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Beyond Cervical Length: Association between Postcerclage Transvaginal Ultrasound Parameters and Preterm Birth

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Abstract

Objective—To assess the value of transvaginal ultrasound parameters after cerclage placement in estimating the risk of spontaneous preterm birth.

Study Design—This is a retrospective cohort at a single tertiary care center from 2013 to 2016. Women carrying a singleton, nonanomalous fetus with cerclage in situ and at least one postcerclage transvaginal ultrasound from $16^{0/7}$ to $25^{6/7}$ weeks' gestation were included. In addition to abstracting maternal demographic and obstetric characteristics, two study investigators separately reviewed each of the images from the first transvaginal ultrasound after cerclage placement, masked to pregnancy outcomes. We measured the angle between the anterior uterine wall and cervical canal at the internal os and external os, closed canal length above and below the stitch, width of the anterior and posterior cervix at the level of the cerclage, and stitch distance from the cervical canal. The presence of additional ultrasound findings such as sludge and cervical funneling was also noted. The main outcomes were preterm birth < 34 weeks and preterm birth < 37 weeks. Transvaginal ultrasound parameters were compared between women with preterm birth and those without preterm birth using chi-square, Fisher's exact, and Wilcoxon's rank-sum tests, as appropriate. Log binomial regression was used to estimate the relative risk of preterm birth for all significant obstetric and ultrasound characteristics.

Results—A total of 102 women met inclusion criteria: 58% had history-indicated, 20% ultrasound-indicated, and 23% exam-indicated cerclages. Of these, 28 (27.5%) women delivered at < 34 weeks' gestation, and 48 (47.0%) women delivered at < 37 weeks' gestation. Preterm birth did not vary by race, maternal age, insurance, smoking, or gestational age of the earliest prior preterm birth (for multiparous women), but women who had preterm birth were more likely to have exam-indicated cerclage. There were several transvaginal ultrasound parameters associated with preterm birth < 34 weeks and preterm birth < 37 weeks. Of these, cervical length below the stitch, stitch distance from the cervical canal, straight cervical canal, funneling to or past the stitch, and presence of sludge had the greatest effect sizes.

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Conflict of Interest

None declared.

Conclusion—Rates of preterm birth are high postcerclage. In addition to measuring cervical length, utilization of postcerclage transvaginal ultrasound to evaluate the location of the cerclage within the cervix, the curvature of the cervical canal, and the presence of funneling and sludge may help identify women who are at the highest risk for preterm birth.

Keywords

cerclage; cervical length; preterm birth; ultrasound; uterocervical angle

Preterm birth is the leading cause of neonatal morbidity and mortality among nonanomalous neonates in the United States.[1] Spontaneous preterm birth complicates approximately 10% of all pregnancies,[2] and accounts for a significant proportion of health care costs totaling more than 2 billion dollars annually.[3] This morbidity can be prevented by placement of transvaginal cervical cerclage in certain populations. Transvaginal cerclage can prolong pregnancy for women with a history of prior mid-trimester pregnancy loss suggestive of cervical insufficiency, those with a history of spontaneous preterm birth who develop a short cervix in the mid-trimester of the current pregnancy, and women with dilated cervix on examination regardless of prior pregnancy history.[4] While cerclage placement is reserved for women at the highest risk for spontaneous preterm birth, up to half of women who undergo cerclage placement still deliver pre-term.[4–7] Antenatal assessment of which women with cerclages are at the highest risk of delivering preterm may allow time for additional interventions such as antenatal corticosteroid administration and referral for delivery at appropriate locations equipped with necessary neonatal care after birth.

Transvaginal ultrasound after cerclage placement has been used to attempt to risk stratify which women remain at elevated risk for spontaneous preterm birth. Sonographic measurements associated with preterm birth have included postcerclage cervical length, cerclage height (defined as distance from external os to cerclage suture), and anterior uterocervical angle (defined as angle formed by intersecting lines drawn from internal to external os and second line parallel to the lower aspect of the anterior uterine wall).[8–12] These associations, however, have not been consistent across studies.[13–15] Furthermore, the value of assessing other sonographic measurements delineating the stitch position is also unknown. Thus, our primary objective was to assess the value of transvaginal ultrasound parameters after cerclage placement in estimating the risk of spontaneous preterm birth.

Methods

We conducted a retrospective cohort study of women who had transvaginal ultrasound surveillance after cervical cerclage placement at a single tertiary care center from 2013 to 2016. We queried the electronic medical record to identify all women with a singleton gestation who underwent cervical cerclage placement. Women were included regardless of the indications for cerclage placement. History-indicated cerclage was defined as cerclage placement after 1 or more prior mid-trimester pregnancy losses suggestive of cervical insufficiency. Ultrasound-indicated cerclage was defined as cerclage placement in a woman with a history of a prior spontaneous preterm birth and transvaginal ultrasound finding of cervical length less than 25 mm between 16 and 24 weeks' gestation. Finally, exam-

indicated cerclage was defined as cerclage placement after asymptomatic mid-trimester cervical dilation.

At this tertiary care center, cerclages are placed by both generalist obstetricians and maternal–fetal medicine providers with involvement of resident and fellow trainees. Transvaginal cerclages are typically removed between 36 and 37 weeks' gestation unless there are signs and symptoms of intra-amniotic infection or spontaneous preterm labor prior to that time. Additional antepartum therapy with intramuscular 17-hydro-xyprogesterone caproate and vaginal progesterone are reserved for standard obstetric indications including history of spontaneous preterm birth and cervical length less than 20 mm for nulliparous women, respectively. The use of either therapy outside of standard practice (including combinations of these therapies) as well as all other management decisions was at the discretion of the primary obstetric provider. It is not standard of care to perform a transvaginal ultrasound after every cerclage; however, some providers at this institution do routinely perform postcerclage ultrasounds; other women have postcerclage vaginal cervical length assessed at the time of a routine transabdominal obstetric scan if there is concern for cervical shortening by the maternal–fetal medicine provider reading the ultrasound. Women were excluded if they did not have at least one transvaginal ultrasound performed after cerclage placement between $16^{0/7}$ and $25^{6/7}$ weeks' gestation, if they were carrying a fetus with a major anomaly or aneuploidy, or if they delivered at another hospital. If a woman had two pregnancies meeting inclusion criteria during the study period, the most recent pregnancy was considered.

Stored ultrasound images were reviewed beginning with the first examination after cerclage placement. For women with multiple cervical length ultrasounds postcerclage, measurements on the first postcerclage ultrasound were considered. All images were separately reviewed by two study investigators who were masked to clinical outcomes. The best images were selected according to Cervical Length Education and Review (CLEAR) criteria and then were post-processed directly within the ultrasound image program. Additional cervical parameters were measured by each image reviewer after development of specific definitions for each measurement (Fig. 1). In addition to the cervical length routinely measured by sonographers at the time of transvaginal ultrasound, the length of the cervix from stitch to internal os and stitch to external os was measured. Cervical cerclage depth was obtained by measuring the distance from the anterior stitch to the cervical canal and from the posterior stitch to the cervical canal. Widths of the anterior cervix and posterior cervix were measured at the level of the stitch in a similar fashion except with measurements taken from the anterior-most and posterior-most borders of the cervical stroma to the cervical canal. Two different uterocervical angles were obtained using a line drawn along the anterior uterine wall as the referent point. First, an angle was measured from anterior uterine wall to line drawn from internal os to external os. Second, an angle was measured from anterior uterine wall to line drawn from internal os along proximal cervical canal. Finally, the curvature of the cervical canal was measured by comparing these two angles, and the canal was considered straight when the difference between these angles was less than 5 degrees. Additional data were abstracted from the electronic medical record including maternal demographics, obstetric history, antepartum course, timing and indication for delivery, as well as maternal and neonatal outcomes. The main outcomes were (1) preterm

birth less than 34 weeks, compared with no preterm birth less than 34 weeks and (2) preterm birth less than 37 weeks, compared with no preterm birth less than 37 weeks.

Demographic and baseline clinical data and ultrasound measurements were compared between those with and without preterm birth. Chi-square, Fisher's exact, and Wilcoxon's rank-sum test were used for bivariable data analysis as appropriate. Pairwise correlation coefficients were calculated to determine whether the variables significant in bivariable analysis were collinear with each other. Relative risks (RRs) with 95% confidence intervals (CIs) were estimated using binomial regression models for each of the significant obstetric and ultrasound characteristics and preterm birth < 34 weeks as well as preterm birth < 37 weeks. All tests were two tailed and $p < 0.05$ was used to define significance. All data were analyzed using STATA version 14.0 (StataCorp, College Station, TX). This study was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill (15–3233).

Results

During the study period, 102 women met inclusion criteria (Fig. 2). Of these, 59 (58%) women had history-indicated cerclage, 20 (20%) women had ultrasound-indicated cerclage, and 23 (23%) women had exam-indicated cerclage. Overall, 28 (27.5%) delivered at less than 34 weeks' gestation, and 48 (47.0%) women delivered at less than 37 weeks' gestation. Only six (5.9%) women delivered at less than 24 weeks' gestation. The frequency of preterm birth less than 34 weeks did not vary by race, smoking, or gestational age of prior preterm birth for multiparous women (Table 1). Women with preterm birth at 34 weeks were more likely to have had an exam-indicated cerclage, compared with ultrasound-indicated or history-indicated cerclage and less likely to have used Mersilene suture, compared with other suture types. While vaginal progesterone use was also more common among women who delivered before 34 weeks, the proportion of women receiving 17-α hydroxyprogesterone caproate did not differ among women with or without preterm birth. Comparison of the demographic and obstetric characteristics among women who had preterm birth less than 37 weeks, compared with those who did not, yielded similar results to these described for preterm birth less than 34 weeks except for maternal body mass index which was significantly different between women who had preterm birth less than 37 weeks versus those who did not (Supplementary Table S1 [available in the online version]).

In addition to obstetrical characteristics, there were several ultrasound parameters after cerclage placement that differed between women who had preterm birth less than 34 weeks' gestation, compared with those who did not (Table 2). In addition to shorter total cervical length, the cervical length above and below the cerclage was shorter among women with preterm birth less than 34 weeks, compared with those without. Women with preterm birth less than 34 weeks were more likely to have a thinner anterior cervical width, shorter distance from the anterior stitch to the cervical canal, and shorter stitch depth within the inner third of cervical stroma, compared with women without preterm birth less than 34 weeks. There were no significant differences noted between the uterocervical angles of women with and without preterm birth less than 34 weeks. Other ultrasound findings that were noted to be different included presence of intra-amniotic sludge, funneling membranes,

and a straight endocervical canal. Again, the relationship between these ultrasound characteristics among women who had preterm birth less than 37 weeks, compared with those who did not was similar to those with preterm birth less than 34 weeks (Supplementary Table S2 [available in the online version]).

Given the high degree of collinearity between the significant obstetric and ultrasound characteristics, we were unable to fit a multivariable regression model for either preterm birth less than 34 weeks or preterm birth less than 37 weeks, but instead reported the RRs and 95% CIs of preterm birth for each characteristic to assess the magnitude of association and precision of each estimate (Table 3). Longer cervical length between the cerclage stitch and the external os was associated with a lower risk of preterm birth < 34 weeks (RR: 0.26, 95% CI: 0.18–0.37), compared with no preterm birth < 34 weeks as well as a lower risk of preterm birth < 37 weeks (RR: 0.53, 95% CI: 0.44–0.63), compared with no preterm birth < 37 weeks. The distal cervical length had a greater magnitude of association than the RR for total cervical length (RR: 0.53, 95% CI: 0.45–0.64 for < 34 weeks and RR: 0.77, 95% CI: 0.69–0.87 for < 37 weeks). The location of the cerclage within the inner third of the cervix and a shorter distance between the anterior cerclage stitch and the cervical canal were associated with higher risk of preterm birth < 34 weeks, compared with no preterm birth < 34 weeks (RR: 3.55, 95% CI:1.97–6.41 and RR: 0.24, 95% CI: 0.10–0.59, respectively). Funneling membranes to or past the cerclage (RR: 4.71, 95% CI: 2.32–9.59), presence of sludge (RR: 3.33, 95% CI: 1.84–6.03), and a straight cervical canal (RR: 5.65, 95% CI: 2.09–15.33) were also among the factors with the highest RR of preterm birth < 34 weeks, compared with no preterm birth < 34 weeks. Overall, the factors associated with preterm birth < 34 weeks were the same as those associated with preterm birth < 37 weeks, although the magnitude of association was greater for preterm birth < 34 weeks.

Discussion

We found that ultrasound findings can be used to provide additional risk stratification to determine which women remain at highest risk of preterm birth after cerclage placement. Approximately half of women who had cervical cerclage placement delivered at less than 37 weeks and almost one-third delivered at less than 34 weeks, consistent with prior studies.[6,8,10,16] On the first ultrasound after cerclage, women with short cervical length between cerclage stitch and external os, cerclage stitch located in the inner third of cervical stroma, funneling membranes to or past the cerclage, presence of intra-amniotic sludge, and a straight endocervical canal have the highest risk of preterm birth less than 34 weeks and less than 37 weeks. Obstetric characteristics that are also important to consider when assessing a woman's risk of preterm birth after cerclage include indication for cerclage placement as women with exam-indicated cerclage are at higher risk for preterm birth than those with history or ultrasound indication as well as use of vaginal progesterone. While vaginal progesterone was associated with an increased risk of preterm birth, we do not believe this to be a causal relationship. Rather, we believe this likely reflects the fact that women who were treated with vaginal progesterone for a short cervix prior to cerclage placement were at even higher risk for preterm birth because they had a short cervix.

While previous studies have suggested an association between uterocervical angle and risk of preterm birth,[9,10] we did not observe this finding on postcerclage ultrasound examination. We did not compare pre- and postcerclage uterocervical angles; thus, it is possible that the difference was associated with preterm birth or that this measurement is more useful prior to cerclage placement. In contrast to the findings of Uquillas et al, we found that the presence of a straight cervical canal was associated with preterm birth. One potential explanation for this difference is that our study population included only women with cerclage, whereas these women were excluded from the prior study.[16] Similar to the theories explaining the association with uterocervical angles and preterm birth,[10,16] we speculate that an angled (compared with straight) cervix may reduce the physiologic stress on the cervix and reduce mechanical forces contributing to premature dilation.

We theorize that the location of the cerclage within the cervical stroma may also play a role in the mechanical strength provided by the cerclage suture. If the cerclage is located too close to the cervical canal (in our study, located within the inner third), it may not provide as much support to the surrounding cervical stroma and thus may explain our findings of a higher risk of preterm birth among women whose cerclage was placed in this area. In addition to the theories related to mechanical forces, it is also possible that placement of a cerclage too close to the cervical canal may cause an inflammatory response within the cervical mucosa. While we did not have precerclage ultrasounds for comparison, we did find an association between presence of intra-amniotic sludge and preterm birth which supports this alternate theory of inflammation and subclinical infection.[17] While previous studies have inconsistently reported an association between postcerclage cervical length and pregnancy outcomes,[12,15] our findings suggest that postcerclage cervical length is associated with preterm birth, and the length of the cervix distal to the cerclage has a stronger association with preterm birth than the total cervical length. Similarly, our results support previous studies that have found an association between funneling membranes and preterm birth,[18] and extend these findings as we demonstrated that the extent of funneling with respect to cerclage location has a stronger association with preterm birth than the presence of any funneling, and further note the importance of the placement of the stitch in relation to the cervical canal.

Our study has many strengths. This was a high-risk cohort of women with high rates of prior preterm birth at early gestational ages, suggesting that even in the setting of management by multiple providers, the cerclage procedures were indicated. Further, inclusion of women receiving a cerclage for different indications increases the generalizability of postcerclage ultrasound parameters in assessing risk of preterm birth. Each image and ultrasound measurement were reviewed by two study investigators masked to obstetric outcomes to minimize bias, but unfortunately, the data were not saved in a manner such that we could calculate interobserver variability. While this study did not consider precerclage ultrasound findings, it evaluated the utility of different postcerclage ultrasound measurements, in addition to cervical length, that could easily be obtained by any ultrasound-trained provider without the need for complex computer programming techniques such as those necessary for heterogeneity calculations. After future validation of these findings, postcerclage ultrasound could potentially be used to assess residual risk of preterm birth as well as guide surgical technique with regard to optimal cerclage placement. However, this study is not without

limitations. We were unable to assess for independent associations between each of the ultrasound measurements and preterm birth risk due to high degree of collinearity between each of these parameters and obstetric characteristics such as the indication for cerclage. While some providers routinely performed a postcerclage transvaginal ultrasound, others did not and thus there was potential for selection bias in our cohort. However, women with and without postcerclage ultrasounds had similar cerclage indications, cerclage types, rates of preterm birth less than 34 and less than 37 weeks (all $p > 0.10$), which suggests that our study cohort was representative of all women who received a cerclage during the study period. Finally, given that this study was conducted at a single site and cerclage placement was not a common procedure, we did not have sufficient power to evaluate preterm birth outcomes stratified by cerclage indication.

In summary, our results demonstrate that postcerclage transvaginal ultrasound parameters are associated with preterm birth. While the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine do not currently recommend cervical length surveillance after cerclage placement,[4] further research may show that transvaginal ultrasound can be used after cerclage placement to modify a woman's residual risk of preterm birth. Knowledge of which women are at the highest risk of preterm birth could then be used to improve neonatal outcomes by increasing antenatal surveillance, optimizing timing of antenatal betamethasone, and ensuring delivery at a tertiary care facility.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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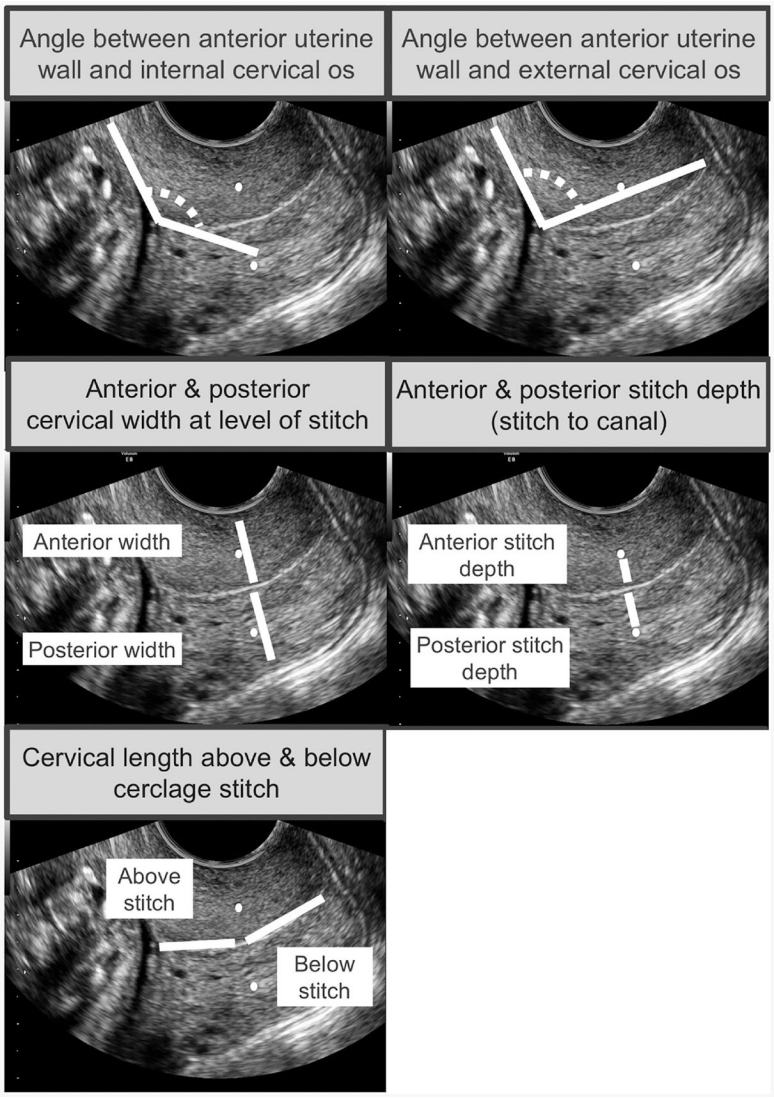

Fig. 1.

Transvaginal ultrasound parameter measurements. Other parameters assessed included the presence of intra-amniotic sludge, presence of funneling membranes at the level of the internal cervical os, and presence of funneling membranes to or past the level of the cerclage stitch.

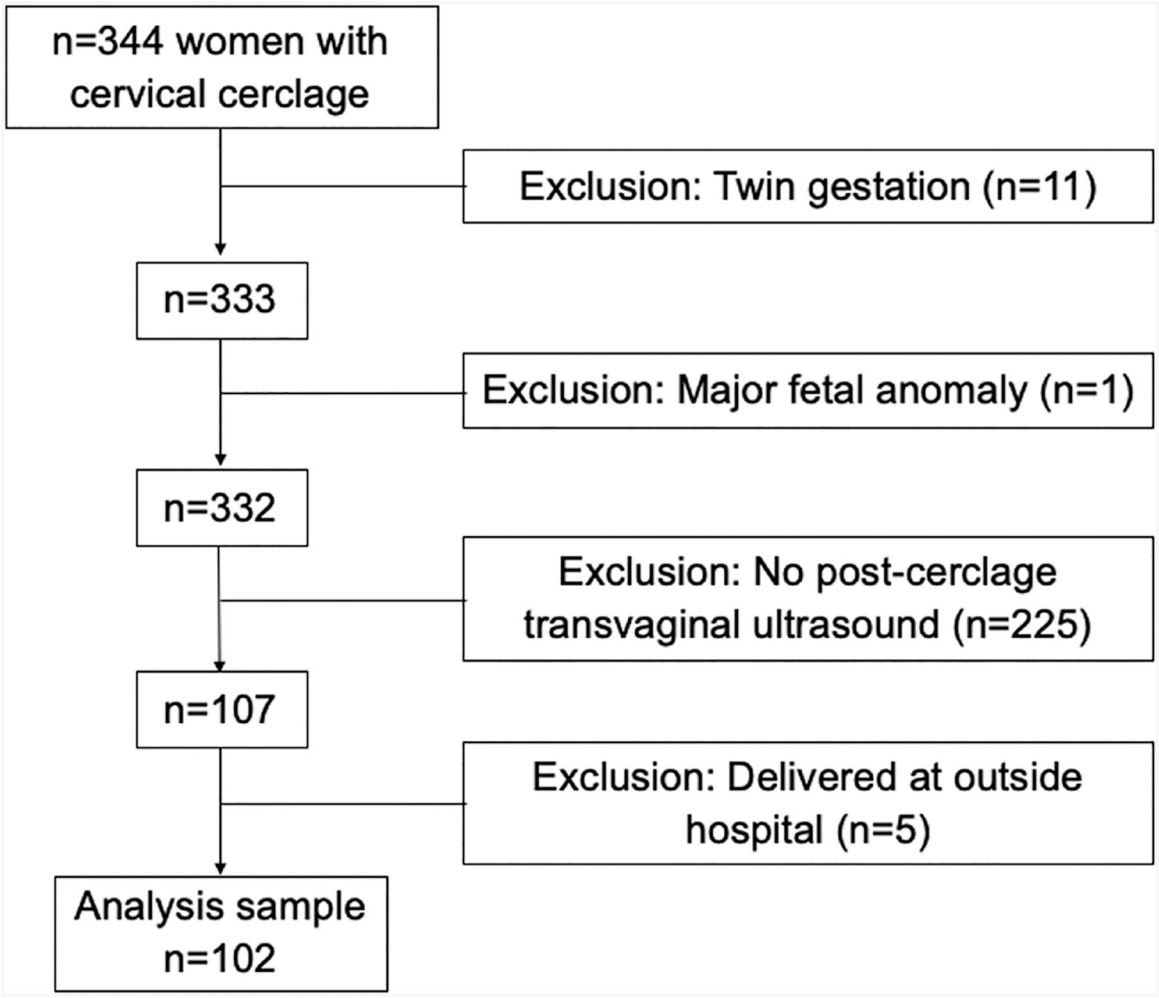

Fig. 2.
Flow diagram of study cohort.

Table 1

Maternal demographics, baseline obstetric characteristics, and cerclage placement details by preterm birth less than 34 weeks' gestation

	Total (*n* = 102)	Preterm birth <34 weeks (*n* = 28)	No preterm birth <34 weeks (*n* = 74)	*p*-Value
Maternal age (y)	32 (28–35)	33 (32–35)	30 (27–35)	0.09
Maternal race/ethnicity				
Non-Hispanic black	55 (55.6)	14 (50.0)	41 (57.8)	0.65
Non-Hispanic white	23 (23.2)	7 (25.0)	16 (22.5)	
Hispanic	15(15.1)	4 (14.3)	11 (15.5)	
Other	6 (6.1)	3 (10.7)	3 (4.2)	
Maternal BMI (kg/m^2)[a]	28.9 (23.8–35.5)	27.4 (24.2–34.6)	29.4 (23.8–37.2)	0.68
Tobacco use during pregnancy	5 (9.1)	1 (6.3)	4 (10.3)	0.64
One or more prior spontaneous preterm deliveries, among multiparous women	63 (76.8)	18 (85.7)	45 (73.8)	0.26
Gestational age of earliest prior delivery (wk)	20.0 (17.9–23.0)	20.0 (17.9–23.6)	20.0 (17.9–23.0)	0.68
Gestational age at cerclage placement (wk)	14.3 (13.0–18.7)	16.6 (13.7–20.3)	14.1 (13.0–18.4)	0.09
Indication for cerclage placement				
History-indicated	59 (57.8)	10 (35.7)	49 (66.2)	0.01
Ultrasound-indicated	20 (19.6)	6 (21.4)	14 (18.9)	
Physical exam-indicated	23 (22.6)	12 (42.9)	11 (14.9)	
Type of cerclage procedure				
McDonald	69 (68.3)	24 (88.9)	45 (60.8)	0.06
Shirodkar	22 (21.8)	2 (7.4)	20 (27.0)	
Cervicoisthmic	8 (7.9)	1 (3.7)	7 (9.5)	
Abdominal	2 (2.0)	0	2(2.7)	
Type of cerclage suture				
Mersilene	58 (58.6)	8 (29.6)	50 (69.4)	<0.001
Ethibond	37 (37.4)	15 (55.6)	22 (30.6)	
Prolene	3 (3.0)	3 (11.1)	0	
Other	1 (1.0)	1 (3.7)	0	
Intramuscular progesterone use	74 (73.3)	20 (71.4)	54 (74.0)	0.80

	Total (*n* = 102)	Preterm birth <34 weeks (*n* = 28)	No preterm birth <34 weeks (*n* = 74)	*p*-Value
Vaginal progesterone use	38 (40.3)	16 (59.3)	22 (32.8)	0.02

Abbreviation: BMI, body mass index.

Note: Data are *n* (%), median (interquartile range), or mean ± standard deviation.

[a]Data available for *n* = 59 women.

Table 2

Ultrasound characteristics at the time of first ultrasound postcerclage by preterm birth less than 34 weeks' gestation

Characteristic	Preterm birth <34 weeks *n* = 28	No preterm birth < 34 weeks *n* = 74	*p*-Value
Gestational age at ultrasound measurement (wk)	20.0 (18.1–21.6)	19.3 (18.1–21.3)	0.34
Interval from cerclage to first ultrasound (wk)	2.1 (1.0–5.1)	4.1 (2.3–6.1)	0.02
Cervical length (mm)	11.7 (4.8–21.4)	34.5 (23.5–44.2)	<0.001
Cervical length above cerclage (mm)	1.7 (0–14.0)	16.8 (6.7–26.4)	<0.001
Cervical length below cerclage (mm)	8.6 (30.6–13.6)	16.6 (9.7–21.9)	<0.001
Distal cerclage	13 (46.4)	13 (17.6)	<0.01
Angle between anterior uterine wall and line drawn along cervical canal nearest to internal os (degrees)	95 (68–114)	106 (89–120)	0.08
Angle between anterior uterine wall and straight line connecting internal to external os (degrees)	95 (68–114)	96 (76–110)	0.65
Straight endocervical canal	19 (82.6)	23 (33.3)	<0.001
Width of the anterior cervix at level of cerclage (mm)	12.7 (9.7–16.3)	15.2 (13.1–18.8)	0.02
Distance between anterior suture and cervical canal (mm)	6.7 (4.1 −9.2)	9.5 (7.8–12.6)	<0.01
Width of the posterior cervix at level of cerclage (mm)	14.8 (10.8–21.3)	16.3 (14.2–18.0)	0.51
Distance between posterior suture and cervical canal (mm)	5.8 (3.3–7.7)	6.5 (5.0–8.6)	0.17
Cerclage stitch located in the inner third of the cervical stroma	5 (21.7)	4 (5.9)	0.03
Funneling membranes to or past the level of the cerclage stitch	15 (53.6)	10 (13.5)	<0.001
Funneling membranes at the level of the internal os	20 (71.4)	15 (20.6)	<0.001
Intra-amniotic sludge present	15 (53.6)	19 (25.7)	<0.01

Note: Data are *n* (%) or mean ± standard deviation.

Table 3

Relative risk of obstetric and ultrasound characteristics significantly associated with preterm birth less than 34 weeks' gestation and less than 37 weeks' gestation

Characteristic	Preterm birth < 34 weeks RR (95% CI)[a]	Preterm birth < 37 weeks RR (95% CI)[a]
Physical exam-indicated cerclage	2.58 (1.43–4.63)	1.72 (1.17–2.51)
Vaginal progesterone use	2.14 (1.12–4.10)	1.54 (1.02–2.33)
Cervical length (mm)	0.53 (0.45–0.64)	0.77 (0.69–0.87)
Cervical length above cerclage (mm)	0.51 (0.38–0.68)	0.76 (0.63–0.91)
Cervical length below cerclage (mm)	0.26 (0.18–0.37)	0.53 (0.44–0.63)
Distal cerclage	2.53 (1.40–4.59)	1.75 (1.20–2.56)
Straight endocervical canal	5.65 (2.09–15.33)	2.56 (1.53–4.29)
Width of the anterior cervix at level of cerclage (mm)	0.44 (0.19–1.02)	0.47 (0.38–0.58)
Distance between anterior suture and cervical canal (mm)	0.24 (0.10–0.59)	0.37 (0.28–0.49)
Cerclage stitch located in the inner third of the cervical stroma	3.55 (1.97–6.41)	1.88 (1.22–2.89)
Funneling membranes to or past the level of the cerclage stitch	4.71 (2.32–9.59)	1.69 (1.15–2.48)
Funneling membranes at the level of the internal os	2.31 (1.24–4.28)	1.97 (1.32–2.93)
Intra-amniotic sludge present	3.33 (1.84–6.03)	2.33 (1.62–3.35)

Abbreviations: CI, confidence interval; RR, relative risk.

[a]Unable to perform multivariable regression due to collinearity between characteristics above.