Pregnancy outcome after cervical conization: risk factors for preterm delivery and the efficacy of prophylactic cerclage

Ka Hyun Nam, Ja Young Kwon, Young-Han Kim, Yong-Won Park
Department of Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, Korea

Objective: This study examined the risk factors for preterm birth and the efficacy of prophylactic cerclage in patients who had undergone cervical conization due to cervical intraepithelial neoplasia before pregnancy.

Methods: We reviewed the medical records of all patients who gave live singleton births between May 1996 and April 2009, after having cervical conization. Delivery before 37 gestational weeks was considered as preterm birth. The pregnancy outcomes were analyzed with independent sample t-test, chi-square test, and multiple logistic regression using the SPSS ver. 12.0.

Results: Sixty five cases were found. The mean gestational age at delivery was 37 weeks (SD, 3.5). Eighteen patients (27.7%) had preterm delivery. The type of conization, the volume of the specimen, and second trimester cervical length were related to preterm birth (p ≤ 0.001, p=0.019, p ≤ 0.001, respectively). In multivariate analysis, only mid-trimester cervical length was statistically significant for preterm birth (p=0.012; odds ratio, 0.194; confidence interval, 0.055 to 0.693). Six out of 65 patients had undergone prophylactic cerclage, and three (50%) of them had preterm births, while 15 (25%) patients without cerclage had preterm births.

Conclusion: The type of conization, the volume of specimen, and second trimester cervical length may be the risk factors for preterm birth in patients who have a prior history of cervical conization. Prophylactic cerclage may not be helpful in preventing preterm birth, therefore more careful consideration should be paid in deciding cerclage after conization during prenatal counseling.

Key Words: Conization, Preterm birth, Cervical cerclage

INTRODUCTION

The incidence of abnormal cervical cytology is rising; especially among women of reproductive age. Consequently, we can expect a higher percentage of pregnancies with a previous conization than before. To treat cervical intraepithelial neoplasia (CIN), various procedures including conization, cryotherapy, laser, and loop electrosurgical excision procedure (LEEP) have been used. Among them, LEEP has become the most widely used method. LEEP is cheaper, does not require general anesthesia or an operating room facility, and is an office-based procedure that is therefore more convenient for both the physician and the patient than cold knife conization. Although it is still controversial, conization of the cervix for the treatment of CIN is known to be related with adverse pregnancy outcomes in subsequent pregnancies, including preterm delivery, low birth weight infants, incompetent cervix, and cervical stenosis.

Most of all, preterm birth is the most notable complication because it can be a major cause of perinatal morbidity and mortality. In particular, infants who are born at earlier gestational ages are at the greatest risk of illness, injury, and handicap. The rate of preterm birth is generally increasing despite improvements in perinatal care over the past two decades. Regarding the risk factors of preterm birth in patients with prior conization, many factors have been suggested, including cervical length, specimen volume, and the interval between LEEP procedure and delivery. As for the need for prophylactic cerclage, controversy still exists.

Therefore, in this study, we investigated the risk factors for preterm birth and the efficacy of prophylactic cerclage in pregnant women who had undergone cervical conization due to cervical intraepithelial lesions prior to the pregnancy.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of all pa-
Table 1. Patient characteristics and univariate analysis for preterm delivery

<table>
<thead>
<tr>
<th></th>
<th>Total (n=65)</th>
<th>Preterm delivery (n=18)</th>
<th>Term delivery (n=47)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)*</td>
<td>31±3.7</td>
<td>30.8±3.8</td>
<td>31.2±3.7</td>
<td>0.707</td>
</tr>
<tr>
<td>Parity (n)‡</td>
<td>1 (0-3)</td>
<td>1 (0-2)</td>
<td>1 (0-3)</td>
<td>0.649</td>
</tr>
<tr>
<td>Prior preterm history†</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>0.999</td>
</tr>
<tr>
<td>Gestational age at delivery (wk)*</td>
<td>37.2±3.5</td>
<td>32.9±3.8</td>
<td>38.9±1.1</td>
<td></td>
</tr>
<tr>
<td>Interval between conization and delivery (mo)*</td>
<td>20.5±12.5</td>
<td>20.1±12.7</td>
<td>20.6±12.5</td>
<td>0.124</td>
</tr>
<tr>
<td>Times of conization†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Once</td>
<td>55 (84.6)</td>
<td>13 (23.6)</td>
<td>42 (76.4)</td>
<td></td>
</tr>
<tr>
<td>Twice</td>
<td>10 (15.4)</td>
<td>5 (50)</td>
<td>5 (50)</td>
<td></td>
</tr>
<tr>
<td>Type of conization†</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>LEEP</td>
<td>51 (78.5)</td>
<td>9 (17.6)</td>
<td>42 (82.4)</td>
<td></td>
</tr>
<tr>
<td>Cold knife</td>
<td>14 (21.5)</td>
<td>9 (64.3)</td>
<td>5 (35.7)</td>
<td></td>
</tr>
<tr>
<td>Volume of specimen (cm³)*</td>
<td>6.0±3.5</td>
<td>7.7±4.1</td>
<td>5.4±3.0</td>
<td>0.019</td>
</tr>
<tr>
<td>Mid-trimester cervical length (cm)*</td>
<td>2.4±0.9</td>
<td>1.7±0.9</td>
<td>2.7±0.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Cerclage</td>
<td>6 (100)</td>
<td>3 (50)</td>
<td>3 (50)</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented mean±SD or numbers (%).
LEEP: loop electrosurgical excision procedure.
*p-value by t-test. †p-value by chi-square test (Fisher’s exact test). ‡p-value by Mann-Whitney U-test.

Table 2. Multivariate analysis for preterm delivery

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% Confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Interval between conization and delivery</td>
<td>0.962</td>
<td>0.870</td>
<td>1.063</td>
</tr>
<tr>
<td>Times of conization</td>
<td>1.364</td>
<td>0.147</td>
<td>12.685</td>
</tr>
<tr>
<td>Type of conization</td>
<td>4.621</td>
<td>0.398</td>
<td>53.687</td>
</tr>
<tr>
<td>Volume of specimen</td>
<td>1.383</td>
<td>0.984</td>
<td>1.944</td>
</tr>
<tr>
<td>Cervical length*</td>
<td>0.194</td>
<td>0.055</td>
<td>0.693</td>
</tr>
</tbody>
</table>

p-value by logistic regression.
*Statistically significant.
Table 3. Patients with prophylactic cerclage

<table>
<thead>
<tr>
<th>Gestational weeks at operation</th>
<th>Indication</th>
<th>Mid-trimester cervical length (cm)</th>
<th>Gestational weeks at delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Preoperative</td>
<td>Postoperative</td>
</tr>
<tr>
<td>1</td>
<td>Prior preterm birth</td>
<td>3.6</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>Short cervical length</td>
<td>1.1</td>
<td>2.7</td>
</tr>
<tr>
<td>3 *</td>
<td>Prior preterm birth</td>
<td>3.5</td>
<td>N/A</td>
</tr>
<tr>
<td>4 *</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>6 *</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

All underwent McDonald’s operation.
N/A: not available.
*Cerclage operations were performed at other institutions, both consisting of cold knife conization rather than loop electrosurgical excision procedure.

Table 4. Cerclage according to mid-trimester cervical length

<table>
<thead>
<tr>
<th>Cervical length</th>
<th>Cerclage (n=6)</th>
<th>No cerclage (n=59)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2.5 cm</td>
<td>3 (1*)</td>
<td>16 (8*)</td>
<td>19</td>
</tr>
<tr>
<td>&gt;2.5 cm</td>
<td>1 (0*)</td>
<td>19 (2*)</td>
<td>20</td>
</tr>
<tr>
<td>Not mentioned</td>
<td>2 (2*)</td>
<td>24 (5*)</td>
<td>26</td>
</tr>
</tbody>
</table>

*The number of preterm deliveries before 37 gestational weeks.

DISCUSSION

Cervical cancer is still the most common malignancy affecting Korean women, but the mortality rate has declined with the efforts to detect precancerous lesions earlier using cervical cytology and colposcopy.20 As the most prevalent age is in the 30's, the need for conservative treatment is rising.21 Since the introduction of cervical conization in the late 1950's, many studies on cervical conization and pregnancy outcomes have been published. In particular, many studies have emphasized on the relationship between conization and preterm birth.7,14,22-26 Even though some authors found no relationship,25,27 many authors have agreed on the significant correlation between cervical conization and preterm delivery.7,14,23-26 They suggested various associated factors including short cervical length,28-30 size of the specimen removed,9,12,31,32 the time interval between conization and delivery,4,15,33 and type of conization.34

In this study, the results showed that the type of conization, the volume of specimen, and second trimester cervical length were related to preterm birth in univariate analysis, and in multiple regression analysis, second trimester cervical length was found to influence the gestational age at birth.

The results are consistent with previous studies. Michelin et al.34 demonstrated that LEEP was the procedure of choice for the patients who wanted to be pregnant, because more miscarriages and preterm pregnancies occur in conization cases than in LEEP cases.

As for the size of the conization specimen, few studies are available; especially regarding the "volume" rather than the "depth" of conization have been seldom published. Leiman et al.9 suggested that a large cone of more than 4 mL of volume is associated with preterm delivery.

Many studies performed on the cervical length measurement by transvaginal ultrasonography.16,19,28,29,35 They reported that cervical length measurement by transvaginal ultrasonography is an accurate and valid method of measuring the cervix,35 and may be a useful method of predicting who is at risk for preterm delivery.16,19 This hypothesis turned out to be true with postconization patients.28 The cervical length appears to be inversely proportional to the risk of preterm birth.19 Our study strongly supports this result.

Our study also revealed the interval between conization and delivery is inversely proportional to the risk of preterm birth. Many studies demonstrated that the healing process is completed in 3 months after conization.31,36 Himes and Simhan33 suggested that a short conization-to-pregnancy interval, especially shorter than 2-3 months, increases the risk of preterm delivery. The length of the cervix is shortened when measured by ultrasonographic measurement just after conization.35 However, after adequate healing time after LEEP, the length does not remain shortened.4 Not much is known regarding the times of conization. It is...
The benefit of prophylactic cerclage in women with a history of conization is not clear. Leiman et al. concluded that all postcone pregnancies should be regarded as high risk, and recommended cerclage in pregnancies following extensive cone biopsy. In contrast, Kullander and Sjoberg concluded that cerclage should be avoided because they were unable to show that it reduces the incidence of preterm delivery in women after conization. Myllynen and Karjalainen and Zeisler et al. proposed that prophylactic cerclage should be used more sparingly, because it does not prevent preterm delivery, and tends to induce preterm uterine contractions. They reported that cerclage itself may be a risk factor. Sutures can act as a foreign body and lead to uterine irritability and contractions after a cerclage procedure. Moreover, some authors reported a significant increase in pathogenic flora in the vagina and cervix after cerclage. They insisted that the release of prostaglandins by bacteria in the vagina may induce chorioamnionitis, preterm premature rupture of membranes, preterm delivery, and sepsis. In this study, preterm births occurred in 50% (n=3) of patients after cerclage. The number of patients was too small to compare the efficacy of the cerclage, but cerclage may not be helpful in preventing preterm delivery, and can only add complications following operative procedures. A further study with a large number of patients may be done on the efficacy of cerclage according to the cervical length, the gestational age at delivery, and the indication of cerclage.

In previous studies on pregnancy outcome after conization, most studies have dealt whether there are adverse perinatal outcomes such as preterm birth, low birth weight, or whether conization itself may be a risk factor for preterm birth. We focused on the associated factors for preterm birth, and we integrated all associated factors together rather than as a single factor. There are few studies on the risk factors for preterm birth after conization. We included "volume removed" rather than "depth (or height)" of the specimen that most previous studies have dealt with.

This study contains the largest numbers of Korean patients ever published on this subject, but the sample size is still small. Moreover, as this study was a retrospective cohort study, there may have been confounders not identified or controlled. A further prospective study with a larger sample size is needed.

In conclusion, in patients with a prior history of cervical conization, the type of conization, volume of conization, and second trimester cervical length influence preterm delivery with statistical significance. Thus close observation, especially with the mid-trimester cervical length is needed for the management of such patients. Since the need for prophylactic cerclage remains questionable in this study, we suggest that prudent decision should be made regarding prophylactic cerclage during prenatal counseling.

**CONFLICT OF INTEREST**

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

**REFERENCES**

16. Berghella V. Novel developments on cervical length screening
Pregnancy outcome after cervical conization


