Published in final edited form as:

Obstet Gynecol. 2013 January ; 121(1): 39–45.

Risk of Cesarean Delivery After Loop Electrosurgical Excision Procedure

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Abstract

Objective—To estimate if previous loop electrosurgical excision procedure (LEEP) affects the risk of cesarean delivery.

Methods—A secondary analysis of a multicenter retrospective cohort study was performed. Women who underwent a prior LEEP were compared to two unexposed cohorts: 1) women with prior screening cervical cytology only; and 2) women with prior cervical punch biopsy. The pregnancy evaluated in this analysis was the first pregnancy of a duration more than 20 weeks after the identifying cervical procedure. Stratified and multivariable logistic regression analyses were used to control for confounding.

Results—Five hundred ninety-eight women with prior LEEP, 588 women with screening cytology only, and 552 women with cervical biopsy were included in this study. After adjusting for relevant confounders, similar rates of cesarean were seen in women with prior LEEP (31.6%) and women with prior cervical cytology only (29.3%, aOR 1.06, 95% CI 0.79–1.41). Likewise, no differences were found in rates of cesarean when women with prior LEEP were compared to those with a prior punch biopsy (29.0%, aOR 0.99, 95% CI 0.74–1.33). Among women who had a cesarean, arrest of labor was the indication for cesarean in a similar proportion of women in the groups (LEEP compared with cytology only, $p=0.12$; LEEP compared with biopsy, $p=0.50$). LEEP specimen size did not vary by delivery mode. Length of time between LEEP and subsequent pregnancy also did not influence delivery mode.

Conclusion—LEEP does not affect mode of delivery in the subsequent pregnancy.

Introduction

Excisional procedures are necessary for the diagnosis and treatment of high-grade cervical intraepithelial neoplasia, (1) but they may lead to structural and functional changes of the cervix. The correct timing and successful execution of cervical remodeling is a critical

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Financial Disclosure

The authors did not report any potential conflicts of interest.

Presented as a poster at the 32nd Annual Meeting of the Society of Maternal-Fetal Medicine, February 10, 2012, Dallas Texas..

component of parturition. (2) The majority of published research on the effects of surgical excisional therapies, including cold-knife conization and loop electrosurgical excision procedure (LEEP), on pregnancy outcomes has focused on the gestational age of subsequent deliveries and prematurity-related neonatal outcomes. (3–6) The ability of the cervix after an excisional procedure to undergo the dynamic intrapartum changes of dilation and effacement to result in a successful vaginal delivery has been inadequately studied.

As the current treatment of choice for cervical intraepithelial neoplasia, LEEP is commonly preformed in women of childbearing age. (7–11) Like all excisional procedures, LEEP may result in loss of cervical tissue (12) and can lead to scarring of the cervix, (13) which in theory, could influence the ability of the cervix to dilate in labor. Arrest of dilation is one of the most common indications for cesarean in the United States. (14) Thus, we hypothesized that LEEP could affect the risk of cesarean in subsequent pregnancies. In this study, we estimated the effect of LEEP on risk of cesarean delivery in a large retrospective cohort, and secondarily estimated the risk of cesarean for arrest, as well as the effect of specimen size and time from LEEP to delivery on risk of cesarean.

Materials and Methods

This study is a secondary analysis of a multicenter retrospective cohort study. In the parent study, women with prior LEEP were compared to age-matched controls without prior cervical excisional procedure and controls with prior cervical biopsy to assess the association of LEEP and spontaneous preterm birth prior to 34 weeks of gestation. Approval for the study was granted by the Institutional Review Boards at each participating hospital. Women with LEEP performed between 1996 and 2006 as well as age-matched controls with screening cervical cytology or cervical punch biopsy performed the same calendar year were identified from clinical databases of surgical pathology at nine participating hospitals by searching for the key words: “*Pap (Papanicolaou) smear*”, “*cervical cytology*”, “*cervical biopsy*”, and “*LEEP*”. Trained research nurses contacted the participants by telephone and collected information, including maternal demographics and details regarding all pregnancies both prior to and after the procedure. With informed consent, medical records were obtained from each pregnancy. Pathology and cytology reports were also acquired from all prior cervical procedures. In cases of inconsistencies between the patient recall and chart obtained data, the medical records information was preferentially used. All research data was stored in a secure, central, electronic study database.

In the present study, risk of cesarean among women with a prior LEEP procedure was compared to risk in women without a prior surgical excisional procedure. There were two unexposed cohorts in this study, both of which were identified from the surgical pathology databases. The first unexposed group consisted of women with only prior screening cervical cytology (Papanicolaou test). Women in the second unexposed group had a prior cervical punch biopsy performed for evaluation of cervical dysplasia. The pregnancy evaluated in this analysis was the first pregnancy of a duration more than 20 weeks after the classifying procedure (LEEP, Papanicolaou test, or cervical biopsy). In the unexposed cohorts, women who reported any history of LEEP or other cervical excisional procedure were excluded. Women with a multiple gestation in the index pregnancy were also excluded. Those women with missing data regarding pregnancy history, mode of delivery in the index pregnancy, or the dates of the cervical procedure or delivery were excluded, as were any women for whom medical records were unavailable.

Demographic information at the time of the index pregnancy was obtained during a structured phone interview and confirmed by inpatient medical records. Data collected included maternal age, parity, height, weight, race, and history of prior cesarean delivery.

Documented gestational age at delivery, use of induction agents during labor and infant birth weight in the index pregnancy were extracted from the records. Preterm was defined as delivery less than 37 weeks gestation. Medical history at the time of the index pregnancy was reviewed. Gestational diabetes was defined as glucose ≥ 140 g/dl on a screening glucose tolerance test followed by at least 2 abnormal values on a 3-hour glucose test using the National Diabetes Data Group criteria. (15) Pre-gestational diabetes was defined as the diagnosis of either type 1 or type 2 diabetes mellitus prior to pregnancy. Criteria used to identify women with preeclampsia or gestational hypertension included persistent blood pressure >140 mm Hg systolic or >90 mm Hg diastolic with or without proteinuria. (16) Pathology reports were examined to determine the grade of cervical dysplasia on screening cytological specimens for all women.

The primary outcome assessed was mode of delivery. Secondly, indication for cesarean was evaluated in women who had a cesarean in the index pregnancy. Indication for cesarean delivery was abstracted from the operative report. The indication was coded as arrest of labor if the documented reason for cesarean included “arrest of dilation”, “failure to progress”, “failed induction of labor,” “cephalopelvic disproportion,” or “cervical stenosis” or “scarring.” Failed operative vaginal delivery and “arrest of descent” was not classified as an arrest of labor. Cesareans performed for indications other than arrest of labor were classified as “other.” In cases in which multiple indications for delivery were documented, the indication was coded as arrest of labor if any one of the indications included one of the criteria used to define labor arrest.

Women with prior LEEP were compared to women with screening cytology only (Control Group 1) and women with history of cervical punch biopsy (Control Group 2) in independent analyses. Baseline characteristics of the groups were compared using chi-square analysis. The distribution of all continuous variables in this study was assessed using the Kolmogorov-Smirnov test. Median maternal age was compared using the Mann-Whitney U test as the values were not normally distributed. Unadjusted relative risks and 95% confidence intervals for cesarean delivery after LEEP were calculated using each reference group. Stratified analyses were performed based on gestational age at delivery, history of cesarean, and induction of labor. The indications for cesarean in the exposed and unexposed groups were compared. Multivariable logistic regression was performed to adjust for confounders identified in the literature as risk factors for cesarean as well as those factors found to be significant in bivariate analysis including infant birth weight, parity, race, prior cesarean, maternal diabetes, maternal body mass index (BMI), and age. (17–19) The final logistic regression model created using a backwards, stepwise approach for the primary outcome, cesarean delivery, included parity, prior cesarean, birth weight, maternal BMI, and maternal age. The likelihood ratio test was used to assess the impact of removal of covariates from the model.

In the group of women with prior LEEP, the relationship between LEEP specimen size and risk of cesarean was examined. Using the dimensions of the specimens described in the pathology reports, total volumes for the specimens were calculated. Median specimen volumes were compared using the Mann-Whitney U test in women who had a cesarean in the index pregnancy and those women who delivered vaginally because the volume data were not normally distributed.

The effect of time from procedure on delivery mode was also evaluated in the group of women with prior LEEP. Median length of time from LEEP to index pregnancy was compared in women who had a cesarean and women delivered vaginally using the Mann-Whitney U test. Risk of cesarean in women who delivered within 12 months of the LEEP

was compared to risk of cesarean in women who delivered >12 months after the procedure. A similar comparison was conducted using delivery within 24 months of the LEEP.

The parent cohort study was powered to detect differences in preterm birth. All women enrolled in the study with a postprocedure pregnancy of more than 20 weeks of gestation were included in this secondary analysis, and a post hoc power analysis was performed. Tests with $p < 0.05$ were considered statistically significant. All statistical analyses were performed using STATA 10.0 (special edition, Stata-Corp, College Station, TX).

Results

A total of 1,738 women in the initial cohort study met inclusion criteria for this secondary analysis. The exposed group consisted of 598 women with a history of LEEP procedure. The unexposed groups were composed of 588 women with a history of only cytological screening (Control Group 1) and 552 women with a prior cervical punch biopsy (Control Group 2). Baseline demographic characteristics were similar between the exposed cohort and the unexposed control groups in regards to parity, maternal body mass index, history of prior cesarean, rates of preeclampsia or gestational hypertension, and rates of gestational and pre-gestational diabetes at the time of the index pregnancy. Women with a prior LEEP were older than women in either control group. White women were more likely to have had a prior LEEP than women of other races whereas control groups were comprised of a significantly higher percentage of black women. Gestational age at delivery, use of induction agents, and birth weight of the infant in the index pregnancy were not significantly different among the groups. Women with a prior LEEP were more likely to have had cytology demonstrating high-grade cervical dysplasia prior to their procedure than women in the unexposed cohorts (Table 1).

We observed similar rates of cesarean delivery in women with a history of LEEP and women without a history of cervical biopsy or excisional procedure (Control group 1) (31.6% vs. 29.3%, aOR 1.06, 95% CI 0.79–1.41). Stratified analyses by gestational age at delivery, labor induction, and history of prior cesarean demonstrated similar rates of cesarean delivery among LEEP exposed and unexposed women. Evaluation of indication for cesarean demonstrated similar rates of cesarean for arrest of labor in women with a prior LEEP and women in Control group 1 after controlling for relevant confounders (Table 2).

In a comparison of women with a history of LEEP and those in the second unexposed group with a history of prior cervical biopsy, no difference in rate of cesarean was seen (31.6% vs. 29.0%, aOR 0.99, 95% CI 0.74–1.33, $p=0.98$). Similar to the Control Group 1 analysis, stratified analyses based on gestational age at delivery, history of cesarean and induction of labor also revealed no association between prior cervical procedure and risk of cesarean delivery. Similar indications for cesarean were documented in both groups (Table 3).

Among women with a history of prior LEEP, the size of the LEEP specimen was compared among women who had a cesarean in the index pregnancy and those who delivered vaginally. No difference in median LEEP specimen volume was found (1.81 cm³ in the cesarean group vs. 1.70 cm³ in the vaginal group, $p=0.71$). Similarly, the specimen size did not significantly vary among women who underwent cesarean for labor arrest in the index pregnancy compared to all women who did not require cesarean for arrest (1.35 cm³ vs. 1.77 cm³, $p=0.10$). The effect of specimen size was further examined by comparing rates of cesarean among those women who had a prior LEEP with the smallest specimen volumes (<10th percentile) to other women with LEEP. Rates of cesarean were statistically similar (37.3% vs. 31.1%, $p=0.36$). Likewise, women with particularly large LEEP specimens (>90th percentile) also did not have an increased rate of cesarean (32.7% vs. 31.3%, $p=0.78$).

The effect of interval of time between LEEP and subsequent pregnancy on cesarean delivery rate was assessed. No difference in median length of time from LEEP was demonstrated in women who subsequently had a cesarean in the index pregnancy and those who delivered vaginally (33.4 months vs. 33.0 months, $p=0.42$). There was also no difference in the time interval between procedure and delivery in women who had a cesarean for arrest and those who did not require cesarean for arrest (25.7 months vs. 33.0 months, $p=0.82$). Among women with prior LEEP, delivery within 12 months of the procedure was not associated with increased cesarean delivery risk (29.8% vs. 31.8%, $p=0.78$), nor was delivery within 24 months of the procedure (31.1% vs. 31.9%, $p=0.84$).

A post hoc power analysis to estimate our ability to detect meaningful differences in rates of cesarean in this secondary analysis was performed. Based on the sample sizes of the exposed and unexposed cohorts and assuming an alpha equal to 0.05, we would be able to detect a 1.5-fold difference in rates of cesarean deliveries among the groups with a 90% power.

Discussion

In this study, we estimated the effect of LEEP on subsequent cesarean delivery. We found no statistically significant difference in rates of cesarean in women with prior LEEP compared to two control groups after controlling for relevant confounders. Furthermore, the indications for cesarean, including arrest of labor, did not vary among the groups. The size of the LEEP specimen and the interval of time from the LEEP also did not impact the risk of cesarean in the subsequent pregnancy.

Few studies have previously examined the relationship between prior LEEP and cesarean birth. (12, 13, 20–24) Of these studies, many have small sample sizes and thus may not be adequately powered to evaluate mode of delivery (13, 20–22), and in some studies cesarean data has been presented without accounting for possible confounders (20, 22–24). In addition, few studies (13, 23) have reported the indication for cesarean delivery thus restricting the ability to draw meaningful conclusions from the reported data. Lastly, the published data on the effect of cervical procedures on rates of cesarean is inconsistent. While at least one publication reported a decreased rate of cesarean (24) after LEEP and others have found higher rates of cesarean following cervical conization, (25, 26) most studies have reported no significant association between prior cervical excisional procedure and mode of delivery. (12, 20–23, 26–28)

The major limitation of the present study is the retrospective design. The available data for analysis was limited to that which was collected as part of the initial study designed to evaluate preterm birth as the primary outcome. Details regarding labor and indication for cesarean in the index pregnancy were restricted to that which could be extracted from the medical record. In cases of multiple indications for surgery, the data was coded in a manner that favored the classification of arrest of labor over other indications. This methodology was utilized because an alteration in the ability of the cervix to dilate was considered the most biologically plausible link between LEEP and cesarean delivery. However, possible heterogeneity among the women classified as having arrest of labor may have diminished the observed effect of cervical excisional procedures on cervical dilation in labor.

Although this study was retrospective, the amount of data collected was substantial. Our study is one of only a few to examine the indication for cesarean, (13, 23) which is an essential step in understanding whether a link between prior LEEP and cesarean exists. In addition, there was minimal missing data particularly in regards to indication for cesarean (8.5%). All data collected during a structured telephone interview with the study participant was confirmed in medical records that were obtained for each pregnancy prior to and

following the enrollment procedure thus minimizing recall bias and improving the completeness of the data. Our use of two unexposed cohorts also enhanced the ability to draw conclusions from our results since it provided better opportunity to assess confounding and selection bias. Furthermore, information from pathology reports was utilized to assess the effect of LEEP specimen size on risk of cesarean. The lack of association between specimen size and cesarean, even at the smallest and largest extremes, reinforces our conclusion that LEEP does not affect the risk of cesarean.

LEEP has become the primary procedure used in the United States for the diagnosis and treatment of high-grade cervical intraepithelial neoplasia. Although LEEP has been associated with cervical stenosis, (13) our study indicates that a history of LEEP does not increase the risk of cesarean in the subsequent pregnancy, regardless of the size of the LEEP specimen or interval of time since the procedure was performed. Additionally, the evaluation of the indications for cesarean suggests that LEEP does not significantly impair the ability of the cervix to dilate during labor.

Acknowledgments

Supported by NIH grant # 5RO1CA10918604.

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Table 1

Characteristics of Women With a History of Prior Loop Electrosurgical Excision Procedure Compared to Unexposed Controls at Time of Index Pregnancy

	Women Without Biopsy (Control Group 1) (n=598)	P	Women With a History of LEEP (n=598)	P*	Women With Punch Biopsy (Control Group 2) (n=552)
Age *	26 (21–31)	<0.01	28 (25–32)	<0.01	26 (22–30)
Nulliparous	286 (48.6)	0.56	301 (50.3)	0.16	255 (46.2)
Gestational age at delivery Term Preterm	501 (85.2) 87 (14.8)	0.08	487 (81.4) 111 (18.6)	0.36	461 (83.5) 91 (16.5)
BMI BMI <25.0 BMI 25.0–29.9 BMI 30–39.9 BMI 40	64 (10.9) 188 (32.0) 208 (35.4) 128 (21.7)	0.33	58 (9.7) 198 (33.1) 233 (39.0) 109 (18.2)	0.09	49 (8.9) 148 (26.8) 242 (43.8) 113 (20.5)
Race Black White Other	386 (65.6) 168 (28.6) 34 (5.8)	<0.01	204 (34.1) 380 (63.6) 14 (2.3)	<0.01	331 (60.0) 204 (36.9) 17 (3.1)
Induction of labor	156 (26.5)	0.09	185 (30.9)	0.36	157 (28.4)
History of prior cesarean	58 (9.9)	0.43	51 (8.5)	0.82	45 (8.2)
Birth weight in index pregnancy 3500 gm 4000 gm	186 (31.6) 42 (7.1)	0.53 0.89	179 (29.9) 44 (7.4)	0.36 0.76	179 (32.4) 38 (6.9)
Diabetes Gestational Pregestational	16 (2.7) 34 (5.8)	0.77 0.27	18 (3.0) 44 (7.4)	0.19 0.02	10 (1.8) 23 (4.2)
Preeclampsia or gestational hypertension	79 (13.4)	0.37	70 (11.7)	0.61	70 (12.7)
HSIL on pap prior to procedure	6 (1.0)	<0.01	359 (60.0)	<0.01	70 (13.1)

LEEP, loop electrosurgical excision procedure.

Data presented as n (%) except maternal age, which is reported as the median (interquartile range).

p is the *p*-value for the comparison of women with history of LEEP and women without a prior biopsy (control group 1), while *P** is the *P*-value for the comparison between women with a history of LEEP and women with a prior cervical punch biopsy (control group 2).

Rates of Cesarean Delivery in Women With a History of Loop Electrosurgical Excision Procedure Compared to Controls without Biopsy (Control Group 1)

Table 2

	Women With a History of LEEP (n=598)	Women Without Biopsy (n=588)	Relative Risk (95% CI)	Adjusted Odds Ratio (95% CI)	P
All women *	189 (31.6)	172 (29.3)	1.08 (0.91–1.28)	1.06 (0.79–1.41)	0.69
Preterm †	50 (45.0)	40 (46.0)	0.98 (0.72–1.33)	0.77 (0.41–1.44)	0.41
Term ‡	139 (28.5)	132 (26.3)	1.08 (0.88–1.33)	1.18 (0.84–1.65)	0.34
Excluding women with prior cesarean §	143 (26.1)	121 (22.8)	1.15 (0.93–1.41)	1.07 (0.79–1.45)	0.65
Induction of labor ¶	41 (22.2)	42 (26.9)	0.82 (0.57–1.20)	0.83 (0.49–1.41)	0.50
Indication for cesarean // Arrest Other	31 (16.4) 158 (83.6)	39 (22.7) 133 (77.3)	0.72 (0.47–1.11) 1.08 (0.98–1.20)	0.64 (0.37–1.12) 1.56 (0.89–2.74)	0.12 0.12

LEEP, loop electrosurgical excision procedure.

Data presented as n (%).

* Adjusted for maternal age, parity, prior cesarean, body mass index, birth weight

† Adjusted for maternal age, parity, prior cesarean, birth weight

‡ Adjusted for maternal age, parity, prior cesarean, body mass index

§ Adjusted for maternal age, parity, body mass index, birth weight

// Adjusted for maternal age, prior cesarean, birth weight

Table 3

Rates of Cesarean Delivery in Women With a History of Loop Electrosurgical Excision Procedure Compared to Controls with Punch Biopsy (Control Group 2)

	Women With a History of LEEP (n=598)	Women With Punch Biopsy (n=552)	Relative Risk (95% CI)	Adjusted Odds Ratio (95% CI)	P
All women *	189 (31.6)	160 (29.0)	1.09 (0.91–1.30)	0.99 (0.74–1.33)	0.98
Preterm †	50 (45.0)	38 (41.8)	1.08 (0.78–1.48)	0.79 (0.41–1.51)	0.47
Term ‡	139 (28.5)	122 (26.5)	1.08 (0.88–1.33)	1.02 (0.73–1.43)	0.89
Excluding women with prior cesarean §	143 (26.1)	123 (24.3)	1.08 (0.87–1.33)	0.95 (0.70–1.28)	0.73
Induction of labor ¶	41 (22.2)	43 (27.4)	0.81 (0.56–1.17)	0.70 (0.42–1.18)	0.18
Indication for cesarean //	31 (16.4) 158 (83.6)	27 (20.0) 128 (80.0)	0.82 (0.52–1.28) 1.04 (0.95–1.15)	0.82 (0.46–1.47) 1.22 (0.68–2.20)	0.50 0.50

LEEP, loop electrosurgical excision procedure.

Data presented as n (%).

* Adjusted for maternal age, parity, prior cesarean, body mass index, birth weight

† Adjusted for maternal age, parity, prior cesarean, birth weight

‡ Adjusted for maternal age, parity, prior cesarean, body mass index

§ Adjusted for maternal age, parity, body mass index, birth weight

// Adjusted for maternal age, parity, prior cesarean, birth weight