

An electrical scalpel conization versus Shimodaira-Taniguchi conization procedure for cervical intraepithelial neoplasia

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Abstract

The incidence of cervical intraepithelial neoplasia (CIN) among reproductive-aged women has increased in Japan. Cervical conization is commonly applied for local cervical treatment to preserve fertility. The Shimodaira-Taniguchi (S-T) conization procedure is widely used in Japan. S-T conization uses a high-frequency current and a triangular probe with a linear excision electrode to remove cervical tissue as a single informative specimen. However, alternative of an electrosurgical scalpel (ES) has the advantage of adjusting the surgical margin to the transformation zone in order to preserve the maximum amount of healthy cervical tissue with good hemostasis. The aim of this study is to retrospectively analyze data regarding surgical margin status, perioperative adverse events, cervical stenosis, and preterm birth between S-T and ES.

Between January 2009 and December 2014, the medical records of 1166 patients who were diagnosed as CIN II, III, or stage 1a1 cervical cancer and who were treated with conization in 7 hospitals in Gunma Prefecture, Japan were enrolled for this retrospective study. The clinicopathological data was analyzed to statistically compare outcome between S-T and ES conization.

There was no difference for age or post-operative follow-up period between ES and S-T treatments. However, positive surgical margins were significantly less frequent in patients who were treated with S-T than in those treated with ES, resulting in a reduced incidence of re-treatment for S-T in comparison with ES patients. In perioperative adverse events, S-T had more patients who were administered antibiotics. The incidence of preterm delivery and cervical stenosis did not differ significantly between the groups.

We demonstrate here that S-T is an alternative procedure for cervical conization with a low risk of recurrence and acceptably low rate of adverse events such as cervical stenosis and preterm delivery. The results of this study can provide useful information for future management of patient with cervical intraepithelial neoplasia.

Abbreviations: CIN = cervical intraepithelial neoplasia, ES = electrosurgical scalpel, HPV = human papillomavirus, LEEP = loop electrosurgical excision, S-T = Shimodaira-Taniguchi.

Keywords: cervical intraepithelial neoplasia, conization, Shimodaira-Taniguchi procedure

1. Introduction

The incidence of cervical intraepithelial neoplasia (CIN) has recently increased in Japan, and the peak incidence of the disease occurs in women aged 40 to 45 years.^[1] These data suggest that many women at diagnosis have not completed child bearing. From the 1970s to 1980s, conservative treatments such as electrocautery, cryotherapy, and laser ablation were adopted. Although meta-analysis demonstrated that those conservative therapies have

comparable efficacy to cervical excision techniques,^[2] the concern that ablative therapies are less effective against cervical lesion^[3,4] has led to cervical excision being adopted in the last 2 decades as the most common procedure to treat high-grade CIN and micro-invasive carcinoma (stage 1a1) for women who desire to maintain their fertility. According to the annual report of the Committee on Gynecologic Oncology of the Japan Society of Obstetrics and Gynecology, the rate of conization to treat CIN III has increased to 79% in 2008 from 33% in 1990.

Historically, cold knife conization was used as a primary method for cervical excision to treat CIN. Alternative methods, such as electrosurgical scalpel (ES) conization, laser conization, and loop electrosurgical excision (LEEP),^[5] were subsequently developed. However, numerous studies have demonstrated that cervical excision is associated with adverse obstetric outcomes, resulting in increased spontaneous miscarriage, preterm birth, and perinatal morbidity.^[6–10] In Japan, the Shimodaira-Taniguchi (S-T) conization procedure was introduced in 1992, and it has subsequently been widely adopted since S-T conization has the advantages of being associated with less bleeding and of removing cervical lesions as single cone-shaped specimen. Several studies have concluded that S-T conization presents a viable alternative method, which has acceptable post-operative complications^[11–13] and comparable efficacy to other methods in terms of rate of positive margin and residual tumor formation.^[14]

Editor: Bernhard Schaller.

The authors have no conflicts of interest to disclose.

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Medicine (2018) 97:41(e12640)

Received: 20 May 2018 / Accepted: 7 September 2018

<http://dx.doi.org/10.1097/MD.0000000000012640>

Table 1**Patient characteristics.**

	Electrosurgical scalpel (n = 477)	Shimodaira-Taniguchi (n = 689)	P value
Age (years)	32.01 (19–39)*	32.26 (19–40)*	.36**
Post operative follow-up period (months)	36.36 (0–94)*	36.81 (0–107)*	.76**
smoking status			<.001***
no	351	342	
yes	100	65	
unknown	26	282	
Delivery history before operation			.79***
no	201	270	
yes	276	383	
unknown	0	36	
Delivery history after operation			.02***
no	308	456	
yes	102	107	
unknown	67	126	

* Average (range).

** t-test or.

*** Chi-squared test was used, respectively.

In our local medical society of Gunma Prefecture, ES and S-T conization procedures have been routinely used for the treatment of early cervical lesions. In the present study, we compared these methods in terms of adverse outcomes by analyzing retrospective data from patients who underwent the excision of cervical tumors.

2. Methods

Between 2009 and 2014, the medical records of 1166 CINII, CINIII and stage Ia1 patients who underwent conization were obtained for this retrospective study from 7 institutions belonging to Gunma medical local society: Gunma Prefectural Cancer Center, Gunma University, Isesaki Municipal Hospital, JCHO Gunma Chuo Hospital, Takasaki General Medical Center, Kiryu Kosei General Hospital, and Tone-Chuo-Hospital. Informed consent was not obtained from each participant because this was a retrospective study. Instead, all participants were given the right to withdraw their data from the study. The protocol of this study was approved by the individual institutions' ethical committees.

Data regarding patient age, follow-up period, smoking status, and delivery history before and after conization are summarized in Table 1. Preterm birth was defined as delivery before 37 weeks of gestation. The surgical margins of the conization specimens

were evaluated using pathological findings. Contact of CINIII or other lesions to the surgical margin was defined as a surgical margin positive sample. In addition, cervical canal curettage was executed for patients with adenocarcinoma in situ, since adenocarcinoma can form skip lesions. After conization, surveillance was conducted as follows: a pap test was taken at every visit and those with positive pap test results underwent a cervical biopsy to diagnose recurrence of CINIII or cervical cancer. Cervical stenosis was determined based on surgical intervention to solve clinical symptoms such as hematometra. All patients received regular follow-up care according to each hospital's standard policy. Missing data were excluded before statistical analysis.

Patient characteristics (age, postoperative follow-up period, smoking status, delivery history before operation, and delivery history after operation) were compared between the ES and S-T conization groups using *t*-tests and chi-squared tests to determine statistically significant differences (Table 1).

The odds ratios and 95% confidence intervals for clinical data regarding margin status after conization, recurrence after conization, preterm delivery, and cervical stenosis based on the difference in conization method were also calculated using logistic regression analysis (Table 2). Odds ratios and 95%

Table 2
The odds ratio and 95% confidence for clinical outcomes after conization by Shimodaira-Taniguchi method to conization by electrosurgical scalpel.

	electrosurgical scalpel	Shimodaira-Taniguchi	Odds ratio	95% CI	P value*
Surgical margin status positive					
negative	377	627	0.38	0.27–0.54	<.001
positive	97	62			
Recurrence after conization					
No	452	667	0.6	0.33–1.07	.08
Yes	25	22			
Preterm delivery					
No	81	81	1.36	0.59–3.13	.53
Yes	11	15			
Cervical stenosis					
No	465	654	1.5	0.70–3.21	.29
Yes	10	21			

CI = confidence interval.

* Logistic regression was used.

Table 3**The rate of recurrence by the margin status.**

	Recurrence	Odds ratio	95% CI	P value*
Electrosurgical scarpel				
Surgical margin status		0.21	0.04–0.48	<.001
Negative (n=377)	12 (3.2%)			
Positive (n=97)	13 (13.4%)			
Shimodaira-Taniguchi				
Surgical margin status		0.1	0.04–0.25	<.001
Negative (n=627)	12 (1.9%)			
Positive (n=62)	10 (16.1%)			

CI = confidence interval.

* Chi-squared test was used.

confidence intervals were determined for the rest of statistical analysis using chi-squared tests (Table 3, 4, 5, and 6). All the tests were 2-tailed, and a *P* value of <.05 was considered statistically significant. All statistical analyses were performed using SAS ver. 9.4.

3. Results

A total of 1,166 patients were enrolled in this retrospective study from 7 institutions in the local medical society of Gunma Prefecture. The characteristics of the ES and S-T groups were comparable concerning age (*P* = .36), post-operative follow-up period (*P* = .76), and delivery history before operation (*P* = .79). Smoking status (*P* < .0001) and delivery history after operation (*P* = .02) were higher in ES group than in S-T group. In both the ES and S-T groups, there were a few patients who had 0 months of follow-up as they were lost to follow up after relocation. Those patients were excluded from further analysis. Table 2 lists clinical outcomes after conization. In the multivariate logistic regression, ES was statistically associated with a positive surgical margin, which was the most important factor to predict tumor recurrence or relapse. However, the recurrence after conization was not statistically different between the 2 groups (*P* = .08). Similarly, there was not a significant difference in preterm delivery or cervical stenosis between ES and S-T groups. Thus, we further investigated factors which could be involved in surgical margin status, preterm delivery, and cervical stenosis.

Three cases in the ES group, in which the margin status was not clear, were excluded from the analysis. We first examined margin status by delivery history and age group (categorized into 3 groups of < 30, 30–34, and ≥ 35 years). We found that there was no significant difference in the margin status associated with either delivery history or age, between the ES and S-T groups (data not shown). As expected, the rate of recurrence was significantly higher in margin-positive than margin-negative patients for both ES (odds ratio 0.21, 95% CI 0.04–0.48, *P* < .001) and S-T (odds ratio 0.10, 95% CI 0.04–0.25, *P* < .0001; Table 3) groups. However, patients with a negative surgical margin did not differ in recurrence rate (3.2% for ES versus 1.9% for S-T). In fact, 47 patients suffered from recurrent cervical lesions: 26 patients were diagnosed with CINIII and 21 patients were diagnosed as having microinvasive tumors. All patients with CINIII had re-conization, whereas patients with microinvasive tumors were treated by re-conization in 10 cases, and simple hysterectomy in 11 cases, respectively.

We also checked the adverse events during the perioperative period (Table 4). Although the total number of events was low, the number of patients who were administered antibiotics was

Table 4**The adverse events after conization.**

	Electrosurgical scarpel (n=477)	Shimodaira-Taniguchi (n=689)	Odds ratio	95% CI	P value*
Infection	1	12	8.5	1.09–65.3	<.05
Bleeding	62	76	0.83	0.58–1.19	.32

CI = confidence interval.

* Chi-squared test was used.

higher in the S-T group than that in ES group (odds ratio 8.5, 95% CI 1.09–65.3, *P* < .05). In contrast, there was no statistical difference in patients who needed treatment such as gauze compression and suture for bleeding after conization (odds ratio 0.83, 95% CI 0.58–1.19, *P* < .32).

Several studies and meta-analyses have shown that local cervical treatment is associated with preterm birth. Thus, we analyzed this issue in our cohort patients. Overall, the incidence of preterm delivery was not different between ES and S-T patients (Table 2). However, when considering preterm birth history, the risk for preterm delivery in which patients had preterm delivery before conization was significantly higher (odds ratio 4.51, 95% CI 1.09–18.63, *P* = .02). We also found that women who had conization by S-T after preterm delivery experienced a higher incidence of preterm delivery (odds ratio 16.33, 95% CI 2.11–126.28, *P* = .02), compared to those who had conization by ES (odds ratio 2.50, 95% CI 0.28–22.34, *P* = .38; Table 5).

In addition to tumor recurrence and preterm delivery, cervical stenosis associated with an excisional procedure is another major factor that determines fecundity. The frequency of cervical stenosis did not differ between ES and S-T patients, occurring in 10 of 475 ES patients and 21 of 675 S-T patients (Table 2). We also examined whether age at the time of the operation affected cervical stenosis; age at operation did not raise cervical stenosis incidence for either ES or S-T patients (Table 6).

4. Discussion

Conization of the cervix is a standard treatment for patients with high-grade CIN or microinvasive carcinoma (stage 1a1) to prevent progression and to preserve fertility. Conization is also a

Table 5**Comparison of preterm delivery dependent on preterm delivery history after conization.**

	Preterm delivery after conization		Odds ratio (95% CI)	P value*
	No	Yes		
Electrosurgical scarpel			2.50 (0.28–22.34)	.38
Preterm delivery before conization				
No	175	10		
Yes	7	1		
Shimodaira-Taniguchi			16.33 (2.11–126.28)	.02
Preterm delivery before conization				
No	196	12		
Yes	2	2		

CI = confidence interval.

* Chi-squared test was used.

Table 6
Comprison of cervical stenosis by age group.

	Cervical stenosis after conization		P value*
	No	Yes	
Electrosurgical scalpel			.72
Age			
<30	132	4	
30–34	176	3	
35≥	157	3	
Shimodaira-Taniguchi			.47
Age			
<30	176	4	
30–34	229	10	
35≥	248	7	

* Chi-squared test was used.

widely-accepted diagnostic method for suspicious invasive carcinomas. To date, a variety of treatment methods such as electrocautery, cryotherapy, laser ablation, cold knife conization, hot knife conization, and LEEP have been applied to local cervical intraepithelial tumors. In our local medical area, ES and S-T have been widely used for treatment and diagnosis of cervical lesions. In this study, data from 1166 women who underwent conization by either ES or S-T were analyzed with regard to surgical margin status, preterm birth, and cervical stenosis between ES and S-T.

The results drawn by logistic analysis (Table 2) indicate that positive surgical margin status is the only significant difference between S-T and ES. The recurrence rate after conization by ES was higher when compared with S-T, although it was not statistically different. In our cohort patients, the rate of recurrence with or without positive margin for both methods was comparable (Table 3), consistent with previous reports.^[15,16] Earlier studies also found no difference in residual disease^[17] or cancer incidence^[18] between different methods. But 1 study reported that cold knife conization was inferior to other methods in terms of future cancer risk.^[19] However, since the average period after operation in our study was 36.36 months for ES and 36.81 months for S-T patients, (Table 1), we were not able to address this issue; longer observation times would be required.

As mentioned above, a major benefit of S-T conization is that cervical lesions are removed as single a cone-shape specimen for pathologists to can easily diagnose margin status. However, the depth of excised cone by the triangle probe in S-T conization (Fig. 1) is fixed based on the size of the transformation zone, whereas with ES, the cone size can be tailored excised cone size. This means that S-T may remove additional endocervical margin, particularly in the case of a small transformation zone, which can result in better outcomes for S-T in terms of margin status.

As shown in Table 4, the adverse events in the perioperative period were evaluated. There was a significant difference in the number of cases requiring intervention for post-operative infection between ES and S-T, whereas there was no difference in bleeding after conization. Currently, we cannot address the reason for the high incidence of infection in S-T but speculate that open wounds are more likely to develop infection since the wound was not sutured in 95.2% of the S-T group versus 21.0% of the ES group in our cohort cases. On the other hand, a high-frequency current and a triangular probe utilized by S-T have good hemostatic effect; therefore, there was no difference in the levels of bleeding between the 2 groups after conization.

Numerous studies have discussed the effect of conization on preterm birth, and the association of cervical excision with preterm birth is well-accepted.^[6–8,10,20] Thus, we investigated whether preterm birth after conization is specifically linked to preterm birth history or conization method. Patients with preterm history had an increased chance of preterm delivery in subsequent births. Interestingly, S-T further increased this risk when compared with ES (Table 5). In accordance with meta-analysis on post-treatment human papillomavirus (HPV) infection^[21], 10% of patients were diagnosed with persistent infection at 24 months. Moreover, HPV infection of the cervix has been shown to be related to adverse pregnancy outcomes and preterm birth.^[21,22] Thus, we assume that patients with preterm birth history have an elevated risk in subsequent pregnancies. However, at this stage, we do not have a clear rationale for why S-T increases the risk of preterm birth. We speculate that S-T might remove more cervix than ES, since S-T is associated with margin status.

Of all the conization-related complications, cervical stenosis most affects patients' later life, causing dysmenorrhea, infertility,

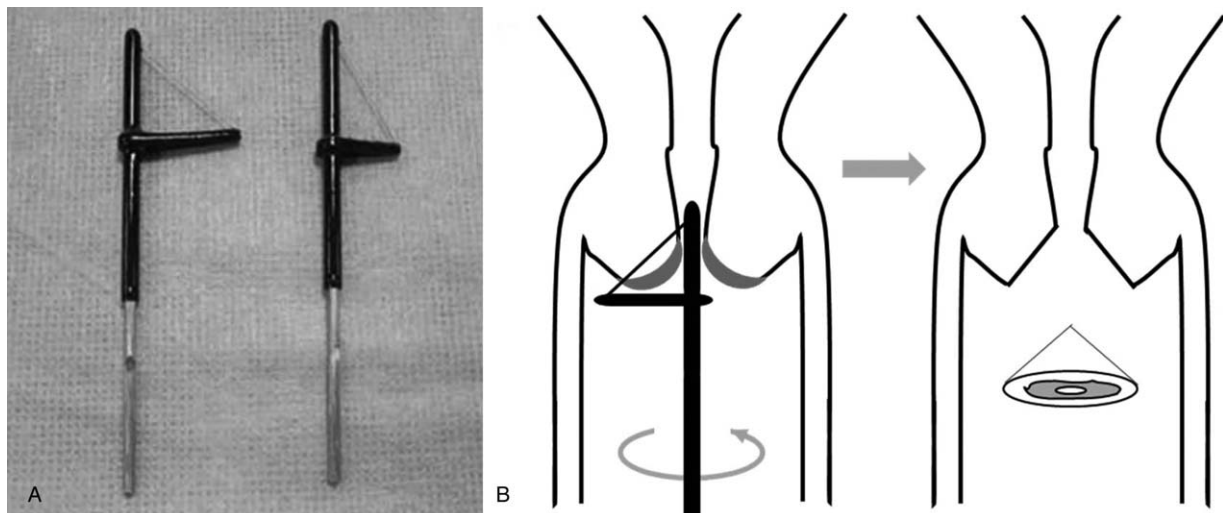


Figure 1. Shimodaira-taniguchi conization procedure. Cutting electrode probes (A) are used based on the width of S-C junction. A probe is inserted into cervical canal and rotated to obtain a specimen (B).

and difficulty in cytology screening during follow-up surveillance. In this study, the rate of stenosis was 2.1% for ES and 3.1% for S-T. Tanaka et al reported that 28 out of 522 patients (5.4%) who underwent conization by S-T developed cervical stenosis,^[13] which was comparable to our study in which 21 out of 627 patients suffered from cervical stenosis. Tanaka et al also pointed out that those who underwent conization when they were \geq 46-years-old or within 12 months of delivery had increased risk of cervical stenosis. Since our patient cohort was \leq 40 -years old, we did not find any difference between age groups in this study (Table 6). Although we do not have data regarding the interval between childbearing and conization, the prevalence of cervical stenosis was higher in patients who underwent S-T after delivery (data not shown). To address these questions in the future, we will need to collect more precise information and increase the sample size to strengthen the statistical power.

In conclusion, we demonstrated that S-T is a useful method to treat and diagnose cervical lesions with an acceptable rate of complications and recurrence. To the best of our knowledge, to date, no prospective randomized trial has been conducted to study the feasibility of S-T. Although this retrospective study included a limited number of patients, the results can provide useful information for further consideration in the management of patients with CIN.

Author contributions

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