

Surgical, oncological and obstetric outcomes of the Shimodaira-Taniguchi conization method

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Abstract. The present study aimed to investigate the surgical, oncological and obstetric outcomes of the Shimodaira-Taniguchi (S-T) conization method. A total of 858 cases of high-grade intraepithelial lesions treated with S-T conization were retrospectively reviewed, and the surgical, oncological and obstetric outcomes were analyzed. The χ^2 test was used to compare the clinical characteristics between patients with and without cervical stenosis. The factors associated with recurrent/persistent disease were analyzed using univariate and multivariate analyses with a Cox hazards regression model. The obstetric outcomes after conization were also evaluated. Cervical stenosis and recurrent/persistent disease occurred in 2.2 and 4.9% of the patients, respectively. Older age [≥ 45 years; hazard ratio (HR), 3.22; 95% CI, 1.73-6.02] and surgical margin involvement (HR, 6.39; 95% CI, 3.44-11.8) were independently associated with recurrent/persistent disease. In particular, older patients with endocervical margin involvement showed a higher rate of recurrence (3-year recurrence rate, 28.1%). The proportion of patients who experienced cervical stenosis was significantly higher in older patients (0.95 vs. 5.7%; $P < 0.001$). Among the 66 deliveries after conization, term delivery was observed in 62 cases (93.9%). The proportion of patients who experienced preterm delivery after conization was significantly higher in patients with a short interval from conization to conception ($P = 0.045$). In conclusion, the S-T conization method was effective in terms of surgical, oncological and obstetric outcomes. A careful follow-up is required for older patients with positive surgical margins, particularly those with positive endocervical margins. In addition, a short interval of ≤ 3 months from conization to conception should be avoided to expect term pregnancy.

Introduction

Cervical intraepithelial neoplasia (CIN) is a premalignant lesion that can be divided into three stages (1, 2 and 3). In particular, CIN2 and 3, also known as a high-grade squamous intraepithelial lesion (HSIL), are high-risk stages of cervical cancer (1). It is estimated that, in 70% of affected women, CIN 2 and 3 can persist or progress to cervical cancer after 10-20 years (2). For this reason, early diagnosis and management of the premalignant lesions is important to reduce the natural progression of these lesions to cervical uterine cancer.

Cervical conization is the gold standard for the treatment of precancerous diseases of the uterine cervix, and various conization methods have been described in previous literature (2-4). Depending on which surgical method is used, the incidence rates of perioperative and postoperative complications differ (2,3). In Japan, 11.6% of patients who underwent therapeutic conization were treated with using the Shimodaira-Taniguchi (S-T) conization method (4). The S-T conization method is associated with decreased thermal damage, improved margin interpretability, and an increased likelihood of excision of a single, non-traumatized specimen that can be easily evaluated to determine the histologic type, grade, glandular involvement, and margin status using high-frequency current with a triangular probe and rigid linear electrode (5). However, English-language articles on S-T conization are limited (3,5-7), and the surgical, oncological and obstetric outcomes of S-T conization have not yet been fully described. The aim of the present study was to investigate the surgical, oncological, and obstetric outcomes of the S-T conization method. The present study also reviewed the previous literature regarding the S-T conization method.

Materials and methods

Data source. The Institutional Review Board (IRB) of Osaka Rosai Hospital approved the present study (IRB approval number: 2021-62, date of approval: September 30, 2021). The medical records of patients managed at the Osaka Rosai Hospital between January 2010 and December 2018 were retrospectively reviewed. A total of 858 cases in which the therapeutic S-T conization method was used for HSIL were

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identified. Patients with diagnostic S-T conization were excluded from the study. The resected specimens were evaluated by pathologists according to the WHO Classification of Tumors of Female Reproductive Organs.

Surgical procedures and postoperative follow-up. All the included women provided their written informed consent for the therapeutic procedures. For the present study, the Institutional Review Board granted an opt-out recruitment approach and waived the requirement for written informed consent for participation from each patient. We routinely performed cervical conization using the S-T method with an Honest Medical High Frequency Surgical Unit (MGI-202; Honest Medical, Tokyo, Japan) under intravenous or spinal anesthesia. The probes used for the S-T conization method are illustrated in Fig. 1. The cutting probe was inserted into the cervical canal and rotated to extract a cone of tissue as a single informative specimen (Video S1), which can be easily performed regardless of the skill of the surgeon. The cervical tissue resected by conization was carefully divided into 12 specimens, and a pathological diagnosis was made by a pathologist. Within 3-4 months after conization, cervical cytology was conducted in 813 of the 858 cases. The cervical cytology results were reported according to the Bethesda System 2001.

Outcome measurements. The surgical outcomes, including operative time, number of resected specimens, and complication rates, were evaluated. The patient characteristics were compared between patients with and without cervical stenosis, a surgical complication. Cervical stenosis was defined as cervical narrowing that limited or prevented the insertion of collection devices for obtaining cervical cytology samples or uterine sounds, closure requiring surgical intervention, or any other cases where a clinician recorded the presence of stenosis in the medical records. Although decrease in menstrual blood flow may be complication, we did not have the data regarding the menstrual blood flow before and after conization. Therefore, we did not define decrease in menstrual blood flow as a complication. We also analyzed the factors potentially associated with recurrent/persistent disease after conization. Recurrent/persistent disease after conization was defined as the occurrence of HSIL, diagnosed by histopathological evaluation of a biopsy specimen or subsequent surgical specimen, at any time after the initial conization procedure. Obstetric outcomes after conization were also reviewed and potential factors were compared between the patients with term and preterm delivery in subsequent pregnancies.

Statistical analysis. The proportions of categorical variables were analyzed for statistical significance using the χ^2 test (8). The probability of recurrence-free status was analyzed using the Kaplan-Meier method and was evaluated for statistical significance using the log-rank test. Univariate and multivariate analyses were performed to identify the factors that could potentially affect the risk of recurrent/persistent disease after conization. We used multivariate regression analysis to control selection bias. Nominal variables were dichotomized arbitrarily (presence vs. absence). Variables of

Table I. Patient characteristics (n=858).

Characteristics	Value
Median age, years (IQR)	38 (33-45)
Median BMI, kg/m ² (IQR)	20.7 (19.2-22.6)
Parity, n	
Yes	561
No	297
Smoking status, n	
Yes	220
No	638
Histology, n	
CIN2	27
CIN3	831
Conization within 1 year after delivery, n	
Yes	61
No	797

CIN, cervical intraepithelial neoplasia; IQR, interquartile range.

interest were entered into a regression model using the Cox proportional hazards model. $P < 0.05$. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) (9), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of the R commander designed to add statistical functions frequently used in biostatistics.

Results

Patients' characteristics. The characteristics of the 858 patients included in this study are shown in Table I. The median age was 38 years (Interquartile range (IQR): 33-45); and BMI was 20.7 (IQR: 19.2-22.6). Of the 858 patients, 297 (34.6%) were nulliparous, 220 (25.6%) were smokers, and 831 (96.9%) had CIN3. Sixty-one (7.1%) women underwent conization within 12 months of childbirth.

Surgical outcomes. The surgical outcomes are shown in Table II. The median operative time was 5.0 min (IQR: 3-8). Among the 858 patients, 834 (97.2%) had intraoperative blood loss of ≤ 50 ml. The number of specimens obtained by the S-T method was also evaluated; in most cases (81.3%), a single adequate specimen was extracted. Postoperative complications that occurred in the patients were as follows: postoperative bleeding, n=71 (8.3%); cervical stenosis, n=19 (2.2%); postoperative fever, n=1 (0.1%); and abdominal pain, n=2 (0.2%).

As shown in Table III, 6 of the 631 (0.95%) younger patients (<45 years of age) experienced cervical stenosis. In contrast, 13 of 227 (5.7%) older patients (≥ 45 years) experienced cervical stenosis. The proportion of older patients with cervical stenosis was significantly higher ($P < 0.001$). Factors such as the number of resected specimens, conization within

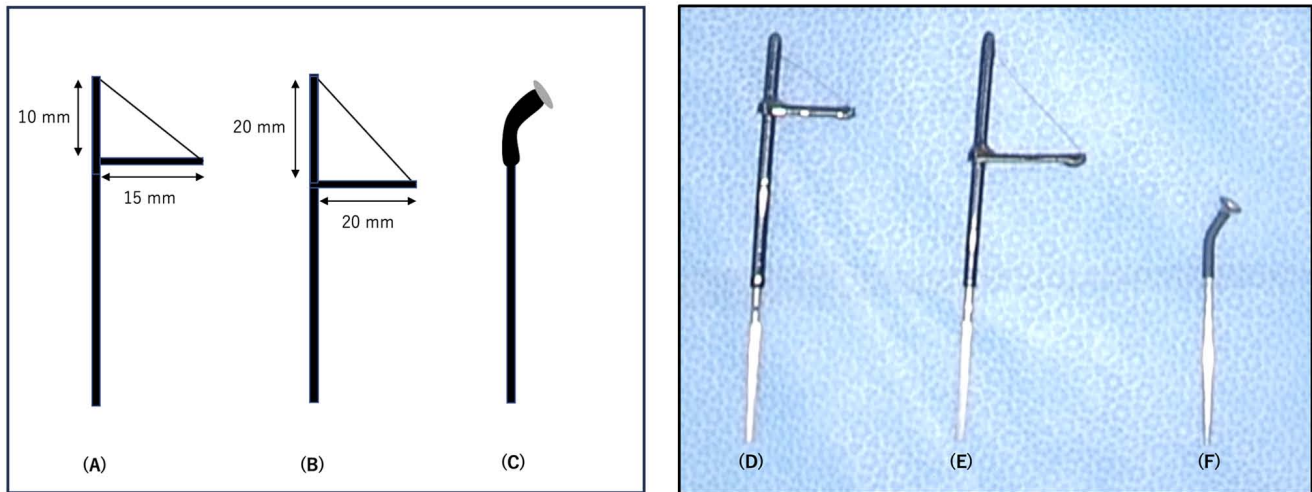


Figure 1. Probes used in Shimodaira-Taniguchi conization. (A) Illustration of triangular probe with a base length of 15 mm and a height of 10 mm. (B) Illustration of triangular probe with a base length of 20 mm and a height of 20 mm. (C) Illustration of coagulation probe. (D) Original image of triangular probe shown in (A). (E) Original image of triangular probe shown in (B). (F) Original image of coagulation probe shown in (C).

one year after delivery, intraoperative blood loss (≥ 51 ml), and suturing for hemostasis did not have any statistically significant impact on the occurrence of cervical stenosis.

Factors associated with recurrent/persistent disease after conization. As shown in Table II, the median follow-up period was 28 months (IQR: 14-49). Among the 858 patients, 42 (4.9%) developed disease recurrence during the observation period. A positive surgical margin was observed in 159 (18.5%) of the 858 patients. Of the 159 patients with a positive surgical margin, 86 (10.0%) had a positive endocervical margin and 73 (8.5%) had no endocervical involvement. As shown in Table IV, the following baseline factors showed a significant association with a higher recurrence rate in univariate analysis: age ≥ 45 years ($P < 0.001$) and positive surgical margin status ($P < 0.001$). The number of resected specimens and the smoking status were not statistically significant. In multivariate analysis, age ≥ 45 years (hazard ratio (HR) 3.22, 95% confidence interval (CI) 1.73-6.02, $P < 0.001$) and positive surgical margin status (HR 6.39, 95% CI 3.44-11.8, $P < 0.001$) also showed an independent association with recurrent disease.

The recurrence-free survival rates in older patients according to surgical margin status are shown in Fig. 2. Older patients with endocervical margin involvement had a higher recurrence rate (3-year recurrence rate, 28.1%).

Obstetric outcomes after conization. The obstetric outcomes are shown in Table V. The study included 62 pregnant women and 66 live births. Among the 66 deliveries, there were 62 term deliveries (93.9%) and 4 were preterm deliveries (6.1%). The proportion of patients with maternal comorbidities and smoking status did not differ significantly between the patients with term and preterm pregnancies. Two of the 10 patients (20%) who had a short interval from conization to conception (≤ 3 months) experienced preterm delivery. In contrast, 2 of the 56 patients (3.6%) with a > 3 months interval from conization to conception experienced term pregnancy. The proportion of patients who experienced

Table II. Surgical outcomes.

Variables	Value
Median operative time, min (IQR)	5.0 (3.0-8.0)
Blood loss, n (%)	
≤ 50 ml	834 (97.2)
≥ 51 ml	24 (2.8)
Median weight of resected specimen, g (IQR)	3.0 (2.0-3.8)
Number of resected specimens, n (%)	
1	698 (81.3)
≥ 2	160 (18.7)
Complication, n (%)	
Postoperative bleeding	71 (8.3)
Cervical stenosis	19 (2.2)
Fever	1 (0.1)
Abdominal pain	2 (0.2)
Surgical margin status, n (%)	
Negative	699 (81.5)
Positive	159 (18.5)
Endocervical margin involvement, n (%)	
Yes	86 (10.0)
No	73 (8.5)
Median follow-up duration, months (IQR)	28.0 (14-49)
Cervical cytology within 3-4 months after conization, n (%)	
Negative for intraepithelial lesion and malignancy	701 (81.7)
Other	112 (13.1)
N/A	45 (5.2)
Recurrence, n (%)	
Yes	42 (4.9)
No	816 (95.1)

IQR, interquartile range; N/A, not applicable.

Table III. Factors potentially associated with cervical stenosis after conization.

Factors	Stenosis		P-value
	Yes	No	
Age, years			<0.001
<45	6	625	
≥45	13	214	
Number of resected specimens			0.358
1	17	681	
≥2	2	158	
Conization within 1 year after delivery			0.558
No	17	780	
Yes	2	59	
Intraoperative blood loss, ml			0.455
≤50	19	815	
≥51	0	24	
Suturing for hemostasis			0.338
No	16	761	
Yes	3	78	

Table IV. Univariate and multivariate Cox regression analyses for recurrent/persistent disease after conization.

Variables	Univariate analysis ^a			Multivariate analysis ^a		
	HR	95% CI	P-value	HR	95% CI	P-value
Age, years						
<45	1			1		
≥45	3.170	1.724-5.828	<0.001	3.220	1.730-6.020	<0.001
Number of resected specimens						
1	1					
≥2	0.755	0.318-1.793	0.524	0.665	0.273-1.560	0.342
Surgical margin status						
Negative	1					
Positive	6.098	3.313-11.20	<0.001	6.390	3.440-11.800	<0.001
Smoking						
No	1					
Yes	1.129	0.567-2.249	0.730	1.210	0.607-2.431	0.581

^aCox proportional hazards model. HR, hazard ratio.

preterm delivery after conization was significantly higher in those with a short interval from conization to conception (P=0.045).

Discussion

We searched the PubMed database for all English-language articles related to S-T conization published by July 10, 2022, using the following key words and combinations of key words: ‘Shimodaira-Taniguchi’ and ‘conization.’ Only five articles regarding S-T conization for HSIL have been previously

reported (3-7) (Table VI). The overall recurrence rate was reported to be 1.3-5.8% and a positive surgical margin was observed in 13.4-39.1% of the patients, which was consistent with the present study. However, postoperative complications and obstetric outcomes after S-T conization have not been fully described in the previous literature. The strengths of the current study were to evaluate not only the oncological outcomes, but also the surgical and obstetric outcomes of S-T conization and to review the previous literature regarding S-T conization.

The incidence of cervical stenosis after conization in previous studies varies up to 29% (10), depending on the

Table V. Obstetrical outcomes after Shimodaira-Taniguchi conization.

Variables	Term pregnancy, n	Preterm pregnancy, n	P-value
Number of live births	62	4	0.918
Comorbidity			
No	55	4	
Myoma	2	0	
Obesity	3	0	
Asthma	2	0	
Smoking			0.763
No	42	3	
Yes	20	1	
Interval from conization to conception			0.045
≤3 months	8	2	
>3 months	54	2	
Gestational age			0.783
≤27 weeks 6 days	0	1	
28 weeks 0 days to 31 weeks 6 days	0	1	
32 weeks 0 days to 33 weeks 6 days	0	0	
34 weeks 0 days to 36 weeks 6 days	0	2	
≥37 weeks 0 days	62	0	
Mode of delivery			0.783
Vaginal delivery	50	3	
Cesarean section	12	1	

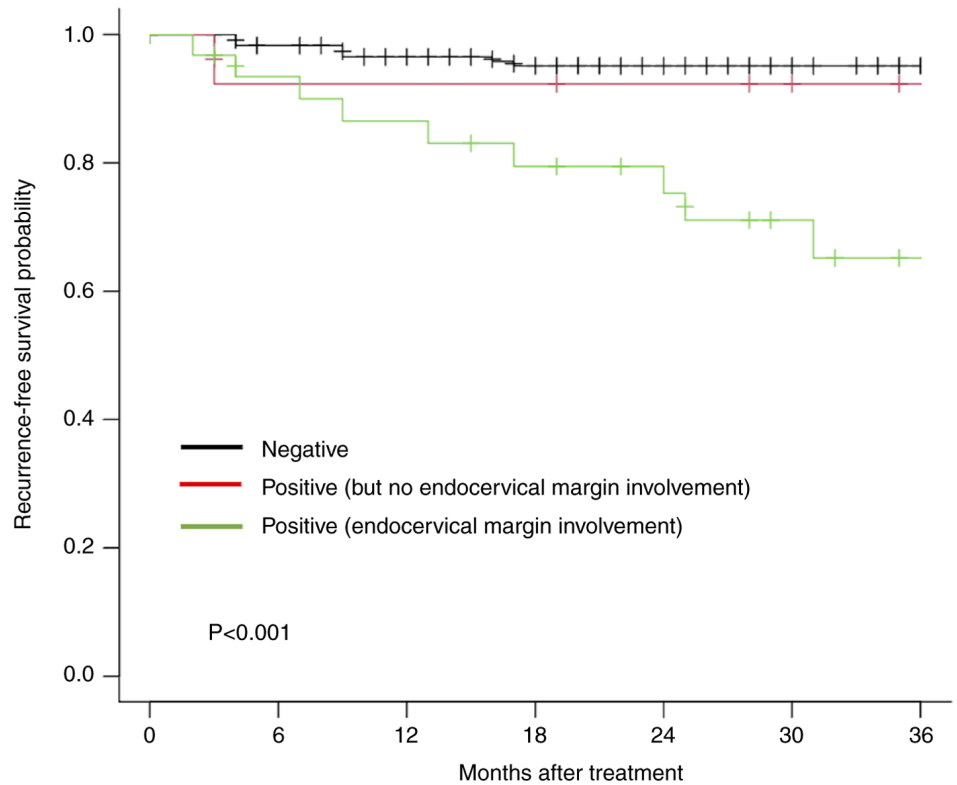
Table VI. Summary of previous studies regarding Shimodaira-Taniguchi conization for high-grade squamous intraepithelial lesions.

First author/s, year	Number of patients	Median or mean postoperative follow-up duration, months (range)	Recurrent and residual disease, n (%)	Margin positive, n (%)	Cervical stenosis, n (%)	Total number of deliveries after conization	Preterm delivery, n (%)	(Refs.)
Tanaka <i>et al</i> , 2017	522	19 (20-83) ^a	25 (4.8)	87 (16.7)	28 (5.2)	N/A	N/A	(3)
Ikeda <i>et al</i> , 2021	1,024	N/A	N/A	184 (18.0)	N/A	N/A	N/A	(4)
Matsumura <i>et al</i> , 2010	455	(13-60)	6 (1.3)	178 (39.1)	15 (3.3)	N/A	N/A	(5)
Miyoshi <i>et al</i> , 2012	243	18.8 (1-100) ^a	14 (5.8)	45 (19)	N/A	N/A	N/A	(6)
Kigure <i>et al</i> , 2018	689	36.8 (0-107) ^b	22 (3.2)	62 (13.4)	21 (3.0)	107	15 (14.0)	(7)
Present study	858	28 (14-49) ^a	42 (4.9)	159 (18.5)	19 (2.2)	66	4 (6.1)	-

^aMedian (range). ^bMean (range). N/A, not applicable.

definition employed. Various factors, including age, deep incision, and time within one year of delivery, are associated with cervical stenosis (3,11). In the current study, cervical stenosis was more likely to occur in individuals older than 45 years. These findings might be due to the migration of the transformation zone to the cervical canal with increasing age and after menopause (12). In contrast to younger patients, the

squamocolumnar junction (SCJ) in older patients is usually located in the endocervix. Therefore, deep conization is required to excise precancerous lesions in these patients, which may lead to cervical stenosis. Furthermore, cervical stenosis after conization in elderly patients may be associated with amenorrhea or a decreased frequency of menstruation. The lack of natural dilatation of the cervical canal by



	Patients at risk							
	Negative	181	168	153	132	111	94	74
Positive (but no endocervical margin involvement)	14	11	11	11	9	8	6	6
Positive (endocervical margin involvement)	32	27	25	22	19	12	9	9

Figure 2. Recurrence-free survival in elderly patients (age ≥ 45 years) according to surgical margin status. The log-rank test was used for analysis. Elderly patients with endocervical margin involvement had a higher recurrence rate (3-year recurrence rate, 28.1%) than those with a negative surgical margin.

menstrual blood may be the main reason for this complication (3). Cervical stenosis can make it difficult to check for the deeper side of the cervical canal. Cervical stenosis can lead to an unsatisfactory follow-up after conization with a risk of unseen relapse. Therefore, a careful follow-up of older patients is required.

Surgical margin status is a well-known prognostic factor for persistent or recurrent disease. There is no consensus on the safety margin when performing conization for HSIL. In the present study, the rate of positive surgical margins was 18.5%. In comparison to the loop electrosurgical excision procedure (LEEP) (11.2%) or cold knife conization (CKC) (8.1%), it seems higher (13-15). However, the overall recurrence rate after the S-T method was approximately 5%, which was comparable to that after LEEP (8.1%) and CKC (2.1%) (13-15). Although a precise explanation for the low recurrence rate with the S-T method is unclear, it may be associated with the use of a coagulation probe. A small flat probe, as shown in Fig. 1, was applied to the entire cervical stump to coagulate the remaining part of the lesion. This step may help prevent recurrence in patients with positive surgical margins.

We found that older age (≥ 45 years) was not only an independent prognostic factor for recurrence after conization, but also an independent prognostic factor for cervical stenosis, which may lead to unsatisfactory follow-up. In particular, focusing on surgical margin status, older patients with endocervical margin involvement showed a higher rate of recurrence (3-year

recurrence rate: 28.1%) (Fig. 1). When residual disease is present in the endocervix, postsurgical stenosis can prevent adequate follow-up. Therefore, when endocervical margin involvement is confirmed in older patients with no visible SCJ, it is beneficial to recommend the performance of a subsequent hysterectomy.

Few studies have investigated obstetric outcomes after S-T conization. In the current study, the rate of preterm delivery was 6.1%, which was consistent with the rate of preterm delivery in the general Japanese population (5.6%) (16). We found that a short interval between conization and pregnancy (≤ 3 months) was associated with preterm delivery (Table V). Some authors have suggested that a 3- to 4-month interval from conization to pregnancy increases the risk of preterm delivery (17,18), while others have suggested that the time interval from conization is not associated with preterm delivery (19,20). Various other factors are potentially associated with preterm birth after conization, including cone depth (21), size of the resected specimen (22) and pre- and post-treatment cervical length (23). Therefore, whether the interval from conization to conception is associated with preterm birth remains controversial. The cervical length was reported to heal to nearly the same length as the pretreatment level at 6 months of posttreatment follow-up in patients who delivered at term in a subsequent pregnancy (23). Although it is difficult to determine the optimal interval from conization to pregnancy, an interval of at least 6 months would be reasonable, considering the risk of preterm birth and the time required for regeneration of cervical length.

The present study is associated with some limitations. First, the data used in this study were retrospective, and the sample size was relatively small. A larger sample size is needed to support our results. Second, confounding factors for recurrent disease, such as preoperative and postoperative HPV infection status, were not analyzed. This type of information strengthened the results of our study. Third, a comparison with a different surgical method, such as CKC or LEEP, would be helpful for demonstrating the validity of the S-T conization method.

In conclusion, the Shimodaira-Taniguchi conization method was found to be effective regarding the surgical, oncological, and obstetric outcomes. We found that older patients with endocervical margin involvement had a higher incidence of recurrence and postoperative cervical stenosis after therapeutic conization than younger patients. A careful follow-up is required, and a secondary hysterectomy should be considered in older patients with endocervical margin involvement. Furthermore, to increase the likelihood of term pregnancy after conization, a short interval of ≤ 3 months between conization and conception should be avoided.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

SH, YT, TD and YS conceptualized the study. SH, YT, MS and YS contributed to the methodology. SH and YT handled the software used. TD and MS validated the data. SH and YT confirm the authenticity of all the raw data. SH and YT analyzed the data. SH, YT, TD, MS and YS curated the data, wrote the original draft, and reviewed and edited the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval for the present study was obtained from the Ethics Committee of Osaka Rosai Hospital (approval no. 2021-62; date of approval, September 30, 2021; Sakai, Japan), and it was conducted in line with the guidelines of The Declaration of Helsinki. The Institutional Review Board granted an opt-out recruitment approach and waived the requirement for written informed consent from each patient. The document of ethical approval for the present study is available on the website of Osaka Rosai Hospital.

Patient consent for publication

Patient consent for Video S1 was obtained.

Competing interests

The authors declare that they have no competing interests.

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