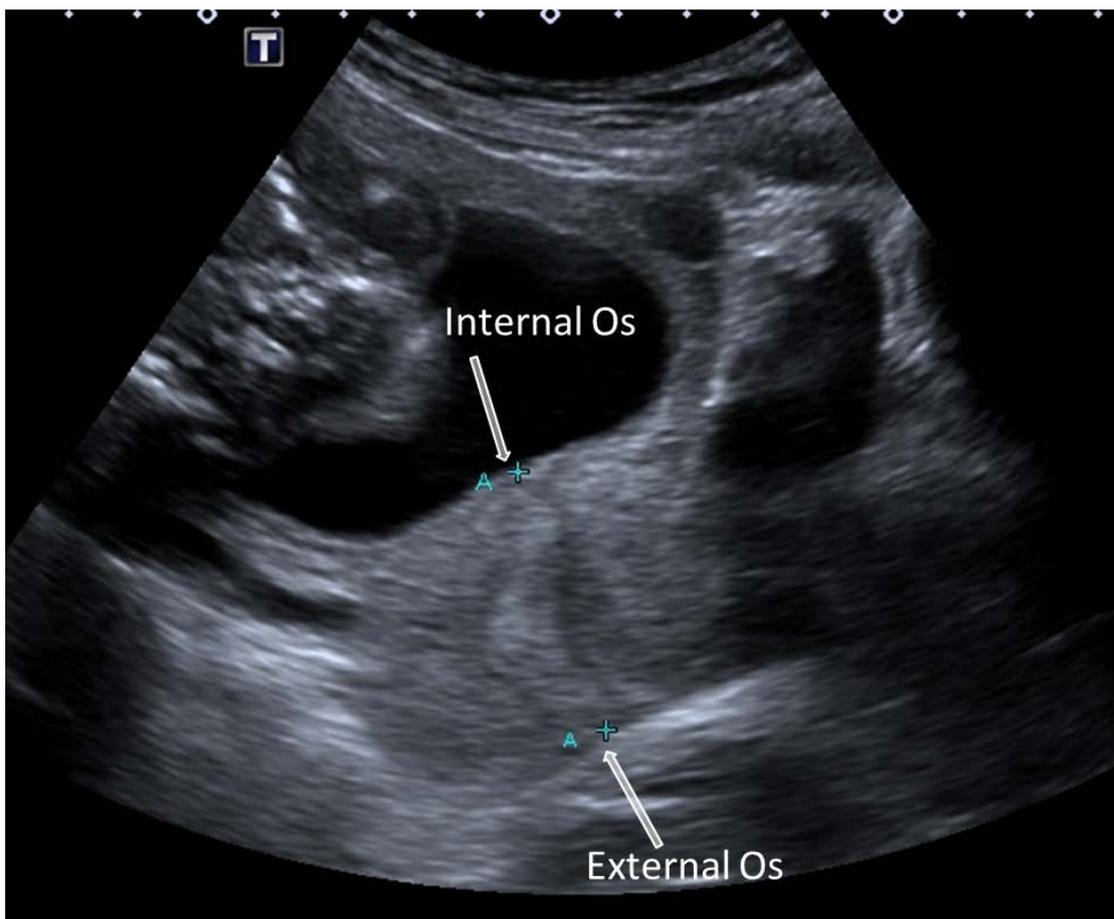


Figure 6. Transabdominal ultrasound cervical length with an empty bladder

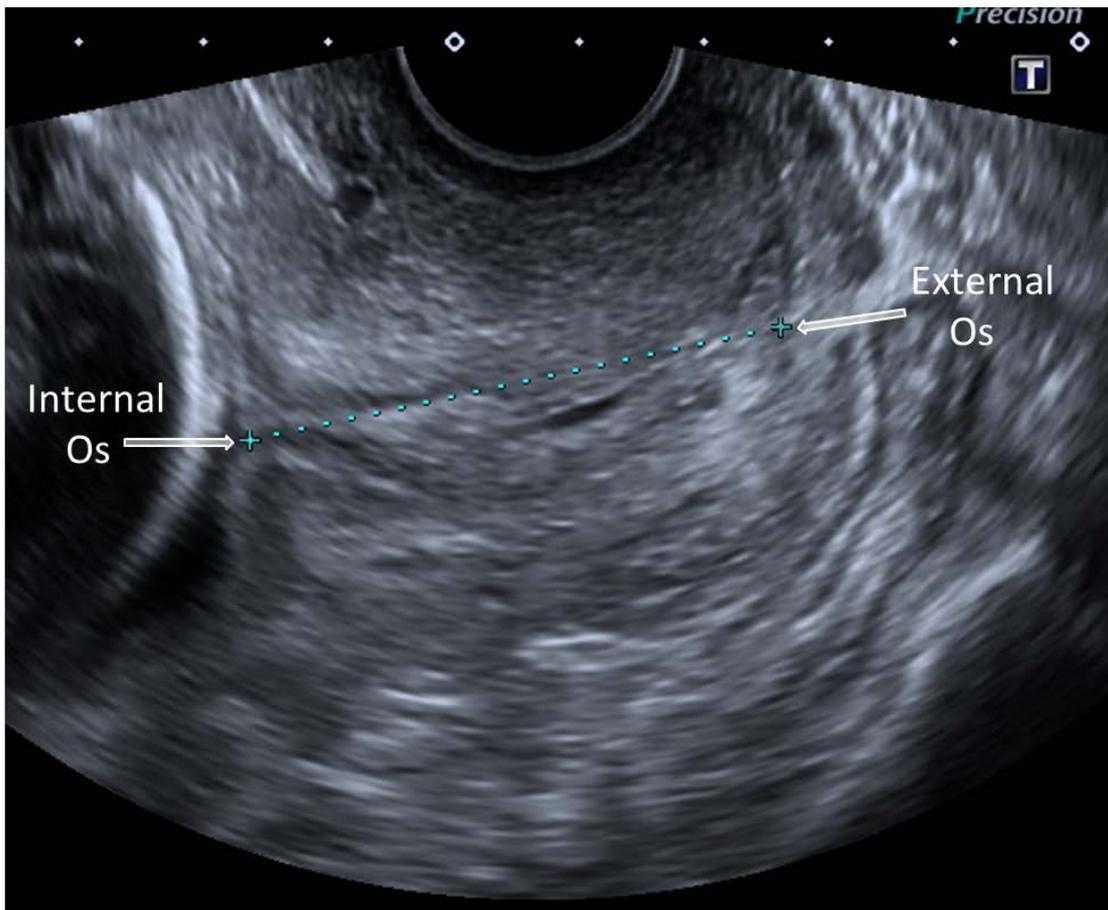


Figure 7. Transvaginal ultrasound cervical length of 45mm with good technique

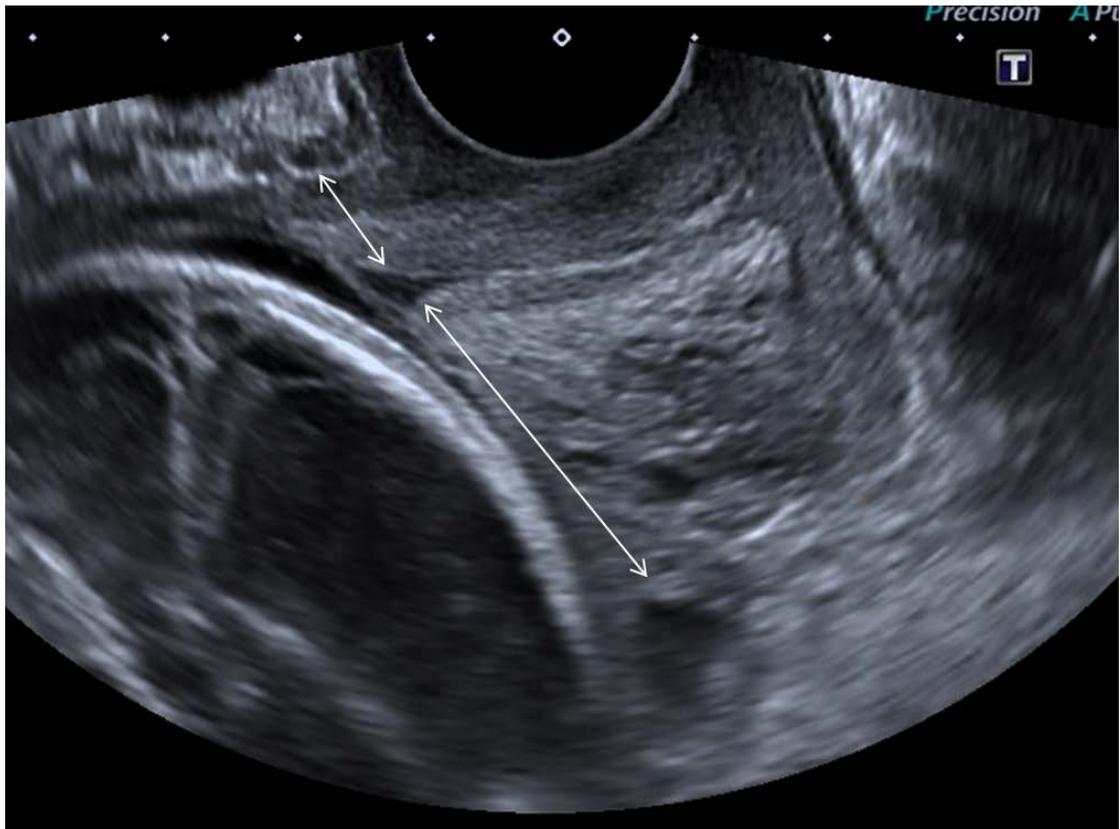


Figure 8. Transvaginal cervical length artifactually lengthened due to too much probe pressure, exhibiting unequal anterior and posterior cervix

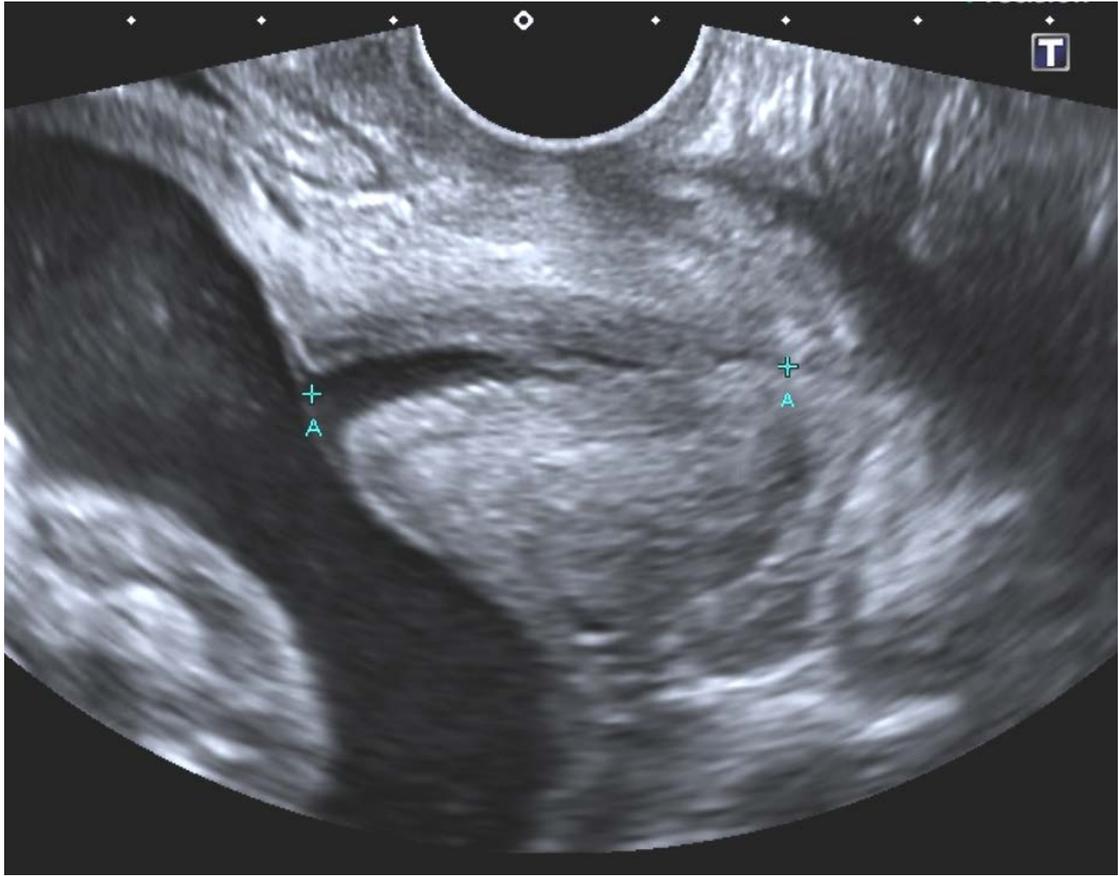


Figure 9. Transvaginal ultrasound cervical length with prominent mucus plug – caliper for internal os placed at amnion

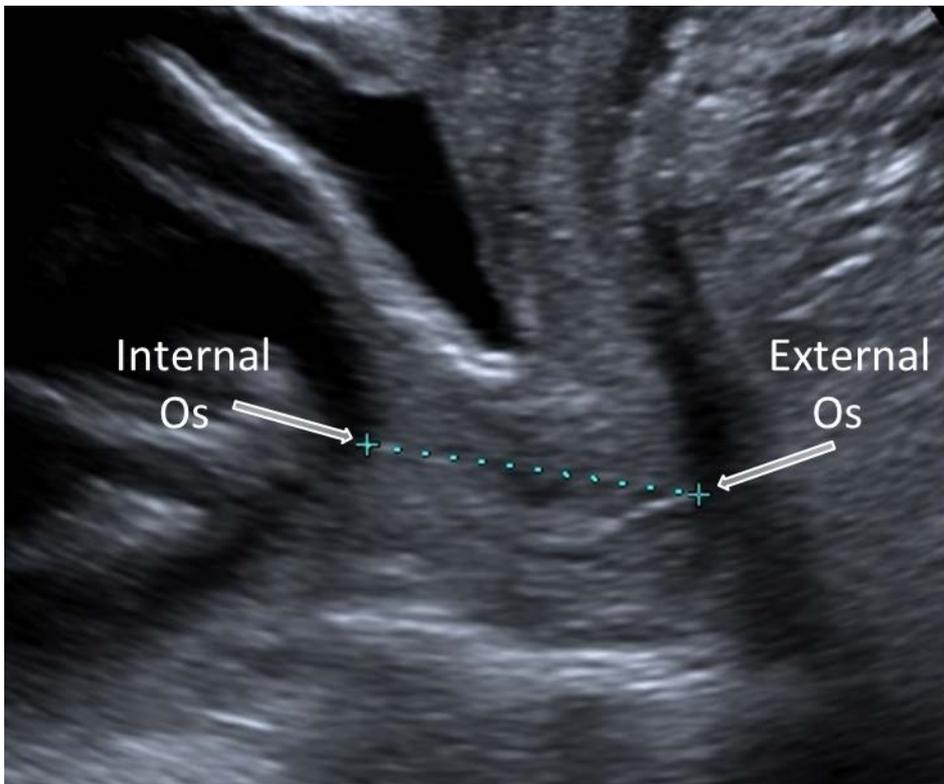


Figure 10. Transperineal ultrasound cervical length

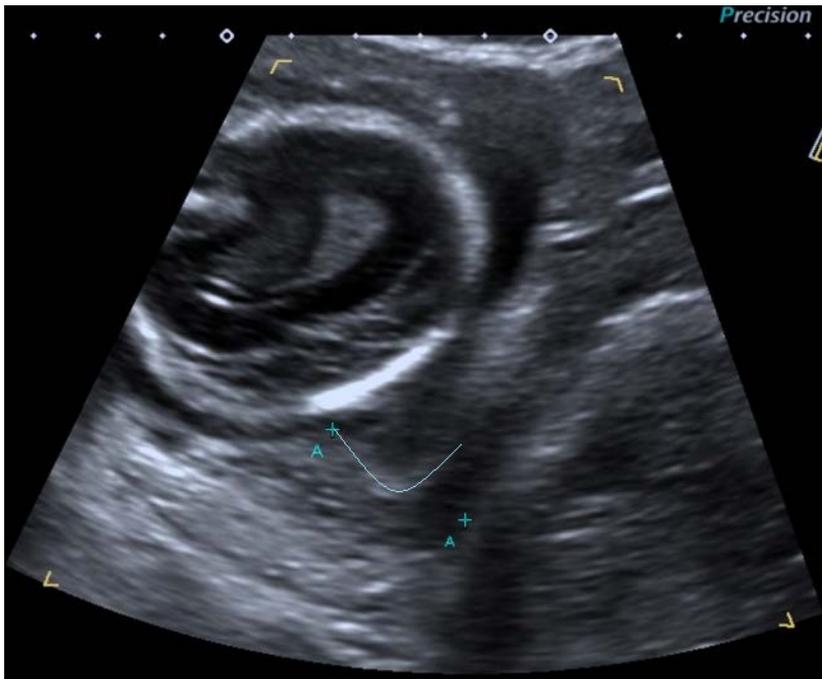


Figure 11. Transabdominal empty bladder cervical length with an undeveloped lower uterine segment exhibiting incorrect caliper placement for the external os (cervical canal is highlighted in the image)

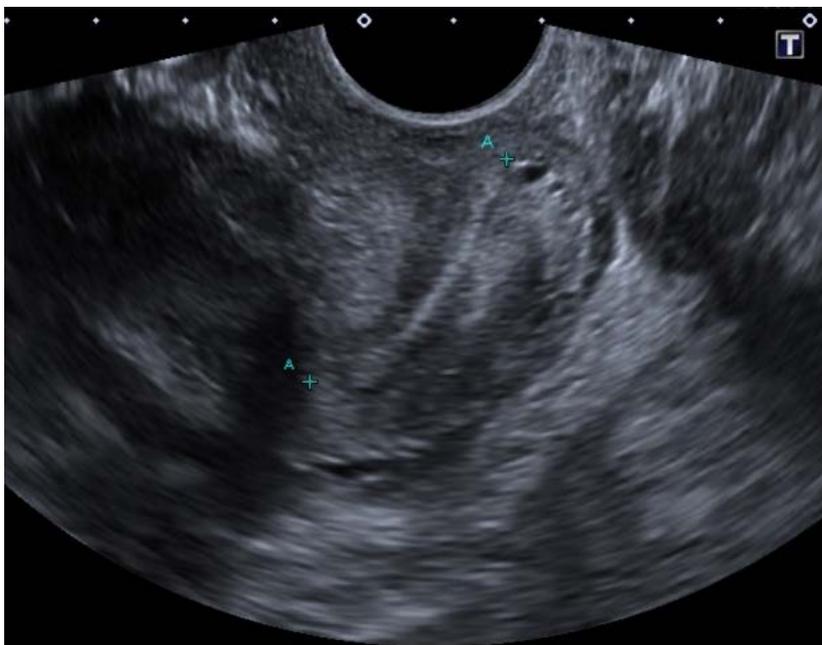


Figure 12. Transvaginal cervical length with an undeveloped lower uterine segment



Figure 13. Transvaginal cervical length with a lower uterine contraction



Figure 14. Transvaginal cervical length measurement of remaining functional cervical length registering 12mm

