The role of prophylactic cerclage in preventing preterm delivery after electrosurgical conization

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Objective: To evaluate pregnancy outcomes after electrosurgical conization.

Methods: We retrospectively analyzed the outcomes of 56 singleton pregnancies after electrosurgical conization of the uterine cervix. Of the 56 cases, 25 women underwent prophylactic cerclage with McDonald procedure (cerclage group), and 31 were managed expectantly (expectant group). Pregnancy outcomes including rate of preterm delivery were compared, and the effect of potential risk factors such as depth of cone, interval between conization and pregnancy, and cervical length on the risk of preterm delivery was assessed.

Results: The rate of preterm delivery was significantly higher in women with a history of electrosurgical conization than those without (32.1% vs. 15.2%, $p < 0.001$). However, preterm delivery rate was not different between the two groups (expectant group vs. cerclage group; < 28 week, 6.5% vs. 8.0%, $p = 1.000$; < 34 week, 19.4% vs. 20.0%, $p = 1.000$; < 37 week, 29.0% vs. 36.0%, $p = 0.579$). All obstetric and neonatal outcomes were similar in the two groups. Even when we confined the study subjects to 19 women (19/56, 33.9%) with cervical length less than 25 mm, the preterm delivery rate also was not significantly different between the expectant ($n = 7$) and cerclage group ($n = 12$). Finally, the potential risk factors for preterm delivery were not associated with risk of preterm delivery in patients with a history of electrosurgical conization.

Conclusion: The rate of preterm delivery was significantly higher in women with a history of electrosurgical conization before pregnancy. However, prophylactic cervical cerclage did not prevent preterm delivery in these patients.

Key Words: Conization, Preterm birth, Cervical cerclage

INTRODUCTION

Cervical cancer is the second most common cancer in female worldwide, and it is the leading cause of gynecological cancer-related morbidity and mortality in developing countries.¹ However, well-organized cervical screening programs and the appropriate management of screen-detected intraepithelial lesions has reduced the incidence of cervical cancer by up to 80%.²

Among the treatment options of excisional procedures, large loop excision of the transformation zone, also known as loop electrosurgical excision procedure (LEEP) has become a standard treatment for women with cervical intraepithelial neoplasia (CIN) in the industrialized world.^{3,4} However, the differ-

ence in the excisional procedure may potentially affect the outcomes of subsequent pregnancies, especially the risk of preterm delivery in women with a history of cervical conization.

Cerclage of the uterine cervix has been tried as an effort to reduce the incidence of preterm delivery in patients with a history of conization, but its efficacy still remains unclear. With this background, this study was conducted to evaluate the influence of conization on the following pregnancy, and whether prophylactic cervical cerclage can change the outcome of pregnancy in women with a history of electrosurgical cervical conization.

MATERIALS AND METHODS

We retrospectively reviewed the medical records to evaluate the obstetric and neonatal outcomes of all patients with a singleton pregnancy and a history of conization due to CIN or carcinoma in situ (CIS), who were treated and delivered at the Samsung Medical Center between January 2001 and December 2008. In all patients, thorough history including prior preterm delivery as well as complete clinical and physical examinations were done antenatally. Cervical length was measured by transvaginal ultrasonography before cerclage. Although a cervical length of

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less than 25 mm was considered to be short, the decision of cerclage was made by patients after obtaining explanation of her cervical status and the controversial role of cerclage in preventing preterm delivery after conization. Of the 56 cases, 25 women underwent cerclage (cerclage group) and 31 pregnant women did not want cerclage (expectant group). Pregnancies complicated by fetal death, multiple pregnancy, fetal chromosomal or non-chromosomal anomalies, diabetes, and serious maternal medical diseases were excluded from this study.

The conization procedure is noted as follows. Firstly, a colposcopic examination was taken to identify the margins of the lesion. Then, the electrosurgical conization was performed by using a right-angled triangular loop, carrying a high frequency current which can penetrate tissue more deeply toward the uterine endocervix than the conventional round loop.⁵ Thereafter, a cold coagulator (120°C) was applied to the cone bed for 30-60 seconds after excision for the purpose of hemostasis and destruction of any residual lesion after electrosurgical excision. Fig. 1 shows an example of a sagittal T2-weighted magnetic resonance image of a large iatrogenic cervical defect caused by electrosurgical conization.

Cervical cerclage was performed prophylactically between 14 and 19 gestational weeks by two maternal-fetal medicine specialists. The McDonald technique was used in all patients in the cerclage group. All of them were given perioperative intravenous antibiotics. The knots of the cerclage were removed regardless of membrane status if a patient went into spontaneous preterm labor. Otherwise, the knots were removed electively at 36-37 gestational weeks and patients were allowed to await spontaneous onset of labor, or induction of labor was proceeded

Fig. 1. An abdominopelvic magnetic resonance imaging (MRI) taken after conization for early cervical cancer stage IA1. There is no demonstrable cervical cancer on the current MRI view. Note the large defect in the cervix as a cone shape after electrosurgical conization procedure (arrow).

when indicated. Two consecutive doses of corticosteroid (betamethasone) were administered intramuscularly for fetal lung maturation if there was any sign of preterm delivery (i.e., regular uterine contractions and cervical dilatation despite the cerclage, preterm premature rupture of membranes [PPROM]) in patients with gestational age 24-34 weeks. The use of tocolytics was at the discretion of the attending physician when regular uterine contractions were developed. Tocolytics were used after removal of the cerclage when spontaneous preterm labor was noticed regardless of cervical status.

The antenatal parameters analyzed were maternal demographic characteristics, the indication and method of conization, depth of cone, interval between conization and pregnancy, and cervical length before cerclage. Obstetric outcomes analyzed were antepartum bleeding episodes, abortion, frequency of admission due to preterm labor per patient, admission duration for preterm labor per patient, tocolytics and antenatal corticosteroid use, preterm delivery, PPRM, gestational age at delivery, and mode of delivery. Neonatal outcomes were analyzed with respect to birth weight, Apgar scores, necessity and duration of ventilator therapy, and duration of neonatal intensive care unit (NICU) stay. In addition, neonatal morbidities including respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), periventricular leukomalacia (PVL), grade 3-4 intraventricular hemorrhage (IVH), grade 3-4 retinopathy of prematurity (ROP), stage 2-3 necrotizing enterocolitis (NEC), suspected or proven early and late neonatal sepsis, and mortality were analyzed. RDS was diagnosed in the presence of respiratory grunting and retracting, an increased oxygen requirement ($\text{FiO}_2 > 0.4$) and diagnostic radiographic chest findings. BPD was defined as a need for supplementary oxygen for ≥ 28 days or by diagnostic radiographic or histological findings. IVH and PVL were diagnosed and graded by ultrasonographic examination of the neonatal brain. IVH was defined as intraventricular bleeding with ventricular dilatation (grade 3) or with parenchymal involvement (grade 4). PVL was defined as the presence of an obvious hypochoic cyst in the periventricular white matter. ROP was diagnosed by ophthalmologists and its grading was based on the International Classification of Retinopathy of Prematurity.⁶ NEC was diagnosed on the basis of various clinical and radiological parameters and grouped in 3 stages as per modified Bell's classification.⁷ The diagnosis of neonatal sepsis was based on the presence of a positive blood culture (proven sepsis) or positive laboratory evidence in clinically suspected neonates (suspected sepsis). Composite morbidity was defined as having more than one of the followings: fetal death, RDS, BPD, PVL, IVH ($\geq$ grade 3), ROP ($\geq$ grade 3), NEC ($\geq$ stage 2), and neonatal sepsis.

Data were presented as percent for categorical variables and median (range) for continuous variables. Fisher exact or chi-square tests were used for the statistical analysis of categorical variables, as appropriate, and Mann-Whitney U tests were used for continuous variables. The results were consid-

ered statistically significant when p-values were <0.05.

RESULTS

During the 8-year period of review, 56 cases of patients who met the inclusion criteria of this study were identified among 22,126 deliveries. The rate of preterm delivery was significantly higher in pregnant women having a history of conization than the remainder of the study population (32.1% [18/56] vs. 15.2% [3,355/22,070], $p < 0.001$).

Of the 56 cases, 31 pregnant women were included in the expectant group and 25 women were included in the cerclage group. The demographic characteristics of the patients, indication for conization, cone depth and the interval between conization and pregnancy were similar in the two groups (Table 1). Cervical length of the patients in the conization group was significantly shorter than those in the expectant group. In addition, cervical cerclage rate was higher in patients with cervical length shorter than 25 mm (12/19, 63.2%) compared to those with normal cervical length (13/37, 35.1%), but the difference did not reach statistical significance ($p = 0.055$). The mean interval from admission due to preterm labor (cerclage removal) to delivery in patients who received tocolytics was 3.00 ± 3.69 days in the cerclage group and 6.13 ± 5.94 days in the expectant group ($p = 0.281$).

Obstetric outcomes including frequency of antepartum bleeding episode, admission due to preterm labor, use of tocolytics or antenatal corticosteroid were not significantly different between the two groups (Table 2). The rate of preterm de-

livery and PPROM and median gestational age at delivery were similar in the two groups. The mode of delivery and indication of cesarean delivery of the two groups were also not significantly different. In accordance to this result, the neonatal outcomes were similar in the two groups (Table 3). Composite neonatal morbidity also did not show statistical difference between the cerclage and the expectant group.

Since short cervical length is a well known risk factor for preterm delivery, and the cervical length of the study subjects were different between the two groups, we re-analyzed the data of 19 patients with short cervical length (less than 25 mm). Seven women were managed expectantly and the other 12 women underwent cerclage operation. Maternal age (expectant group vs. cerclage group, 31.0 years [29 to 35] vs. 30.5 years [27 to 40], $p = 0.910$), depth of cone (2.2 cm [1.5 to 2.5] vs. 2.2 cm [2.0 to 3.2], $p = 0.321$), cervical length (2.0 cm [1.5 to 2.4] vs. 2.0 cm [1.1 to 3.1], $p = 0.837$), interval between conization and pregnancy (24 months [7 to 36] vs. 14 months [4 to 96], $p = 0.650$), gestational age at delivery (37.0 weeks [27.3 to 39.0] vs. 38.3 weeks [25.0 to 39.6], $p = 0.343$), rate of preterm delivery (3/7 [42.9%] vs. 3/12 [25.0%], $p = 0.617$) was not significantly different between patients who underwent cerclage and those managed expectantly. All neonatal outcomes also were not different significantly between the two groups (data not shown).

Because cerclage was not preventive for preterm delivery in patients with a history of electrosurgical conization, we tried to find out other risk factors for preterm delivery in these patients. Of the 56 cases, 18 pregnant women delivered pre-

Table 1. Comparison of demographic characteristics and antenatal parameters between the expectant group and cerclage group

	Expectant (n=31)	Cerclage (n=25)	p-value
Age (yr)	32 (28-40)	30 (24-41)	0.136
Height (cm)	162.0 (153.0-172.0)	162.0 (147.0-172.0)	0.535
Weight (kg)	67.0 (51.8-87.2)	62.0 (49.4-81.0)	0.052
Nulliparity	8 (25.8)	13 (52.0)	0.044
History of preterm delivery*	2 (6.5)	2 (8.0)	1.000
Abortion history*	4 (12.9)	3 (12.0)	1.000
IVF-ET pregnancy*	0 (0.0)	2 (8.0)	0.195
Smoking*	1 (3.2)	1 (4.0)	1.000
Indication for conization			
CIN I*	7 (22.6)	3 (12.0)	0.485
CIN II*	5 (16.1)	6 (24.0)	0.514
CIN III	10 (32.3)	7 (28.0)	0.730
CIS	9 (29.0)	9 (36.0)	0.579
Cone depth (cm)	2.0 (1.0-3.0)	2.0 (1.3-3.2)	0.635
Cervical length (cm)	3.0 (1.5-5.8)	2.6 (1.1-3.4)	0.008
≤ 2.5	7 (22.6)	12 (48.0)	0.055
≤ 2.0	4 (12.9)	7 (28.0)	0.176
Funneling	1 (3.3)	2 (8.0)	0.585
Interval between conization and pregnancy (mo)	19 (1-55)	19 (3-96)	0.471

Data were presented as number (%) or median (range). Statistical analyses were performed using chi-square tests and *Fisher's exact tests for categorical variables and Mann-Whitney U tests were used for continuous variables. Statistical significance indicated $p < 0.05$.

IVF-ET: in vitro fertilization-embryo transfer, CIN: cervical intraepithelial neoplasia, CIS: carcinoma in situ.

Table 2. Comparison of obstetric outcomes between the expectant group and the cerclage group

	Expectant (n=31)	Cerclage (n=25)	p-value
Antepartum bleeding episode*	0 (0.0)	3 (12.0)	0.083
Admission due to preterm labor	11 (35.5)	10 (40.0)	0.729
Frequency of admission due to preterm labor per patient	0 (0-2)	0 (0-2)	0.575
Admission duration for preterm labor per patient [†] (day)	11 (1-33)	8 (1-38)	0.750
Tocolytics use	8 (25.8)	7 (28.0)	0.854
Antenatal corticosteroid use	6 (19.4)	6 (24.0)	0.674
Gestational age at delivery (wk)	38.0 (27.3-40.4)	38.2 (25.0-40.6)	0.788
Preterm delivery* (wk)			
Before 28	2 (6.5)	2 (8.0)	1.000
Before 34	6 (19.4)	5 (20.0)	1.000
Before 37	9 (29.0)	9 (36.0)	0.579
Preterm premature rupture of membranes (wk)			
Before 28*	2 (6.5)	2 (8.0)	1.000
Before 32*	5 (16.1)	4 (16.0)	1.000
Before 34	7 (22.6)	5 (20.0)	0.815
Before 37	13 (41.9)	10 (40.0)	0.884
Delivery mode			
Vaginal delivery	18 (58.1)	9 (36.0)	0.100
Cesarean delivery	13 (41.9)	16 (64.0)	0.100
Emergency cesarean delivery*	9/13 (69.2)	11/16 (68.8)	1.000
Cesarean delivery indication			
Secondary arrest of dilatation*	4 (30.8)	2 (13.3)	0.372
Arrest of descent*	0 (0.0)	3 (20.0)	0.226
Previous Cesarean section*	5 (38.5)	2 (13.3)	0.198
Breech presentation*	1 (7.7)	3 (20.0)	0.600
Others*	3 (23.1)	5 (33.3)	0.686
Mean interval between cerclage removal or admission due to preterm labor and delivery (day)	3.0±3.7	6.1±6.0	0.281

Values are presented as number (%) or median (range). Statistical analyses were performed using chi-square tests and *Fisher's exact tests for categorical variables and Mann-Whitney U tests were used for continuous variables. [†] Analyzed with patients who admitted for preterm labor only. Statistical significance indicated $p < 0.05$.

term (preterm group) and 38 women delivered at term (full term group). We compared the demographic characteristics and potential antenatal risk factors for preterm delivery between the two groups (Table 4). However, maternal characteristics, cone depth, cervical length, and interval between conization and pregnancy were not significantly different between the two groups.

DISCUSSION

This study evaluated the outcomes of pregnancy after electrosurgical conization: preterm delivery rate and the effect of the prophylactic cervical cerclage. Our results showed that the risk of preterm delivery was significantly increased in women with a history of electrosurgical cervical conization before pregnancy. However, it is questionable whether prophylactic cervical cerclage is beneficial for these high-risk patients in preventing preterm delivery.

Any surgical procedure of the cervix including conization has a potential of causing cervical incompetence which sub-

sequently leads to abortion or preterm delivery during the following pregnancy. Early study results show that conization does not constitute a hazard to the outcome of future pregnancies.⁸⁻¹⁰ However, recent studies have reported that conization can lead to impaired outcomes of pregnancy.¹¹⁻¹³ The incidence of preterm deliveries following conization varies in recent publications between 14 and 25%.^{11,12} These conflicting findings might be explained by differences in the study period population, and operative techniques such as instruments used for conization, depth, width and volume of the removed cones. Leiman et al.¹⁴ found that the risk of premature delivery and late spontaneous abortion increased in direct proportion to the cone size. In our study, cone depth was not associated with risk of preterm delivery in pregnancies after conization. However, the volume of removed cones was not evaluated, and it might be presumed the electrosurgical conization method using a right-angled, triangular loop with cold coagulation would have removed large volume of cone tissues as shown in Fig. 1.

The overall obstetric outcomes after electrosurgical excision

Table 3. Comparison of neonatal outcomes between the expectant group and the cerclage group

	Expectant (n=31)	Cerclage (n=25)	p-value
Male	17 (56.7)	9 (36.0)	0.126
Low birth weight* (g)	3,000 (1,220-3,700)	3,000 (680-4,200)	0.554
<2,000	6 (19.4)	3 (12.0)	0.487
<1,500	3 (9.7)	2 (8.0)	1.000
<1,000	0 (0.0)	2 (8.0)	0.202
Apgar score			
1 min <4	0 (0.0)	0 (0.0)	-
5 min <7	0 (0.0)	0 (0.0)	-
NICU admission*	7 (22.6)	4 (16.0)	0.737
Duration of NICU stay (day)	17 (5-54)	32.5 (20-90)	0.154
Ventilator treatment	1 (3.2)	3 (12.0)	0.314
Neonatal mortality	0 (0.0)	0 (0.0)	-
Neonatal morbidity			
Respiratory distress syndrome*	0 (0.0)	3 (12.0)	0.083
Bronchopulmonary dysplasia*	0 (0.0)	2 (8.0)	0.195
Periventricular leukomalacia*	0 (0.0)	1 (4.0)	0.446
Intraventricular hemorrhage (≥grade 3)	0 (0.0)	0 (0.0)	-
Retinopathy of prematurity (≥grade 3)*	0 (0.0)	0 (0.0)	-
Necrotizing enterocolitis (≥stage 2)*	1 (3.2)	0 (0.0)	1.000
Suspected or proven early sepsis*	3 (9.7)	1 (4.0)	0.620
Suspected or proven late sepsis	0 (0.0)	0 (0.0)	-
Composite morbidity [†]	4 (12.9)	4 (16.0)	1.000

Data were presented as number (%) or median (range). Statistical analyses were performed using chi-square tests, *Fisher's exact tests for categorical variables and Mann-Whitney U tests were used for continuous variables. Statistical significance indicated $p < 0.05$. [†]Defined as having more than one of the following: respiratory distress syndrome, bronchopulmonary dysplasia, periventricular leukomalacia, intraventricular hemorrhage (≥grade 3), retinopathy of prematurity (≥grade 3), necrotizing enterocolitis (≥stage 2), suspected or proven early and late neonatal sepsis.

NICU: neonatal intensive care unit.

Table 4. Comparison of demographic characteristics and antenatal parameters between the preterm delivery group and full term delivery group

	Preterm delivery (n=18)	Full term delivery (n=38)	p-value
Age (yr)	30 (27-39)	32 (24-41)	0.087
Height (cm)	163.0 (151.0-171.0)	160.0 (147.0-172.0)	0.088
Weight (kg)	61.0 (49.5-78.0)	67.0 (49.4-87.2)	0.160
Nulliparity	6 (33.3)	15 (39.5)	0.658
History of preterm delivery*	3 (16.7)	1 (2.6)	0.093
Smoking*	2 (11.1)	0 (0.0)	0.099
Indication for conization			
CIN I*	3 (16.7)	7 (18.4)	1.000
CIN II*	2 (11.1)	9 (23.7)	0.473
CIN III	6 (33.3)	11 (28.9)	0.739
CIS	7 (38.9)	11 (28.9)	0.457
Cone depth (cm)	2.0 (1.5-2.6)	2.0 (1.0-3.2)	0.885
Cervical length (cm)	2.8 (1.4-3.6)	3.0 (1.1-5.8)	0.327
≤2.5	6 (33.3)	13 (35.1)	0.895
≤2.0	4 (22.2)	7 (18.9)	1.000
Funneling	1 (5.6)	2 (5.4)	1.000
Interval between conization and delivery (mo)	12.0 (3-96)	19.5 (1-60)	0.734
Gestational age at delivery (wk)	32.4 (27.3-36.1)	38.5 (37.0-40.6)	<0.001

Data were presented as number (%) or median (range). Statistical analyses were performed using chi-square tests and *Fisher's exact tests for categorical variables and Mann-Whitney U tests were used for continuous variables. Statistical significance indicated $p < 0.05$.

CIN: cervical intraepithelial neoplasia, CIS: carcinoma in situ.

in our study showed different results from earlier reports by others.¹⁵⁻¹⁷ Common conclusions of earlier studies were that the diathermy loop excision does not affect fertility and pregnancy outcome. However, none of these studies seem to have analyzed the overall rates of pregnancy and preterm delivery after conization, even in a single institute. Because conization itself most often cures the cervical lesion, the patients are not usually required for long term follow-up at a gynecologic oncologic clinic, and a considerable number of patients is lost to follow-up. In our study, we recruited almost all patients who became pregnant after conization in our institute. All excisional procedures used to treat cervical intraepithelial neoplasia have a potential to bring about adverse obstetric morbidity, but only cold-knife conization is proven to significantly increase adverse outcomes that is similar to our results.¹⁸

An increasing number of reproductive-age women with cervical lesions are being treated with local excisional procedures. In particular, the right-angled triangular shape cone biopsy excisors with a ball diathermy is known to be more effective than the U-shaped loop in women who want to preserve fertility because of its higher rate of removing the transformation zone at once, or with fewer times and with a lower rate of margin positive and recurrent rate, and a better maintenance of shape of uterine cervix after the procedure.^{19,20} Despite the advantages, these procedures may alter the cervical environment by damaging the integrity of tissue, and thus might affect cervical competence. These women might also have an increased risk of preterm delivery because cervical conization removes a sizeable part of the connective tissue which can possibly lead to a weakening of cervical tissue, and inability to support the pregnant uterus.²¹ Therefore, cervical cerclage has been performed as an effort to reduce the risk of preterm delivery. However, the cerclage may itself be a risk factor for preterm delivery. Sutures can act as a foreign body which may cause uterine irritability and lead to contractions after a cerclage procedure.²² Moreover, some authors reported a significant increase of pathogenic flora in the vagina and cervix after cerclage.²³ Along with previous reports in which cerclage after conization had no benefit on pregnancy outcomes,²⁴⁻²⁶ our study also showed that cervical cerclage after electrosurgical conization did not convincingly reduce the rate of spontaneous preterm delivery. We performed the McDonald procedure for cerclage in this study, but we are not sure that the Shirodkar procedure would have made a difference in the rate of preterm delivery, because preterm delivery rates were similar whether the cervical length were more or less than 25 mm before cerclage. Therefore, we suggest that using a colposcope-guided conization may be an option to reduce the volume of removed tissue so as to minimize the adverse effects on future pregnancies. We also suggest a more sparing use of cerclage for women with a history of conization because the efficacy and safety of the prophylactic cervical cerclage is still controversial.

To date, there is no randomized trial to evaluate the effect of prophylactic cervical cerclage after conization. The main streng-

th of our study is that almost all patients were followed up for the antenatal care and delivery after conization, and the procedure of each conization and cerclage was performed with the same method in a single institute. However, the main limitation of our study is its non-randomized retrospective nature and the small number of subjects included in the study. Therefore a larger number of prospective randomized controlled trials are needed to confirm the effect of prophylactic cervical cerclage after conization.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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