

OBSTETRICS

The association between cervical excisional procedures, midtrimester cervical length, and preterm birth

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OBJECTIVE: To determine whether a prior cervical excisional procedure (a loop electrosurgical excision procedure or cold knife cone) is associated with a short midtrimester cervical length (<3 cm) and whether having a short cervix explains the relationship between this procedure and preterm birth.

STUDY DESIGN: In this cohort study of women with a singleton pregnancy who underwent routine cervical length assessment between 18 and 24 weeks of gestation, women with a history of a prior cervical excisional procedure were compared with those without such a history. Bivariable and multivariable analyses were performed to identify whether a prior cervical excisional procedure remained an independent risk factor for preterm birth after controlling for cervical length.

RESULTS: Of the 6669 women who met inclusion criteria, 460 (6.9%) had a prior cervical excisional procedure. Mean cervical length was

shorter (4.2 ± 0.9 cm vs 4.5 ± 0.9 cm, $P < .001$) and the proportion of women with a short cervix was higher (6.5% vs 1.5%, $P < .001$) in women with a prior cervical excisional procedure. In multivariable regression, both a short cervix (adjusted odds ratio, 6.19; 95% confidence interval, 3.85–9.95) and a prior cervical excisional procedure (adjusted odds ratio, 1.53; 95% confidence interval, 1.04–2.25) were significantly associated with preterm birth.

CONCLUSION: Women with a prior cervical excisional procedure have shorter midtrimester cervical lengths. Both a prior cervical excisional procedure and a short cervix were independently associated with preterm birth. These data suggest that the risk of preterm birth associated with a prior loop electrosurgical excision procedure or cold knife cone is not merely due to postsurgical shortening of the cervix.

Key words: cervical excisional procedure, cervical length, LEEP, preterm birth

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Loop electrosurgical excision procedures (LEEP) and cold knife cones (CKC) are excisional procedures of the cervix commonly used to treat cervical intraepithelial neoplasia. A prior cervical excisional procedure has been associated with an increased risk of preterm birth.¹⁻⁶

An increased size of the excision confers a higher risk of preterm birth, suggesting

that excision itself yields a direct effect upon the length of the cervix, thereby increasing the risk of preterm delivery.⁷⁻¹⁰

Correspondingly, midtrimester cervical length is shorter in women who underwent an excisional procedure compared with those who did not.¹¹⁻¹³

Causality between excisional procedures and preterm birth has been called into question, however, as confounders, such as socioeconomic status, sexually transmitted infections, and smoking may explain the association reported in prior observational trials. In fact, some studies comparing women with dysplasia but no prior excisional procedure to those with a prior excisional procedure have suggested that it may be the dysplasia itself or risk factors for dysplasia, and not the excisional procedure, that yield the higher risk of preterm birth.¹⁴⁻¹⁷

Understanding the relationship between cervical excisional procedures, midtrimester cervical length, and preterm birth has important clinical implications

for both patient counseling and antenatal surveillance. If the increased preterm birth risk associated with a LEEP or CKC is related to the physical excision of a cervical segment, then increased frequency of a short midtrimester cervical length should account for the relationship between cervical excisional procedures and preterm birth. The objective of this study was to determine whether a prior cervical excisional procedure is associated with preterm birth independent of midtrimester cervical length.

MATERIALS AND METHODS

This is a retrospective cohort study of women undergoing routine cervical length assessment between December 2010 and January 2012 at a single tertiary care institution. Women were included in the cohort if they were at least 18 years of age, had a singleton nonanomalous gestation, and delivered at the institution where the cervical length ultrasound was performed. During the study period,

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transvaginal cervical length was assessed between 18 and 24 weeks at the time of the fetal anatomic survey as a part of routine clinical care in all women. The cervical length was measured transvaginally by staff sonographers and confirmed by the sonologist in accordance with methods previously described by Iams et al.¹⁸ If multiple ultrasounds for cervical length were performed on an individual patient, the measurement taken closest to 20 weeks of gestation was used for analysis.

Records of all women who underwent transvaginal cervical length screening were identified through review of the clinical ultrasound reports. Cervical length was abstracted from the medical record and defined as a short cervix if the length was <3.0 cm (ie, the 10th percentile at this gestational age).^{19,20} A secondary analysis defining a short cervix as an ultrasonographic cervical length of less than 2.5 cm also was performed. A history of a prior cervical excisional procedure (defined as either a LEEP or CKC) and gestational age at delivery was obtained from review of clinical records. Demographic and baseline clinical data, such as maternal age, race/ethnicity, and body mass index (BMI) at delivery were abstracted from the clinical record. Potential confounders of preterm birth such as tobacco use, conception via in vitro fertilization, nulliparity and a prior preterm birth were abstracted as well. Preterm birth was defined as a gestational age at delivery <37 weeks.

Bivariable analyses were performed comparing those with and without a history of a cervical excisional procedure. Student *t* test, Mann-Whitney *U* test or χ^2 analysis was performed for comparisons, as appropriate. To determine whether a prior cervical excisional procedure yielded any effect modification for women with a short cervix, an interaction term between the 2 factors was created. Multivariable logistic regression was used to determine whether a cervical excisional procedure was associated with preterm birth independent of the presence of a short cervix. In the initial regression, variables, with the exception of “prior cervical excisional procedure” and the interaction term,

TABLE 1
Patient characteristics stratified by prior excisional procedure

Characteristic	Cervical excisional procedure n = 460	No cervical excisional procedure n = 6209	P value
Age	33 (31–36)	32 (28–35)	< .001
Race/ethnicity, n (%)			< .001
NonHispanic white	300 (76.1)	3014 (56.9)	
NonHispanic black	27 (6.9)	621 (11.7)	
Hispanic	47 (11.9)	1226 (23.2)	
Asian	13 (3.3)	321 (6.1)	
Other	7 (1.8)	113 (2.1)	
BMI at delivery	28.2 (25.8–31.1)	29.3 (26.5–33.0)	< .001
Smoking in current pregnancy	7 (1.6)	59 (1.0)	.24
IVF conception	23 (5.4)	228 (3.9)	.13
Nulliparous	245 (53.3)	3272 (52.7)	.82
Prior preterm birth	27 (5.9)	284 (4.6)	.20

Data are presented as median (interquartile range) or n (%).
BMI, body mass index; IVF, in vitro fertilization.
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were added to the equation if they had reached statistical significance ($P < .05$) in the bivariable analyses. A second regression was then performed in which the history of a cervical excisional procedure and the interaction term were added to the first equation.

Analyses were performed using Stata version 11.1 (StataCorp College Station, TX). All tests were 2-tailed and a $P < .05$ was used to define statistical significance. Approval for this study was obtained from the Northwestern University Institutional Review Board with a waiver of informed consent.

RESULTS

There were 6669 women who underwent a midtrimester cervical length measurement and met inclusion criteria during the study time period. Of these, 460 (6.9%) had undergone a prior cervical excisional procedure. Baseline patient characteristics dichotomized by prior cervical excisional procedure are shown in Table 1. Women with a prior cervical excisional procedure were significantly older, more likely to be non-Hispanic white, and had a lower BMI.

In bivariable analysis, mean cervical length was statistically significantly shorter, but this difference is unlikely to be clinically important (4.2 ± 0.9 cm vs 4.5 ± 0.9 cm, $P < .001$). However, the proportion of women with a short cervix was significantly higher (6.5% vs 1.5%, $P < .001$) among women with a prior cervical excisional procedure. In terms of timing of delivery, having a prior cervical excisional procedure was associated with an earlier gestational age at delivery (38.8 ± 2.4 weeks vs 39.1 ± 1.9 weeks, $P < .001$). Although this difference is not clinically significant, there was a statistically and clinically significant increased frequency of preterm birth (11.1% vs 7.1%, $P = .001$). A summary of these results in comparison to other studies is shown in Table 2.

In the initial multivariable regression, a short cervical length was significantly associated with preterm birth (Table 3). When a history of the cervical excisional procedure was added to the equation, the magnitude of the association between short cervix and preterm birth was essentially unchanged. A history of a prior cervical excisional procedure was significantly associated with preterm birth as

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