

The problems of cervical conization for postmenopausal patients

K. Hasegawa^{1,2}, Y. Torii³, R. Kato⁴, Y. Udagawa^{1,3}, I. Fukasawa¹

¹Department of Obstetrics and Gynecology, Dokkyo Medical University, Mibu, Tochigi

²Department of Obstetrics and Gynecology, Banbuntane Hotokukai Hospital, Fujita Health University, Nagoya, Aichi

³Department of Obstetrics and Gynecology, Fujita Health University School of Medicine, Toyoake, Aichi

⁴Department of Obstetrics and Gynecology, Tokyo Medical University, Shinjyuku-ku, Tokyo (Japan)

Summary

Purpose: Cervical conization is the definitive treatment for women of any age who have cervical intraepithelial neoplasia (CIN). However, complications of the procedure have not been fully investigated in postmenopausal patients. The aim of this retrospective study was to evaluate the results and complications of cervical conization performed on premenopausal and postmenopausal patients. **Materials and Methods:** This study recruited 405 patients who had undergone cervical laser conization. The median age was 36 years (range 20 to 75), and there were 361 (89.1%) premenopausal and 44 (10.9%) postmenopausal women. **Results:** The length of the cone removed from the postmenopausal patients was significantly longer than the length from the premenopausal patients (17.9 ± 3.9 mm vs. 15.7 ± 3.6 mm, respectively; $p = 0.02$). The rate of positive endocervical cone margins from the premenopausal patients was significantly higher than the rate from the postmenopausal patients (9.1% vs. 0%, respectively; $p = 0.037$). The rate of cervical stenosis was significantly higher in postmenopausal patients than in premenopausal patients (59.1% vs. 8.3%; respectively; $p < 0.0001$). There was no difference in the rates of frequency of intraoperative complications. **Conclusions:** Although deep incision is mandatory for complete excision of CIN in postmenopausal patients, it increases the incidence of cervical stenosis. Cervical conization may be a less invasive surgical procedure for older women with CIN than hysterectomy; however, the risk of postoperative complications remains, causing a dilemma for physicians treating postmenopausal women with CIN.

Key words: Cervical intraepithelial neoplasia; Cervical conization; Postmenopause; Complications; Cervical stenosis.

Introduction

The treatments for cervical intraepithelial neoplasia (CIN) that have been investigated in clinical trials include cervical conization, hysterectomy, cryotherapy, and laser ablation. Cervical conization enables histopathological examination of the resected specimen, whereas cryotherapy and laser ablation have shortcomings because histopathological examination of the frozen or vaporized area cannot be performed. Cervical conization is also a definitive treatment for patients with CIN, leaving no evidence of invasion or residual lesions in the preserved uterus following the procedure. However, hysterectomy can be considered for elderly patients or patients who do not desire preservation of reproductive function.

Although small in number, there are some patients with microinvasive or invasive carcinoma among those preoperatively diagnosed with CIN3. It is therefore appropriate to perform cervical conization to obtain the definitive pathological diagnosis and then determine whether a hysterectomy is necessary [1, 2].

CIN lesions are more often localized to the endocervix in postmenopausal patients, because of physiological change

in the location of the squamocolumnar junction (SCJ) after menopause. Therefore, a sufficiently deep cone is needed for complete resection of lesions in postmenopausal women. On the other hand, the intra- and postoperative complications of cervical conization for postmenopausal patients are worrisome. The complications include intra- and postoperative hemorrhage, cervical stenosis or occlusion, and wound infection. Moreover, rare complications include uterine perforation, injury to the bladder or rectum, and pelvic inflammation.

The complications of cervical conization for postmenopausal women have not been fully investigated. The aim of this retrospective study was to evaluate the results and complications of cervical conization performed for women with CIN or microinvasive cervical carcinoma and compare the data from postmenopausal patients with the data from premenopausal patients.

Materials and Methods

Subjects

Cervical conization was performed in 504 patients with CIN after obtaining informed consent from January 1997 to Decem-

Revised manuscript accepted for publication February 24, 2015

Table 1. — *Pathological diagnosis after cervical conization.*

Age (years)	n (%)	CIN1	CIN2	CIN3	MIC	AIS	CIN3+AIS
20~29	71 (17.5%)	0	2	68	0	0	1
30~39	201 (49.6%)	0	4	184	8	3	2
40~49	79 (19.5%)	0	3	74	2	0	0
50~59	32 (7.9%)	2	1	28	1	0	0
≥60	22 (5.4%)	1	3	17	1	0	0
Total (%)		3 (0.7%)	13 (3.2%)	371 (91.6%)	12 (3.0%)	3 (0.7%)	3 (0.7%)

CIN: cervical intraepithelial neoplasia, MIC: microinvasive carcinoma, AIS: adenocarcinoma in situ.

Table 2. — *Clinical factors and ages of patients.*

Age (years)	20~29	30~39	40~49	50~59	≥60
n	71	201	79	32	22
Length of removed cone (mm)	14.7 ± 3.6	15.8 ± 3.6	16.4 ± 3.6	17.2 ± 3.2	17.8 ± 4.5
Positive endocervical cone margin	7 (9.9%)	21 (10.4%)	6 (7.6%)	0	0
Persistence of disease	3 (4.2%)	3 (1.5%)	0	0	0
Cervical stenosis	5 (7.0%)	19 (9.5%)	6 (7.6%)	9 (28.1%)	16 (72.7%)
Intraoperative complications	AH 2(2.8%)	AH 13 (6.5%)	AH 4 (5.1%)	AH 2 (6.3%) PD 1 (3.1%)	AH 1 (4.5%) PD 1 (4.5%)

AH; abnormal hemorrhage, PD; penetration of the Douglas cul-de-sac.

ber 2010 at Fujita Health University Hospital. Among these patients, 99 were excluded from the study for the following reasons: underwent cervical conization via a loop electrosurgical excision procedure (LEEP) or an harmonic scalpel, were diagnosed postoperatively with invasive squamous cell carcinoma or adenocarcinoma and subsequently underwent hysterectomy, or were lost to follow-up within 12 months. The remaining 405 patients underwent cervical conization alone using a potassium-titanyl-phosphate (KTP) laser or neodymium: yttrium-aluminum-garnet (Nd: YAG) laser, and were enrolled in this study. The median age was 36 years (range 20 to 75), and there were 361 (89.1%) premenopausal and 44 (10.9%) postmenopausal women. The median follow-up period was 36 months (range 12 to 136).

The operating surgeons used similar surgical protocols, which is summarized as follows: conization was performed according to the extent of the lesion using a KTP laser with the beam power set at 10 W. Hemostasis was then achieved using laser beam coagulation, which employed the Nd: YAG laser with the beam power set at 20 W, and by vaginal gauze packing with or without Oxcel or Surgicel. In some cases, both incision and coagulation were performed using the Nd: YAG laser only.

This study investigated the following factors: length of removed cone, endocervical cone margin, persistence of disease, cervical stenosis, and intraoperative complications. These factors were compared between patients grouped according to age or pre- versus postmenopause. The following intraoperative complications were investigated: abnormal hemorrhage, defined as hemorrhage volume greater than 200 mL, and accidental penetration of the Douglas cul-de-sac, which was immediately repaired by surgical suturing. The length of the removed cone was defined as the maximum length of the resected cervical specimen. In premenopausal patients, cervical stenosis was defined as symptomatic cervical stenosis with dysmenorrhea or prolonged menstruation resulting in hematometra or hematocervix; or asymptomatic cervical stenosis with cervical narrowing that prevented insertion of a uterine probe. In postmenopausal patients, cervical stenosis was defined as complete occlusion of the cer-

vical canal, or cervical narrowing that prevented insertion of a uterine probe. The current study was approved by the ethical committee of Fujita Health University hospital.

Statistical analysis

The lengths of removed cone are shown as means ± standard deviation, and were analyzed using the Student *t*-test. Other factors were analyzed using the Fisher exact test. A *p* < 0.05 was considered to be statistically significant.

Results

The postoperative histopathological diagnosis of the 405 patients undergoing cervical conization is shown in relation to age categories in Table 1. Patients aged between 30 and 40 years accounted for half of all patients. A total of 371 (91.6%) patients were diagnosed with CIN3, which was the most common diagnosis among all age groups. A few patients had CIN1, CIN2, microinvasive carcinoma, adenocarcinoma in situ (AIS), and CIN3 with AIS (Table 1).

Table 2 summarizes the relationship between the investigated factors and ages of patients, and Table 3 summarizes the relationship between the investigated factors and pre- versus postmenopausal patients. The length of the removed cone was significantly longer in the postmenopausal patients than the length in the premenopausal patients (17.9 ± 3.9 mm vs. 15.7 ± 3.6 mm, respectively; *p* = 0.002). The rate of positive endocervical cone margins from the premenopausal patients was significantly higher than the rate of positive margins from the postmenopausal patients (9.1% vs. 0%, respectively; *p* = 0.037). The difference in disease persistence between the pre- and postmenopausal patients was not significant. The rate of cervical stenosis

Table 3. — Clinical factors and pre- versus postmenopausal patients.

	Premenopause n=361	Postmenopause n=44	p value
Length of removed cone (mm)	15.7 ± 3.6	17.9 ± 3.9	0.0002
Positive endocervical cone margin	33 (9.1%)	0	0.037
Persistence of disease	6 (1.7%)	0	1.00
Cervical stenosis	30 (8.3%)	26 (59.1%)	< 0.0001
Intraoperative complications	AH 19 (5.3%)	AH 3 (6.8%) PD 2 (4.5%) total 5 (11.4%)	0.16

AH: abnormal hemorrhage, PD: penetration of the Douglas cul-de-sac.

was significantly higher in postmenopausal patients than in premenopausal patients (59.1% vs. 8.3%; respectively; $p < 0.0001$) (Table 3). The rate of intraoperative complications, including abnormal hemorrhage and penetration of the Douglas cul-de-sac, was not significantly different between the pre- and postmenopausal patients (5.3% vs. 11.4%, respectively; $p = 0.16$). However, penetration of the Douglas cul-de-sac during the procedure was only seen in two postmenopausal patients.

Of the 361 premenopausal patients, the lengths of the removed cone in the 331 patients not developing cervical stenosis and in the 30 patients developing cervical stenosis were 15.6 ± 3.7 mm and 16.4 ± 2.6 mm, respectively, which was not significant ($p = 0.28$). Of the 44 postmenopausal patients, the lengths of the removed cone in 18 patients not developing cervical stenosis and in the 26 patients developing cervical stenosis were 17.9 ± 3.2 mm and 18.2 ± 4.2 mm, respectively, which was not significant ($p = 0.80$).

Of the 30 premenopausal patients developing cervical stenosis, 13 asymptomatic patients or patients with mild symptoms (abdominal pain or prolonged menstruation) were followed without treatment and 11 underwent outpatient cervical dilatation using Hegar dilators. However, six patients with severe symptoms and signs (dysmenorrhea, cramping, and fertility problems) or with cervical occlusion underwent cervical dilatation and cervicoplasty as inpatients. There were 26 postmenopausal patients who developed cervical stenosis. Because these patients were asymptomatic as expected, they were routinely followed without treatment.

Discussion

Cervical conization has been widely performed as a diagnostic or therapeutic procedure for patients with CIN or early invasive cervical carcinoma. The intra- and postoperative complications of cervical conization are as follows: hemorrhage, cervical stenosis and occlusion, wound infection, cervical incompetence, which may lead to miscarriage

or preterm birth during the second and third trimesters, and rare events such as uterine perforation, injury to the bladder or rectum, and pelvic inflammation.

The occurrence of complete occlusion combined with hematometra after stenosis of the cervical canal as a result of conization is a rare event, based on the methods used for conization [3, 4]. Although cervical stenosis is not a rare event, the extent of severity varies. There are several definitions of cervical stenosis, and, as noted by many investigators, there is no consensus in the literature regarding its definition. Therefore, the reported incidence of cervical stenosis after conization has also varied (from 4% to 17%) [3, 5-8].

Post-treatment cervical stenosis is an important issue, because it prevents adequate cytological follow-up of patients treated for CIN or early invasive cervical carcinoma. Cervical stenosis may necessitate additional excision because of the concern over the possibility of residual disease that may progress to invasive carcinoma. Moreover, cervical stenosis also prevents collection of endometrial cytology to screen for endometrial carcinoma.

Several studies investigating the risk factors associated with cervical stenosis after conization have been reported [5, 7, 9, 10]. Suh-Burgmann *et al.* reported a 6% rate of cervical stenosis after LEEP, and the volume of tissue removed and a history of previous LEEP were significant independent predictors of stenosis [9]. Boulanger *et al.* reported that the rate of cervical stenosis, which was defined as unseen SCJ after conization, was 73.1% and 14.9% in post- and premenopausal women, respectively [10]. Houliard *et al.* reported that cervical stenosis after laser conization was observed in 40 out of 238 patients (16.8%), and that patient age was the only independent factor associated with the risk of stenosis [7]. Baldauf *et al.* reported a 4.3% rate for cervical stenosis after conization, and univariate analysis found that the risk of cervical stenosis was greater for patients older than 50 years of age, for those with completely endocervical lesions, for those with an excision 20-mm deep or greater, and for those undergoing laser conization instead of LEEP, and multivariate analysis determined that excision depth and a completely endocervical lesion were the only independent risk factors [5].

In this study, the rate of cervical stenosis was significantly higher in postmenopausal patients than in premenopausal patients (59.1% vs. 8.3%, respectively; $p < 0.0001$), which is similar to the results of previous studies. However, inconsistent with other reports [11-14], this study found that the rate of positive endocervical margins was significantly higher in premenopausal than postmenopausal patients (9.1% vs. 0%, respectively; $p = 0.037$).

Several reports identified age as a predictor of residual disease [11-14]. Bae *et al.* reported that the rate of endocervical margin involvement was 7.5%, and this was positively associated with disease severity and age and inversely related to cone depth [13]. They mentioned that

the risk for positive endocervical margins increased in patients aged 40 to 59 years and the patients aged 60 years or more compared with the patients aged less than 40 years; the odds ratios were 1.67 (95% confidence interval [CI] 1.06 -2.65) and 3.90 (95% CI 1.84 - 8.25), respectively, by multivariate logistic regression analysis.

The CIN lesions of elderly women are more often localized to the endocervix; therefore, it is necessary to perform sufficiently deep excisions to avoid positive endocervical margins. In this study, there were no postmenopausal patients with positive endocervical margins. Moreover, the length of the cone removed from the postmenopausal patients was significantly longer than the length of cone from the premenopausal patients (17.9 ± 3.9 mm vs. 15.7 ± 3.6 mm, respectively; $p = 0.002$). Therefore, the obtained cone depth was sufficient for avoiding positive endocervical margins among the postmenopausal patients with unsatisfactory colposcopic findings, whose lesions were more often localized to the endocervix.

If the length of the removed cone becomes longer regardless of the age of the patient, the incidence of positive endocervical margins or persistence of disease may decrease; however, the incidence cervical stenosis or occlusion may increase. For complete excision of CIN, a deep incision is mandatory, and when a large volume of specimen is excised, it also increases the risk of intra- and postoperative complications. In this study the intraoperative complication of accidental penetration of the Douglas cul-de-sac was only seen in postmenopausal patients. Regarding postoperative complications in younger patients, the effects of cervical conization on subsequent pregnancy and delivery have attracted considerable attention [15, 16].

Since increased age becomes a significant risk factor of cervical stenosis after conization, Boulanger *et al.* proposed that hysterectomy might be preferable for the postmenopausal patients with CIN [10]. Houliard *et al.* also concluded that older patients should be informed of the risk for cervical stenosis after laser conization and of other surgical options, such as hysterectomy, which may be considered for patients aged 40 years or older [7].

Several approaches for treating severe cervical stenosis have been investigated. For example, the following devices were studied: urinary catheter stent [17], coated nitinol stent [18], and nylon threads tied up to an intrauterine contraceptive device [19]. To date, however, effective and reliable treatment options for cervical stenosis are not available.

There is a report that use of hormone replacement therapy (HRT) was associated with a low risk of cervical stenosis [6]. HRT may become an option for preventing cervical stenosis in postmenopausal patients after further confirmation of these results.

Cervical conization may be a less invasive surgical procedure than hysterectomy for older patients with CIN; how-

ever, the risks of intra- and postoperative complications or problems remain, causing a dilemma for physicians treating postmenopausal women with CIN. It is important to take some care in choosing the treatment procedure for CIN occurring in postmenopausal women.

References

- [1] Ueda M., Ueki K., Kanemura M., Izuma S., Yamaguchi H., Nishiyama K., *et al.*: "Diagnostic and therapeutic laser conization for cervical intraepithelial neoplasia". *Gynecol. Oncol.*, 2006, 101, 143.
- [2] Yamaguchi H., Ueda M., Kanemura M., Izuma S., Nishiyama K., Tanaka Y., Noda S.: "Clinical efficacy of conservative laser therapy for early-stage cervical cancer". *Int. J. Gynecol. Cancer*, 2007, 17, 455.
- [3] Mathevet P., Chemali E., Roy M., Dargent D.: "Long-term outcome of a randomized study comparing three techniques of conization: cold knife, laser, and LEEP". *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2003, 106, 214.
- [4] Brun J.L., Youbi A., Hocké C.J.: "Complications, sequelae and outcome of cervical conizations: evaluation of three surgical techniques". *Gynecol. Obstet. Biol. Reprod.*, 2002, 31, 558.
- [5] Baldauf J.J., Dreyfus M., Ritter J., Meyer P., Philippe E.: "Risk of cervical stenosis after large loop excision or laser conization". *Obstet. Gynecol.*, 1996, 88, 933.
- [6] Penna C., Fambrini M., Fallani M.G., Pieralli A., Scarselli G., Marchionni M.: "Laser CO2 conization in postmenopausal age: risk of cervical stenosis and unsatisfactory follow-up". *Gynecol. Oncol.*, 2005, 96, 771.
- [7] Houliard S., Perrotin F., Fourquet F., Marret H., Lansac J., Body G.: "Risk factors for cervical stenosis after laser cone biopsy". *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2002, 104, 144.
- [8] Monteiro A.C., Russomano F.B., Camargo M.J., Silva K.S., Veiga F.R., Oliveira R.G.: "Cervical stenosis following electrosurgical conization". *Sao Paulo Med. J.*, 2008, 126, 209.
- [9] Suh-Burgmann E.J., Whall-Strojwas D., Chang Y., Hundley D., Goodman A.: "Risk factors for cervical stenosis after loop electrocautery excision procedure". *Obstet. Gynecol.*, 2000, 96, 657.
- [10] Boulanger J.C., Gondry J., Verhoest P., Capsie C., Najas S.: "Treatment of CIN after menopause". *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2001, 95, 175.
- [11] Moore B.C., Higgins R.V., Laurent S.L., Marroum M.C., Bellitt P.: "Predictive factors from cold knife conization for residual cervical intraepithelial neoplasia in subsequent hysterectomy". *Am. J. Obstet. Gynecol.*, 1995, 173, 361.
- [12] Kalogirou D., Antoniou G., Karakitsos P., Botsis D., Kalogirou O., Giannikos L.: "Predictive factors used to justify hysterectomy after loop conization: increasing age and severity of disease". *Eur. J. Gynaecol. Oncol.*, 1997, 18, 113.
- [13] Bae H.S., Chung Y.W., Kim T., Lee K.W., Song J.Y.: "The appropriate cone depth to avoid endocervical margin involvement is dependent on age and disease severity". *Acta Obstet. Gynecol. Scand.*, 2013, 92, 185.
- [14] Shaco-Levy R., Eger G., Dreier J., Benharroch D., Meirovitz M.: "Positive margin status in uterine cervix cone specimens is associated with persistent/ recurrent high-grade dysplasia". *Int. J. Gynecol. Pathol.*, 2013, 33, 83.
- [15] Kyrgiou M., Koliopoulos G., Martin-Hirsch P., Arbyn M., Prendiville W., Paraskevaidis E.: "Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis". *Lancet*, 2006, 367, 489.
- [16] Arbyn M., Kyrgiou M., Simoons C., Raifu A.O., Koliopoulos G., Martin-Hirsch P., *et al.*: "Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: meta-analysis". *BMJ*, 2008, 337, a1284. doi: 10.1136/bmj.a1284.

- [17] Tan Y., Bennett M.J.: "Urinary catheter stent placement for treatment of cervical stenosis". *Aust. N. Z. J. Obstet. Gynaecol.*, 2007, 47, 406.
- [18] Grund D., Köhler C., Krauel H., Schneider A.: "A new approach to preserve fertility by using a coated nitinol stent in a patient with recurrent cervical stenosis". *Fertil. Steril.*, 2007, 87, 1212.e13.
- [19] Nasu K., Narahara H.: "Management of severe cervical stenosis after conization by detention of nylon threads tied up to intrauterine contraceptive device". *Arch. Gynecol. Obstet.*, 2010, 281, 887.

Address reprint requests to:
K. HASEGAWA, MD, Ph.D.
Department of Obstetrics and Gynecology
Dokkyo Medical University
880 Kitakobayashi, Mibu
Tochigi 321-0293 (Japan)
e-mail: hasek@dokkyomed.ac.jp