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Prevention of preterm birth based on a short cervix: cerclage

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Abstract

In an attempt to prevent preterm birth, clinicians have recommended cerclage for women with shortened cervical length and other worrisome sonographic cervical features in the mid-trimester, although randomized trials have not supported this practice. Emerging data suggests that preterm birth is a complex and poorly understood syndrome comprising several anatomic and functional components. As a result, preventive efforts have been mostly empiric and generally ineffective. Plausibly, effective preterm birth therapies exist, but matching the effective treatment with the correct patient has been problematic. Mid-trimester cervical changes visualized with vaginal sonography likely represent a pathologic process of premature cervical ripening and not real mechanical disability which has been traditionally treated with suture support. Cerclage may be an effectively reduce preterm birth in carefully selected women who have experienced a prior early preterm birth and who have shortened mid-trimester cervical length.

Background and Scope

Preterm birth remains an unrelenting obstetrical problem. With annually increasing incidence, it now affects nearly 13% of all gravidas in the United States¹. Most of these births are spontaneous (not the result of maternal-fetal indications), and comprise the spontaneous preterm birth syndrome². This syndrome encompasses several anatomic and related functional components with numerous inciting factors and pathways; the underlying pathophysiology is complex and poorly understood. One component of this syndrome is diminished cervical competence, now termed cervical insufficiency.

Although a traditional paradigm depicted the cervix as competent or incompetent, contemporary evidence suggests that, in congruence with other biologic processes, cervical competence functions on a continuum of reproductive performance.^{3–6} Some women whose obstetric histories suggest a cervical component actually have tangible evidence of poor cervical integrity; however, most women with a clinical diagnosis of cervical insufficiency have ostensibly normal cervical anatomy. In a proposed model of cervical competence as a continuum, a poor obstetric history more likely results from a process of *premature cervical ripening* (in the absence of clinical labor) caused by one or more underlying factors including subclinical infection, local inflammation, hormonal effects or genetic predisposition. If and when the mechanical (and secondarily, the immunologic) integrity of the cervix is

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compromised, other processes may be stimulated, appearing clinically as the preterm birth syndrome.

Because the underlying mechanisms and interactions with anatomic components associated with preterm birth remain elusive, the specific series of events leading to spontaneous preterm birth cannot be accurately determined, either during pregnancy when the syndrome is recognized and managed, or by a careful retrospective analysis of the past obstetrical events. Thus, prevention and treatment strategies have been largely empirically based and, not surprisingly, ineffective.

The term “cervical incompetence” was first used in the *Lancet* in 1865 (*would you have a reference?*), but the contemporary concept was not widely accepted until the mid-1900s when two authors independently described interval repair of anatomic cervical defects associated with an obstetric history of recurrent spontaneous mid-trimester birth. Shirodkar in 1955⁷ and McDonald in 1957⁸ described the cerclage procedures that are still utilized in contemporary obstetric practice. Nevertheless, in spite of its wide acceptance as a presumably effective therapy, the literature on cerclage and cervical insufficiency has largely been a chronicle of surgical techniques to correct anatomic disruption of the internal os in women who had experienced recurrent painless dilation and mid-trimester birth. Evidence-based guidelines for many aspects of this diagnosis and management are still lacking, and randomized trials prior to the 1980’s were rarely performed. Because cervical insufficiency is a clinical diagnosis made retrospectively, after poor obstetric outcomes have occurred (or are in evolution), reasonably, clinicians have sought criteria which might lead to a prospective and more objective diagnosis, coupled with an effective intervention.

Cerclage for Risk Factors

Although beyond the scope of this report, we should mention that, to date, there have been four well-designed randomized trials^{9–12} of history-indicated (also called prophylactic) cerclage in women with “risk factors” for cervical insufficiency, and whose managing physicians were unsure if they would benefit from a prophylactic cerclage. All but the largest⁹ failed to demonstrate a benefit.

This multinational trial of history-indicated cerclage was performed by the Royal College of Obstetrics and Gynecology⁹ between 1981 and 1988. The research teams enrolled 1292 women who lacked a typical clinical history of insufficiency, but whose managing physicians wondered if cerclage was indicated based on any of 6 historical risk factors. Delivery before 33 weeks’ gestation was significantly lower (RR, 0.75; 95% C.I., 0.57–0.98) in cerclage-treated women (83 of 647, 13%) than in the controls (110 of 645, 17%), but because most untreated women delivered near term regardless, this benefit amounted to saving one preterm birth for every 25 treated with this form of history-indicated cerclage. Moreover, women assigned to cerclage received more tocolytics medications and spent more time in the hospital; puerperal fever was also more common in the cerclage group. Regrettably, this trial predated the now common use of cervical assessment with ultrasound.

In subgroup analyses, the authors divided their participants into six mutually exclusive cohorts: 1) 554 singleton pregnancies with exactly one prior second-trimester abortion or preterm delivery, but no history of cone biopsy or cervical amputation, 2) 196 singleton pregnancies with exactly two second-trimester abortions or preterm deliveries, and no cone biopsy or cervical amputation, 3) 107 singleton pregnancies with 3 or more second-trimester abortions or preterm deliveries, and no cone biopsy or cervical amputation, 4) 138 singleton pregnancies with a history of cone biopsy or cervical amputation, 5) 269 singleton pregnancies with other indications, and 6) 28 twin gestations. There was a significant reduction in the frequency of delivery before 33 weeks’ gestation only in the cohort of 107 women with at least 3 prior

second-trimester pregnancy losses or premature births (8 of 54, 15% in cerclage group versus 17 of 53, 32% in the control group, $p=.02$). There was no significant improvement in neonatal outcome or preterm birth in any of the other 5 subgroups, individually or collectively. The authors concluded that the subgroup with the poorest obstetric history (i.e. 3 or more prior preterm births) should undergo further study. Thus, the available clinical trial data does not suggest a benefit from cerclage in women with most of the abovementioned risk factors. However, the importance of a poor obstetric history (at least 3 preterm births) in possibly defining a valid cerclage indication was recognized.

Cervical Ultrasound and The Prediction of Spontaneous Preterm Birth

If cervical competence functions along a biologic continuum of reproductive performance, then assessment of cervical characteristics should provide useful information regarding at least one element of the preterm birth syndrome. The assessment of cervical length has been well standardized¹³ and is reproducible¹⁴. In addition, cervical length is an objective linear measurement which lends itself well to screening and identifying those women at increased risk of preterm birth. In 1996, the NICHD Maternal-Fetal Medicine Units Network reported the results of a prospective, blinded observational study of nearly 3000 unselected women with a singleton gestation at the 10 university centers⁴. The investigators observed a strong inverse relationship between cervical length and the likelihood of spontaneous preterm birth < 35 weeks' gestation. Using a cutoff of < 26 mm (10th population percentile) at the 24 week scan, the associated positive predictive value for preterm birth < 35 weeks was only 18%. This was attributed in part to the very low incidence of preterm birth in this unselected, generally low-risk population (4.3%). Visualization of funneling did not improve the prediction compared to the sole assessment of cervical length. These findings were significant because, not only did they support the concept that cervical length (as a surrogate measure of cervical competence) functions along a biologic continuum, it cast doubt on whether the recognition of funneling added appreciable biologic information to the measurement of cervical length. Most importantly, this report demonstrated that, in a low-risk population, cervical ultrasound was not an efficient screening tool for spontaneous preterm birth because of the very low positive predictive value (18%) associated with considering that 10% of gravidas had an "abnormal" cervical length.

In a subsequent blinded observational investigation in the NICHD MFM Units Network, women at high risk for spontaneous preterm birth because of a prior early spontaneous preterm delivery (< 32 weeks) were studied¹⁵. Women with a typical history of cervical insufficiency who received "prophylactic" cerclage were excluded. In this high-risk cohort based on obstetric history, women whose cervical lengths were < 25 mm (chosen because it was the observed 10th percentile at the initial evaluation) had a relative risk of spontaneous preterm birth before 35 weeks' gestation of 4.5 (95% CI, 2.7 – 7.6). In a logistic regression model, for every 5 mm increase in the shortest observed cervical length on serial scans, the odds of spontaneous preterm birth before 35 weeks fell by 43%. The less-than-25 mm threshold was associated with a sensitivity of 69%, a specificity of 80% and a positive predictive value of 55%. This study also found that controlling for cervical length there was no additional biologic information from the presence of funneling. Aspects of funneling were more systematically evaluated in this high-risk population by Berghella et al., and the authors reached the same conclusion.¹⁶

In a secondary analysis of these data, the authors hypothesized that if cervical length was a reasonable surrogate for the competency status of the cervix, then spontaneous preterm birth associated with shortened cervical length should preferentially occur earlier as opposed to later in gestation.¹⁷ In support of this hypothesis, they observed an inverse relationship between cervical length and gestational age at birth and that a shortened cervical length (defined as < 25 mm or 25 – 29 mm) was preferentially associated with mid-trimester birth as opposed to

third-trimester preterm birth. The typical delivery pattern associated with the natural history of spontaneous preterm birth (i.e. more births in the late preterm window) was observed only in women with longer cervical lengths (≥ 30 mm). These analyses suggest that shortened mid-trimester cervical length in women with a history of prior early spontaneous preterm birth implies a clinically significant component of diminished cervical competence which might be amenable to therapeutic intervention(s).

Since several other lower uterine segment and cervical characteristics in addition to cervical length can be assessed with mid-trimester endovaginal ultrasound, Yost et al.,¹⁸ in another secondary analysis, further evaluated the predictive value of cervical canal contour (straight/curved), cervical position (vertical/horizontal), posterior cervical width, lower uterine segment thickness and vascularity, minimal degrees of apparent endocervical canal dilation, and whether or not the chorioamnion was well-applied to the internal os or visible as a distinct membrane layer. At the initial sonogram (16 0/7 – 18 6/7 weeks' gestation) membranes visible at the internal os (RR 1.0, CI 1.2 – 3.1) and canal dilation of 2–4 mm (RR 2.6, CI 1.4 – 4.7) were significant predictors of spontaneous preterm birth of less than 35 weeks, but only canal dilation remained statistically significant after controlling for cervical length (OR 5.5, CI 1.1 – 28.6). The authors concluded that endocervical canal dilation of 2–4 mm during mid-trimester endovaginal sonography was associated with an increased risk of recurrent preterm delivery independent of cervical length. The clinical implications of this finding have not yet been systematically assessed.

Collectively, these reports^{4,15,17} support that cervical length acts as a surrogate for cervical competence and operates along a continuum of reproductive performance. However, the actual identification of an appropriate cervical length “action point” remains problematic. It is evident that cervical sonography performs poorly as a screening test in low-risk or unselected women, but it appears to have significant utility in high-risk women, defined as a prior history of early spontaneous preterm birth. Whether cervical ultrasound has similar predictive values in other populations with risk factors such as DES, prior cervical surgery, etc, has not been as well characterized; however, it has been evaluated in a cohort of 109 women with prior cone biopsy and found to be similarly predictive.¹⁹

Evaluation of the Cervix with Vaginal Ultrasonography

For the examination, the patient should have an empty bladder and be placed in dorsal lithotomy position. A high-resolution (≥ 5 MHz) endovaginal probe, protected by a lubricated sterile transducer cover, is gently inserted along the vaginal canal. Essentially all endovaginal probes currently in use are based on a convex, switched array of active elements, which create a fan-shaped image. The sector should encompass at least a 120-degree field of view in order to create an image that facilitates simultaneous visualization of the required landmarks without excessive probe manipulation. The image “trapezoid” should stay in a vertical orientation in order to maintain a sagittal view of the cervix and lower segment.

Three landmarks are crucial for the measurement of cervical length 1) External os, 2) Endocervical canal, and 3) Internal os. By sweeping the probe slightly from left to right, one or more of these landmarks can be visualized. Although there is significant biologic variation among patients (and also over time of gestation), the internal os can usually be recognized as a small notch or triangle at the interface between the amniotic cavity and the endocervical canal. With experience, various patterns of internal os anatomy can be appreciated. In some cases a normal appearing internal os can never be visualized, because either funneling or a poorly developed lower uterine segment are present. These situations will be covered in more detail below.

Once the internal os has been recognized, its image should be maintained while the transducer is manipulated (angled) slightly in order to visualize the entire endocervical canal, ending at the external os. The external os is generally more difficult to visualize than the internal os because the vaginal mucosa is well applied to the ectocervix and has a similar echogenicity. The external os is often characterized by an echogenic area several millimeters inside of cervico-vaginal interface. With high quality sonographic equipment, more details of the external os can be recognized, and it commonly has the appearance of the small triangle or notch. The intervening cervical canal may have a varied appearance, depending on the echogenicity of the glands, mucous and the canal itself. The canal is commonly more echolucent than the surrounding cervical and glandular tissue, but it may also appear as a faint echo-dense line.

When these 3 landmarks are simultaneously visualized, the probe must be manipulated one last time before acquiring the cervical length. The probe should be withdrawn slowly (while maintaining a view of these landmarks) until the image blurs. At this point, the sonologist should increase the insertion pressure slightly, just until a satisfactory image returns. This technique minimizes pressure on the cervix and prevents mechanical distortion of the surrounding anatomy.²⁰ The image should be frozen and electronic calipers used to measure the distance from the internal os to the external os. At times the canal will have a curved or bent contour, and a line connecting the two os will not follow the endocervical canal. This biologic artifact can be avoided by measuring the endocervical canal in two linear segments, which connect at the point of maximum deflection along the canal. If the maximal deflection is at least 5mm, we use the sum of the two linear segments to define the cervical length. It is advisable to repeat the measurement several times in order to find the shortest cervical length associated with the best quality image. Experience has shown that the first measurement is typically several millimeters longer than subsequent assessments. During subsequent image capture, probe insertion pressure (withdrawal/reinsertion) should be adjusted.

If a normal appearing internal os cannot be visualized, the cervix should be assessed further to determine whether funneling is present. The appearance of funnels has been well characterized in the literature.²¹ We generally diagnose a funnel if the “notch” which often defines the internal os, is greater than 5 mm from the end of the endocervical canal to its “shoulder”. Funnels may be sub-categorized as primarily V-shaped or U-shaped, depending upon their dominant appearance. When funneling is seen, the presumption is that the endocervical canal at the internal os has begun to dilate, but one can only estimate its (former) location. In this setting, we measure cervical length from the external os to the *functional* internal os, where the apex of the funnel meets the closed endocervical canal. In rare cases, a funnel can replace essentially the entire endocervical canal and the cervical length is defined as zero. (This phenomenon can also be thought of as complete canal dilation). Funnel measurements are inexact since the landmarks are not always distinct and may even change during the examination. The point along the “shoulder” where the caliper should be placed is highly operator dependent, and at times, asymmetric “shoulders” are recognized. This significantly diminishes the reproducibility of the measurement.

Another confounder of cervical length measurement is a poorly developed lower uterine segment. This phenomenon is probably due to either a delay in the normal maturing process of the lower segment, or, in some cases, the result of spontaneous muscular contractions. It can be visualized in approximately 15% of mid-trimester gestations. Although it is a subjective diagnosis, we have published diagnostic criteria for this phenomenon.¹⁵ In these cases, the internal os cannot be visualized and, thus a cervical length cannot be accurately measured. At times, a poorly developed lower uterine segment may spontaneously resolve during the scan, after which the cervical length can then be assessed normally.

When performing vaginal sonography for cervical length evaluation, we utilize a provocative measure to assess for any dynamic changes. Moderate fundal pressure (insufficient to cause any patient discomfort) is applied by the sonologist's non-dominant hand while maintaining the image of the internal os to determine if a funnel develops or the cervical length shortens. If so, the (shortened) cervical length should be re-measured. Cervical length shortening may also occur spontaneously, and this phenomenon, and the associated shortened cervical length measurement, should also be recorded. We have determined that utilizing the cervical length associated with serial mid-trimester evaluations, and including either fundal pressure-induced or spontaneously occurring dynamic shortening, significantly increases the predictive value of cervical length for spontaneous preterm birth.¹⁵ In order to observe these dynamic changes, we recommend that cervical scans last a minimum of 5 minutes.

Cerclage for Sonographic Indications: Is Cervical Insufficiency a clinical or a sonographic diagnosis (or Both)?

Over the past several decades, numerous investigators have reported that cervical insufficiency can be diagnosed by mid-trimester sonographic evaluation of the cervix. Various sonographic findings have been described, including cervical length shortening (with multiple different cutoffs suggested), the presence of a funnel, and dynamic changes either spontaneously or with provocative measures. These findings have been utilized to select women for treatment, generally cerclage.

To date, four randomized trials of cerclage for shortened cervical length (i.e. ultrasound-indicated cerclage) have been published.^{22–25} Althuisius et al.²² in 2001 published a two-tiered randomized trial of high-risk patients, who were thought to have cervical insufficiency based on obstetric history or symptoms. The women in the first tier were randomly allocated to prophylactic cerclage or cervical ultrasound surveillance. Thirty-five women in the ultrasound surveillance arm were found to have a shortened cervical length less than 25 mm. These 35 women in the second tier underwent a second randomization to either cerclage or no cerclage. Both groups were instructed to use modified home rest. Of those women, 19 were assigned to cerclage and none experienced preterm birth at less than 34 weeks' gestation versus a 44% preterm birth rate in the 16 women assigned to home modified rest without cerclage ($p = 0.002$). Importantly, none of the women who maintained a cervical length of at least 25 mm experienced preterm birth. The outcomes were also similar in those women who randomly received history-indicated (prophylactic) cerclage versus those women who were randomly assigned to undergo ultrasound-indicated cerclage.

Rust et al.²³ in 2001 published a trial of 138 women who had various risk factors for preterm birth, including multiple gestations, and who were randomly assigned to receive McDonald cerclage or no cerclage after their cervical length shortened to less than 25 mm or they developed funneling greater than 25%. The rate of preterm birth less than 34 weeks' gestation in the cerclage group was 35% versus 36% in the no cerclage group ($p = 0.8$).

In a third trial²⁴ that comprised 12 hospitals in 6 countries, 47,123 unselected women were screened at 22–24 weeks' gestation with transvaginal ultrasonography, and 470 (1%) women were identified as having a shortened cervix at or less than 15 mm. Of these 470 women, 253 participated in a randomized trial of Shirodkar cerclage ($n = 127$) versus no cerclage ($n = 126$). The primary outcome was the rate of delivery prior to 33 weeks' gestation. Women assigned to the cerclage group experienced similar rates of preterm birth as the controls, 22% versus 26% respectively ($p = 0.44$). Four stillbirths attributed to birth at 23–24 weeks' gestation and five neonatal deaths attributed to birth at 23–26 weeks' gestation were observed in the control group (9 total). In the cerclage group, the respective counts were three and four (7 total).

In the fourth trial,²⁵ women with various risk factors for preterm birth including prior preterm birth, dilation and curettages, cone biopsy, and DES exposure underwent transvaginal ultrasound surveillance every 2 weeks from 14–23 weeks' gestation. Of those women, 61 had a cervical length less than 25 mm or funneling greater than 25% and were randomized to McDonald cerclage versus no cerclage. Preterm birth at less than 35 weeks' gestation occurred in 45% of the cerclage group and 47% of the control group ($p = 0.91$).

Of these four published randomized trials two^{23,25} seem most applicable to contemporary U.S. obstetrical practice. Neither of these trials supported the use of cerclage for ultrasound findings commonly cited as “abnormal” in women with various types of risk factors. The multinational trial²⁴ confirmed that very shortened cervical length (less than or equal to 15 mm) conferred a high risk for preterm birth; however to find one woman with this risk factor, approximately 100 women would have to be screened. This large randomized trial also demonstrated no clinical benefit from ultrasound-indicated cerclage in a population with no history of preterm birth.

A patient-level meta-analysis²⁶ of these four previously described trials was published by Berghella et al. in 2005 to determine if certain subgroups of women with mid-trimester cervical shortening might benefit from cerclage, defined as a relative risk reduction of preterm birth at less than 35 weeks' gestation. A marginal benefit was observed in singleton gestations, and the benefit was enhanced in those with a prior history of preterm birth (RR 0.61, 95% CI, 0.4 – 0.9). This observed relationship may have been due in part to the inclusion of women with a prior spontaneous preterm birth attributed to a clinical diagnosis of cervical insufficiency²². Nevertheless, their findings raised the question of whether patients who experienced a prior preterm birth attributed to other components of the spontaneous preterm birth syndrome might benefit from ultrasound-indicated cerclage.

To answer this specific question, a large, multicenter randomized trial in high-risk women, defined as women who had one or more early spontaneous preterm births less than 34 weeks' gestation, but who lacked a clinical history of cervical insufficiency, was recently completed.²⁷ In this trial, 1,014 women underwent transvaginal sonographic screening every 2 weeks between 16 and 22 6/7 weeks' gestation if the cervical length was at least 30 mm, while screening was increased to weekly if the cervical length shortened to 25–29 mm. Those women whose cervical length shortened to less than 25 mm were randomly assigned to undergo McDonald cerclage or no cerclage. In addition to multiple gestation, acute cervical insufficiency was one of the exclusion criteria. The primary outcome was the rate of preterm birth before 35 weeks' gestation.

Three hundred eighteen women (30%) developed a cervical length less than 25 mm, and 302 (95%) consented to randomization. The rate of preterm birth in the no-cerclage group was 42% versus 32% in the cerclage group (OR, 0.67, 95% CI, 0.42 – 1.07, $p = 0.09$). Survival analysis also demonstrated an improvement in overall pregnancy prolongation in the cerclage group ($p = 0.053$). In planned secondary analyses, birth less than 37 weeks ($p = 0.01$), previsible birth less than 24 weeks ($p = 0.03$), and perinatal mortality ($p = 0.046$) were less common in the cerclage group. There was a significant ($p = 0.03$) interaction between cervical length at randomization (less than 15 mm versus 15–24 mm) and assigned treatment, demonstrating a beneficial effect of cerclage in the shorter cervical length stratum observed for both preterm birth less than 35 weeks (OR 0.23, 95% CI, 0.08 – 0.66) and longer time to delivery in survival analysis ($p = 0.024$). We concluded that in women with a prior preterm birth less than 34 weeks' gestation and shortened cervical length less than 25 mm between 16 and 22 6/7 weeks' gestation, cerclage did not show a benefit in preventing premature birth before 35 weeks, but did improve previsible birth and perinatal mortality. The effect of cerclage for preventing

preterm birth and prolonging gestation was clearly pronounced when the cervical length is less than 15 mm.

Adjunctive Therapy

Because ultrasound-indicated cerclage is not uniformly efficacious in women with a short cervical length, adjunctive therapies to cerclage have been sought. These therapies include antibiotics, progesterone, indomethacin. Visintine et al.²⁸ published a retrospective cohort study of asymptomatic women with an ultrasound-indicated cerclage placed because of a short cervical length (< 25 mm). Indomethacin therapy consisted of 50 mg administered orally or rectally followed by 25 mg given orally every 6 hours for approximately 48 hours. Of 101 participants, 51 women received indomethacin at the time of cerclage placement and 50 women did not. There was no difference in the rate of preterm birth less than 35 weeks in those women who received indomethacin at the time of cerclage placement versus those who did not. The rates of spontaneous preterm birth were also similar at < 32 weeks' gestation (RR 1.1; 95% CI, 0.6 – 1.9). Logistic regression analysis showed that indomethacin administration at the time of ultrasound-indicated cerclage was not an independent predictor of spontaneous preterm birth. The authors concluded that while there was no difference in the rates of preterm birth, randomized trials were indicated.

Other adjunctive therapies include antibiotic use at the time of ultrasound-indicated cerclage. Antibiotics are commonly used but there is no data to support their efficacy. Prophylactic antibiotics at the time of cerclage would be used to theoretically reduce a surgical site infection. Acute cervicitis and chorioamnionitis would be contraindications to cerclage. Shiffman²⁹ in 2001 reported a study of 10 women with history of failed cerclage in prior pregnancy with short cervical length and funneling in the current pregnancy that underwent ultrasound-indicated cerclage. These women were continuously treated with low dose antibiotics. The outcome was number of weeks of pregnancy gained in the index pregnancy minus the weeks of the prior pregnancy. All 10 achieved fetal viability. Pregnancy was prolonged by a mean of 13.4 +/- 4.2 weeks beyond the previous pregnancy. This was highly statistically significant ($P < .001$). The authors conclude that continuous low-dose antibiotics prolong pregnancy in patients with recurrent second-trimester pregnancy losses and prior failed cerclage. Randomized clinical trials are also needed to confirm the role of antibiotics in these high-risk pregnancies.

Recently, the NICHD Maternal-Fetal Medicine Units Network reported the results of a double-blind trial of 17 α -hydroxyprogesterone caproate for the prevention of spontaneous preterm birth in women with a prior spontaneous preterm birth³⁰. Compared to placebo, weekly intramuscular injections reduced the rate of preterm birth by approximately one third. Current guidelines suggest the use of 17 α -hydroxyprogesterone caproate in women with a prior spontaneous preterm birth³¹ and since essentially all women with a clinical history of cervical insufficiency have experienced this outcome, it should be considered as adjunctive therapy. Whether 17 α -hydroxyprogesterone caproate (or a related congener) is useful in women with shortened cervical length and no prior preterm birth is currently under investigation.

Can cervical ultrasound be used to avoid cerclage?

One ancillary aim of cervical ultrasound surveillance is to reduce the number of unnecessary cerclage surgeries in order to limit the possible complications associated with this surgical procedure and to prevent unnecessary surgical intervention in women who would not benefit from such intervention. Ultrasound surveillance might better identify appropriate candidates for cerclage while achieving pregnancy outcomes comparable to a less selective approach with more liberal cerclage utilization in women with suspected cervical insufficiency (e.g. a single prior mid-trimester loss).

In a systematic review, pregnancy outcomes and cerclage-related complications of ultrasound-indicated versus history-indicated cerclage in patients with suspected cervical insufficiency were compared.³² The authors performed a structured search to identify potentially relevant articles from January 1980 through July 2007 and selected studies if ultrasound-indicated cerclage was compared to history-indicated cerclage in women with a singleton gestation. After critical evaluation for relevance and quality, 6 articles (randomized trials=2, cohort studies=3, case-control study=1) remained.^{33–38} Five of the 6 showed similar pregnancy outcomes (spontaneous preterm birth or pregnancy loss < 24 weeks' gestation) between the ultrasound-indicated and the history-indicated cerclage groups. However, in one prospective cohort study preterm birth was significantly *lower* in the ultrasound-indicated group.³⁸ One possible limitation to the review was that the 6 reports evaluated heterogeneous populations, although the incidence of prior mid-trimester loss was appreciable (Table 1 and 2). Of note, 40–68% of the patients followed with cervical ultrasound were able to avoid cerclage. Unfortunately, the majority of the studies provided insufficient data to draw firm conclusions regarding cerclage-related complications for comparison. The authors concluded that using ultrasound shortened cervical length to select women with suspected cervical insufficiency for cerclage reduces cerclage rates, but yields pregnancy outcomes similar to cases where cerclage was placed on the basis of clinical suspicion alone. Based on this systematic review, women with suspected, but non-classic cervical insufficiency may undergo mid-trimester transvaginal cervical length assessment to optimize surgical candidate selection.

The management of a woman who presents with a history of a prior pregnancy in which a prophylactic cerclage was placed for questionable indications is also unclear, but many clinicians are reluctant to withhold another surgery. Although this was but one of many indications cited in the reports that populated the above-mentioned systematic review,³² Fejgin et al.³⁹ reported a series of 35 women in whom cerclage had been placed in prior pregnancies for indications other than clinically defined insufficiency. A committee of 3 attending obstetricians reviewed each case and decided whether stitches had been placed for classic or non-classic indications. Collectively, these women had been managed through 58 prior pregnancies with cerclage. These investigators followed the cohort through an additional 52 pregnancies managed with clinical examinations and sonography up to 28 weeks' gestation *without* repeat cerclage. Compared to the pregnancies managed with elective cerclage, fewer perinatal losses were observed in the group managed with serial evaluations (0% versus 16%; $P=.01$). However, they failed to report how many patients underwent an exam-indicated or ultrasound-indicated procedure.

Summary

Contemporary lines of evidence indicate that cervical insufficiency is uncommonly a distinct and well-defined clinical entity, but only one component of a larger and more complex syndrome of spontaneous preterm birth. The original paradigm of viewing the cervix as competent or incompetent has been replaced with the new concept of the cervix functioning along a biologic continuum of reproductive performance and premature cervical ripening, likely from one or a combination of multiple interrelated factors and biologic pathways. The interpretation of current clinical data emphasizes that ultrasound screening and treatment regimens should be limited to a highly selected population of women with a prior spontaneous preterm birth and may also be applicable to patients with suspected, but non-classic histories of cervical insufficiency (Figure 1). Women with a prior spontaneous preterm birth represent a population that can clearly benefit from transvaginal ultrasound measurement of cervical length;^{27, 26} the recently completed trial²⁷ emphasizes the inclusion of women with prior early spontaneous preterm birth < 34 weeks. Currently, only women with a preterm birth history should be considered for such routine sonographic screening and cerclage placement. Nevertheless, the findings from this trial²⁷ are not completely prescriptive regarding the

optimal cervical length cutoff for ultrasound-indicated cerclage; however in planned secondary analyses, improved obstetric outcomes were demonstrated using the trial's entry cervical length cutoff of 25 mm, recognizing that the beneficial effect is significantly more pronounced in women with very short cervical length less than 15 mm.

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Figure 1.
Flowchart for cervical ultrasound.

Table 1

Randomized Trials of Cerclage for Sonographic Indications

Author, Year	Population	N	Randomization Criteria	G.A. of U/S Screening	Primary Outcome	Benefit
Owen, 2008 ²⁷	Prior spontaneous preterm birth at 17–33 weeks' gestation	301	Cervical length less than or equal to 25 mm	16–22 ^{6/7} weeks	Preterm birth at less than 35 weeks' gestation	Previability birth and perinatal mortality reduced; effect more clearly pronounced if cervical length <15 mm
Borghella, 2004 ²⁵	Unselected, but most had risk factors	61	Cervical length, less than or equal to 25 mm, or more than 25% funneling	14–23 weeks	Preterm birth at less than 35 weeks' gestation	No
Rust, 2001 ²³	Unselected, but many had risk factors	113	Cervical length less than 25 mm or more than 25% funneling	16–24 weeks	Cerclage (45%) versus No Cerclage (47%)	P = 0.91
To, 2004 ²⁴	Unselected, low risk	253	Cervical length less than or equal to 15 mm	22–24 weeks	Preterm birth at less than 34 weeks' gestation	No
Althuisius, 2001 ²²	High-risk history consistent with cervical insufficiency	35	Cervical length less than 25 mm	Less than 27 weeks	Preterm birth at less than 33 weeks' gestation	P = 0.44
					Cerclage (0%) versus no cerclage (44%)	Yes
						P = 0.002

Table 2

Description of 6 Studies included in the Systematic Review by Blickman et al.³²

Author, Year	N	Study Design	Inclusion Criteria	Prior mid-trim ester birth	Criteria for U/S-indicated cerclage	Underwent U/S-indicated cerclage
Althuisius, 2000 ³⁴	73	RCT	Singletons, spontaneous PTD 15–34 weeks with painless dilatation or PPRM not preceded by contractions, “suspected cervical incompetence”, Singleton PTD (16–33 weeks) or mid-trimester loss	Mean 1.2 in cerclage group versus 0.8 in Observational Group	CL $\leq$ 25 mm at $<$ 27 weeks’ gestation	23%
To, 2002 ³⁵	90	Retrospective Cohort	Singletons, prior spontaneous PTD (16–33 weeks) or mid-trimester loss	27%	CL $\leq$ 25 mm before 24 weeks’ gestation	60%
Berghella, 2002 ³³	177	Retrospective Cohort	Singletons, prior spontaneous PTD or mid-trim ester loss, risk factors for cervical insufficiency	46%	CL $<$ 25 mm, funneling at least 25%, before 24 weeks’ gestation	36%
Higgins, 2004 ³⁸	135	Prospective Cohort	Prior spontaneous PTD (20–36 weeks) or mid-trimester loss, previous forced dilation, cone biopsy	53%	CL $<$ 25 mm at $\leq$ 24 weeks’ gestation	32%
Groom, 2004 ³⁷	81	Case-control	History of spontaneous PTB or mid-trimester loss, history of cervical surgery	Mean 1.2 in cerclage group versus 1.08 in Controls	CL $\leq$ 15 mm, or progressive shortening to $\leq$ 25 mm, funneling of at least 50% before the 3 rd trimester	36%
Beigi, 2005 ³⁶	97	RCT	Singleton pregnancies, history of spontaneous PTD (15–32 weeks) or mid-trimester loss with painless and progressive dilation of the cervix	43%	CL $\leq$ 20 mm at $<$ 24 weeks’ gestation	54%