Clinical significance of atypical squamous cells of undetermined significance after treatment for cervical intraepithelial grade 3 neoplasia: A retrospective single-center cohort study

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Abstract. The aim of the present study was to evaluate the clinical significance of atypical squamous cells of undetermined significance (ASC-US) following cervical conization for cervical intraepithelial neoplasia (CIN) grade 3. This study was a retrospective cohort analysis. The medical records of women treated with conization for CIN 2-3 were reviewed and 142 patients with CIN 3 who had been diagnosed using the conization specimens were selected. The mean follow-up period after conization was 41.8 months. Cytological abnormalities after conization were observed in 19.0% of the patients and consisted of ASC-US (13.4%) and worse than low-grade squamous intraepithelial lesion (LSIL; 5.6%). Recurrence was defined as a diagnosis worse than CIN 2, and the recurrence rate was 29.6% among patients with abnormal cytology. The recurrence rate was 15.7% in the ASC-US group and 71.4% in the worse than LSIL group. There was no significant difference in the time of initial identification of abnormal cytology after treatment between the worse than LSIL and the ASC-US groups (P=0.054). However, the ASC-US group had a significantly better cumulative recurrence-free rate compared with the worse than LSIL group (P<0.05). Women with ASC-US following treatment for CIN appear to be at a relatively high risk. Regarding the risk stratification of women following treatment for CIN, if surveillance cytology shows ASC-US, immediate colposcopy is recommended, along with long-term follow-up.

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Introduction

Cervical conization is the recommended treatment for cervical intraepithelial neoplasia (CIN) grade 3 (1). Based on the available evidence, there is no optimal surveillance strategy following treatment for CIN (2). For early detection of recurrence, long-term follow-up after cervical conization has been recommend by the American College of Obstetricians and Gynecologists (ACOG) guidelines (3).

In Japan, the national screening guidelines for women under the National Health Insurance system state that cervical conventional cytology using Pap smears is a standard screening test for cervical cancer. Human papillomavirus (HPV) DNA testing has not been recommended for population-based screening due to the scarcity of scientific evidence. However, when conventional cervical cytology shows atypical squamous cells of undetermined significance (ASC-US), repeat cervical cytology after 6 and 12 months, immediate colposcopy, or HPV DNA triage have been recommended by the National Cancer Comprehensive Network (NCCN) guidelines (4).

Although ASC-US comprise a wide variety of cervical cells, including benign and malignant cells, the presence of ASC-US has been considered as a low-risk abnormal cervical cytological characteristic (5). However, a substantial proportion of cases displaying ASC-US have underlying high-grade CIN (2 or 3) and, thus, are at an increased risk of developing cervical cancer (6). Based on these facts, it appears reasonable to consider women with ASC-US following treatment for CIN to be at a relatively increased risk of developing cervical cancer compared with women with ASC-US after no treatment. As regards risk stratification for women following treatment for CIN, an appropriate triage method used to identify women with ASC-US who have or will develop a cervical cancer precursor is crucial. The clinical significance of ASC-US following cervical conization for CIN, particularly for CIN 3, which has a high risk of recurrence, has not been fully elucidated. The aims of the present study were to evaluate the clinical significance of ASC-US following cervical conization for CIN 3 and to suggest an appropriate triage method.

Patients and methods

Study population. This was a retrospective cohort study. In order to identify cases with cytological abnormalities following conization, the medical records of patients who received conization as a conservative treatment for CIN 2-3 were reviewed. A total of 142 cases with CIN 3 that had been diagnosed using the conization specimens between February 2005 and May 2015 in our hospital were ultimately considered as eligible for review.

Conization procedure. Conization was performed using yttrium-aluminum-garnet (YAG) laser or ultrasonic scalpel under spinal anesthesia. Prior to resection, the squamous columnar junction (SCJ) was examined using the Schiller test.

The YAG laser procedure was performed as follows: The cervix was sutured, pulling the line to the outside of the SCJ. Towing the line, cervical excision was performed with the YAG laser at 12 W. The resection stump was coagulated with the laser.

The ultrasonic scalpel procedure was as follows: The cervix was sutured, pulling the line to the outside of the SCJ. Cervical excision was performed using output level 3 of the Harmonic Scalpel. The use of equipment was determined by the attending physician.

Surveillance after treatment for CIN 3. A conventional Pap smear was performed after conization at a time left to the discretion of each physician. The physicians conducted the follow-up based on the guidelines determined by the Office of Gynecology in Japan and the NCCN guidelines (4).

Identification of abnormal cytology and recurrence after treatment. Abnormal cytology was defined as worse than ASC-US. ASC-US was determined by one cytoscreener and one cytopathologist based on the Bethesda guidelines (7). Recurrence was defined as a diagnosis worse than CIN 2 in any pathological specimen at any timepoint during the follow-up period. The pathological specimens were independently reviewed by two gynecological pathologists.

HPV testing. Some ASC-US patients underwent high-risk HPV DNA testing (Hybrid Capture test using SurePath (BD Biosciences, Sparks, MD, USA) as the collection method). The high-risk HPV DNA test detects 13 different HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) (8). High-risk HPV DNA testing in patients with ASC-US was left to the discretion of the physicians.

Statistical analysis. Data were analyzed using the SPSS 21.0 software (IBM Corp., Armonk, NY, USA). Based on the postoperative cytology results, patients with abnormal cytology after conization were divided into an ASC-US group and a worse than low-grade squamous intraepithelial lesion (LSIL) group. The data are presented as means ± standard deviation (SD) for quantitative variables and frequencies (%) for qualitative variables. Student's t-test was used to compare means or medians, and the Chi-squared test or Fisher's exact test were used, as appropriate, to compare the frequency distributions of categorical variables. Pearson's χ^2 test was used to analyze categorical variables. Kaplan-Meier survival curves with log-rank tests, with patient status at the time of the last follow-up visit, were used to compare the cumulative recurrence-free rates among the normal, ASC-US, and worse than LSIL groups. A P-value of <0.05 was considered to indicate statistically significant differences.

Results

Patient characteristics. The mean age of the 142 patients was 36.1 years. The mean age was not significantly different between the normal and the abnormal cytology groups. The mean follow-up period after conization was 41.8 months.

Cytological abnormalities after conization were observed in 27 patients (19%), whereas the remaining 115 patients had normal cytological findings. There were no significant differences in age, surgical instrument, postoperative visit frequency, duration, or intervals between the abnormal and the normal cytology groups (Table I).

Identification of abnormal cytology after treatment. Of all the participants in this study, 19 (13.3%) had ASC-US, and 8 (5.6%) had a diagnosis worse than LSIL. There was no significant difference in the mean age between the two groups (35.3 vs. 35.9 years, respectively). The rate of cytological abnormalities did not differ significantly among the negative margin, the positive margin, and the non-assessable margin groups ($\chi^2=0.104$). However, in the abnormal cytology group, there was a significant positive association between the rate of using YAG laser conization and the positive margin status of the excised specimen group ($\chi^2=0.036$; Table II).

ASC-US group. In this group, there were negative margins in 11 patients, positive margins in 7 patients, and a non-assessable margin in 1 patient. There were 3 different approaches to management based on the Japanese and NCCN guidelines. High-risk HPV tests were performed in 11 cases (including 7 negative-margin cases, 3 positive-margin cases and case with a non-assessable margin); the high-risk HPV test was positive in 6 cases (including 2 negative-margin cases using the ultrasonic scalpel, 1 negative-margin case using the YAG laser, 2 positive-margin cases using the YAG laser, and 1 non-assessable margin case using the YAG laser). Colposcopy with cervical biopsy was performed in 4 cases; 2 cases of CIN 1 and 2 cases of CIN 2 were detected (1 positive-margin case using the YAG laser and 1 negative-margin case using the ultrasonic scalpel). One patient underwent re-excision, and the result was negative for dysplasia. A total of 5 patients were negative for high-risk HPV (including 4 negative-margin patients and 1 positive-margin patient). Of those 5 patients, 4 were followed up by repeat cervical cytology, and all the cytological results were negative. In one case, hysterectomy was performed at the patient's request, and the result was negative for dysplasia.

The high-risk HPV test was not performed in 8 cases (including 4 negative-margin and 4 positive-margin cases). Of the 8 cases, 5 (3 negative-margin and 2 positive-margin) were followed up by repeat cervical cytology, and all the cytological results were negative. Immediate colposcopy with cervical biopsy was performed in 1 patient (with a positive margin), and no dysplasia was detected. Two patients (1 negative-margin and

Table I. Patient characteristics (n=142).

Characteristics	Cytological findings after treatment	
	Normal	Abnormal
Number of patients	115	27
Mean age, years	36.2	35.5
Conization procedure, n (%)		
Ultrasonic scalpel	38 (33.0)	12 (44.4)
YAG laser	77 (67.0)	15 (55.6)
Margins status of the excised specimens, n		
Negative	66	13
Positive	32	12
Not assessable	17	2
Postoperative follow-up visits		
Mean total number of visits (median)	7.1 (6)	7.5 (6)
Mean duration, months (median)	42.0 (33)	41.1 (31)
Mean interval, months	5.6	5.2

YAG, yttrium-aluminum-garnet.

1 positive-margin) underwent immediate colposcopy followed by hysterectomy at their request; 1 of the patients had CIN 3, and the other patient had CIN 1 (Table III).

Worse than LSIL group. In this group, there were 2 negative-margin patients, 5 positive-margin patients, and 1 non-assessable margin patient. There were 4 cases of LSIL (3 positive-margin and 1 non-assessable margin), 3 cases of high-grade squamous intraepithelial lesion (HSIL) (2 negative-margin and 1 positive-margin), and 1 case of atypical squamous cells, which cannot exclude high-grade squamous intraepithelial lesion (ASC-H) (a positive-margin case) (Table IV).

Of the 8 patients, 7 underwent immediate colposcopy. Two patients with LSIL (both with non-assessable margin) had negative findings on colposcopy and were then followed up with repeat and cervical cytological examination, which have been normal thus far. Colposcopy with cervical biopsy was performed after 4 re-excisions. All the patients exhibited CIN 3 (including 1 HSIL with negative margins, 2 LSIL with positive margins, and 1 HSIL with positive margins). In the single remaining case, hysterectomy was performed at the patient's request, with ASC-H including a positive margin, and CIN 3 was detected in this case. One patient was lost to follow-up for unknown reasons (Table IV).

Identification of recurrent disease. Based on colposcopy with cervical biopsy, re-excision, and hysterectomy after detecting abnormal cytology, CIN 2 and CIN 3 were diagnosed in 8 of the 142 cases. The recurrence rate of CIN 2 and CIN 3 was 5.6% of all cases and 29.6% (8/27) in the abnormal cytology cases. The recurrence rate was 15.7% (3/19) in the ASC-US group and 71.4% (5/7) in the worse than LSIL group. The cumulative recurrence-free rate was significantly better for the ASC-US group compared with that in the worse than LSIL group (log-rank test P<0.05; Fig. 1). All cases of worse than LSIL that underwent histopathological examination were diagnosed with CIN 3.

Postoperative identification of abnormal cytology and recurrence time. There was no significant difference in the time to first identification of abnormal cytology after treatment between the worse than LSIL and the ASC-US groups (12.12±15.2 vs. 24.73±30.6, respectively; P=0.054; Student's t-test). There was no significant difference in the time to first identification of abnormal cytology after treatment by margin status of the excised specimens (positive, 16±23.5; negative, 28±3.24; non-assessable, 17.4±15.02 months; P=0586; Kruskal-Wallis test). However, there was a significant difference in the time to first identification of abnormal cytology after treatment between the recurrence and the no recurrence groups (32.37±40.18 vs. 16.21±19.19, respectively; P=0.003; Student's t-test).

Discussion

ASC-US was the most common abnormal cytological finding after treatment for CIN 3. Among all participants, 19% displayed cytological abnormalities after treatment in this study; the rate of ASC-US was 13.3%, and that of worse than LSIL 5.6%. The recurrence rate was 15.7% (3/19) in the ASC-US group and 71.4% (5/7) in the worse than LSIL group.

The Bethesda System (2001 revision) was adopted in 1988 (7). ASC-US accounts for 90% of ASC cases in American standard facilities, and ASC-H accounts for 10%. With respect to the frequency of ASC, it has been suggested that good management requires that the ASC:SIL ratio be maintained at <1.5, and the frequency of ASC be maintained at <5% of all cervical screenings (7). With respect to the accuracy of cancer screenings in our institute, the rate of negative cytology results in conventional cancer screenings (95%) was similar to the rate of normal cytology results using conventional cytology (96%) in the Canadian Cervical Cancer Screening Trial (9).

In the population-based screening phase, it has been reported that ASC-US were found in <1% of the cases in a single population-based study (10). Solomon *et al* reported that <4% of U.S. women were given an equivocal cervical cytological diagnosis (ASC-US) annually (11). Based on these facts, the results obtained in the present study revealed a rate of ASC-US that appears to be quite high (13.3%) compared with these previous reports. ASC-US comprises a wide variety of cervical cells, including benign and malignant cells, and it appears reasonable to suggest that a proportion of women who receive treatment for CIN with ASC-US have postoperative inflammation resulting in altered cell morphology.

In addition, it has been reported that, on conventional cervical cytology alone, ASC-US accounts for 6.9% of CIN 2, 2.6% of CIN 3, and 0.18% of cervical cancer cases (12). In the present study, the recurrence rate was 15.7% (3/19) in the ASC-US group. CIN 2 and CIN 3 were the final pathological diagnoses in 2/19 (10.5%) and 1/19 (5.2%) patients, respectively. The 2 CIN 2 cases (1 with a positive margin using

Table II. Association of abnormal cytology and conization procedure with margin status.

Cytology after treatment	Conization procedure	Margin status of the excised specimens, n				P-value (Pearson's χ^2 test)
		Negative	Positive	Unclear	Total	
Normal	YAG laser	42	25	10	77	0.267
	Ultrasonic scalpel	24	7	7	38	
	Total	66	32	17	115	
Abnormal	YAG laser	4	9	1	15	0.036
	Ultrasonic scalpel	9	3	1	12	
	Total	13	12	2	27	
Total	YAG laser	46	34	11	92	0.104
	Ultrasonic scalpel	33	10	8	50	
	Total	79	44	19	142	

A P-value of <0.05 was considered significant. YAG, yttrium-aluminum-garnet.

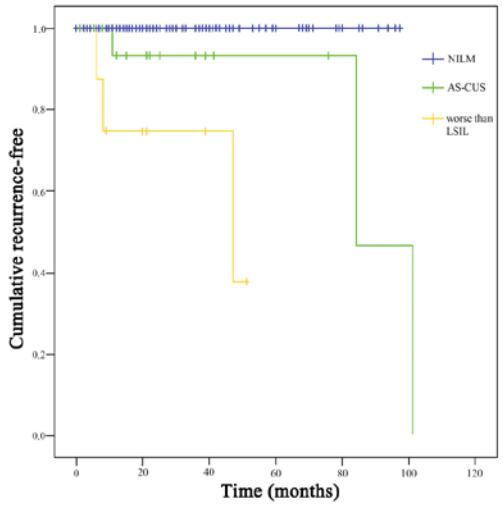

Figure 1. Cumulative recurrence-free rate. Kaplan-Meier survival curves with log-rank tests, with patient status at the time of the last follow-up visit, were used to compare the cumulative recurrence-free rates among the normal, ASC-US and worse than LSIL groups. NILM, negative for intraepithelial lesion or malignancy; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion.

the YAG laser, and the other with a negative margin using an ultrasonic scalpel), were diagnosed with high-risk HPV. The remaining CIN 3 case (negative margin using a YAG laser and unknown, high-risk HPV status) was detected by immediate colposcopy.

On the basis of these facts, it appears reasonable to predict that women with ASC-US who have undergone treatment for CIN would be at a greater risk of developing cervical cancer compared with women with ASC-US in population-based screenings. As regards the risk stratification of women following treatment for CIN, it is crucial to determine an appropriate triage method able to identify women with ASC-US that have or will develop a cervical cancer precursor.

The risk of developing recurrent high-grade CIN (CIN 2 or CIN 3) and cervical cancer with a positive margin after treatment is high. The margin-positive recurrence rate after conization is 9-16% (13), whereas the margin-negative recurrence rate has been reported to be 2-4% (14,15). Melnikow *et al* noted that recurrence was defined by initial CIN grade and treatment type (5). A positive margin after treatment is one of the most important risk factors for recurrence (12), but evaluation of margins after conization may be difficult; therefore, in the present study, margin status was not assessable in some of the cases. Although there was no significant difference in recurrence of CIN 3 between the YAG laser and the ultrasonic scalpel, the use of the ultrasonic scalpel was more frequent in the abnormal group. During conization with a YAG laser, the margins are often cauterized; this may have resulted in a low incidence of abnormal cytological findings. In our hospital, a coin-shaped resection is performed for nulliparous women, often resulting in unclear or positive margins.

However, even women with clear excision margins are at risk for disease recurrence (16). The risk of developing invasive cancer after treatment for high-grade CIN is five times higher compared with that in the general population (17), which justifies closer surveillance of such patients with annual cytology and colposcopy follow-up for 10 years after treatment (18). Therefore, for women treated for CIN 3, it has been recommended that they have cytological follow-up at least 6 and 12 months after treatment, and annual cytology for the next 9 years, before resuming screening at the routine interval (19).

There was a significant difference in the time to first identification of abnormal cytology after treatment between the recurrence and the no recurrence groups (32.37±40.18 vs. 16.21±19.19, respectively; P=0.003; Student's t-test). However, the cumulative recurrence-free rate was a significantly better in the ASC-US group compared with that in the worse than LSIL group (log-rank test P<0.05).

Cytological abnormalities during the early postoperative period are due to persistent lesions or postoperative inflammation resulting in altered cell morphology, whereas those in the late postoperative period are due to the generation of new dysplasia. According to the ACOG guidelines and a Cochrane Database systemic review (2,3), CIN recurrence was

Table III. Course of ASC-US cases.

Case	Age (years)	Conization procedure	Margin status of the excised specimens	Time to first identification of abnormal cytology after treatment (months)	Management after first identification of abnormal	High-risk HPV DNA test	Follow-up after first management	Final evaluation	Follow-up time (months)
1	27	Ultrasonic scalpel	Negative	14	Repeat cervical cytology		Repeat cervical cytology	NILM	35
2	30	Ultrasonic scalpel	Negative	6	Repeat cervical cytology		Repeat cervical cytology	NILM	22
3	30	Ultrasonic scalpel	Negative	8	Repeat cervical cytology		Repeat cervical cytology	NILM	18
4	36	Ultrasonic scalpel	Negative	2	High-risk HPV DNA test	Negative	Repeat cervical cytology	NILM	22
5	35	Ultrasonic scalpel	Negative	1	High-risk HPV DNA test	Negative	Hysterectomy	No dyplasia	11
6	35	Ultrasonic scalpel	Negative	12	High-risk HPV DNA test	Negative	Repeat cervical cytology	NILM	22
7	33	Ultrasonic scalpel	Negative	8	High-risk HPV DNA test	Negative	Repeat cervical cytology	NILM	18
8	31	Ultrasonic scalpel	Negative	11	High-risk HPV DNA test	Positive	Colposcopy with cervical biopsy	CIN 2 followed by ASC-US	27
9	37	Ultrasonic scalpel	Negative	41	High-risk HPV DNA test	Positive	Colposcopy with cervical biopsy	No dysplasia followed by ASC-US	51
10	29	YAG laser	Negative	2	High-risk HPV DNA test	Positive	Re-excision	No dyplasia followed by NILM	44
11	41	YAG laser	Negative	84	Immediate colposcopy		Hysterectomy	CIN 3	103
12	28	Ultrasonic scalpel	Positive	13	Repeat cervical cytology		Repeat cervical cytology	NILM	25
13	41	Ultrasonic scalpel	Positive	5	Repeat cervical cytology		Repeat cervical cytology	NILM followed by pregnancy	15
14	33	YAG laser	Positive	76	High-risk HPV DNA test	Negative	Repeat cervical cytology	NILM	86
15	34	YAG laser	Positive	32	High-risk HPV DNA test	Positive	Colposcopy with cervical biopsy	CIN 1 followed by HSIL	49
16	42	YAG laser	Positive	101	High-risk HPV DNA test	Positive	Colposcopy with cervical biopsy	CIN 2 followed by NILM	121
17	35	YAG laser	Positive	12	Immediate colposcopy		Colposcopy with cervical biopsy	No dysplasia followed by NILM	32
18	62	YAG laser	Positive	9	Immediate colposcopy		Hysterectomy	CIN 1	31
19	32	YAG laser	Not assessable	43	High-risk HPV DNA test	Positive	Colposcopy with cervical biopsy	CIN 1 followed by NILM	46

ASC-US, atypical squamous cells of undetermined significance; NILM, negative for intraepithelial lesion or malignancy; CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesion; HPV, human papillomavirus; YAG, yttrium-aluminum-garnet.

often observed in the first 24 months; however, in the present study, it appeared that follow-up for 48 months after surgery is necessary. Even CIN 3 recurrence was observed 5 years after surgery. Although follow-up for >48 months is necessary,

Table IV. Course of worse than LSIL cases.

Case	Age (years)	Conization procedure	Margin status of the excised specimens	Time to first identification of abnormal cytology after treatment (months)	Cytology findings	Management after first identification of abnormal cytology	Follow-up after first management	Final evaluation	Follow-up time (months)
1	34	YAG laser	Negative	1	HSIL	Colposcopy with cervical biopsy	Re-excision (CIN 3)	CIN 3 followed by HPV, negative ASC-US	49
2	45	YAG laser	Negative	4	HSIL	Unknown			4
3	50	YAG laser	Positive	1	ASCH	Colposcopy with cervical biopsy	Hysterectomy	CIN 3	31
4	26	Ultrasonic scalpel	Positive	47	LSIL	Colposcopy with cervical biopsy	Re-excision (CIN 3)	CIN 3 followed by NILM	69
5	28	YAG laser	Positive	12	LSIL	Colposcopy	Negative findings followed by repeat cytology	NILM	61
6	32	YAG laser	Positive	8	LSIL	Colposcopy with cervical biopsy	Re-excision (CIN 3)	CIN 3 followed by NILM	44
7	35	YAG laser	Not assessable	18	LSIL	Colposcopy	Negative findings followed by repeat cytology	NILM	30
8	37	YAG laser	Positive	6	HSIL	Colposcopy with cervical biopsy	Re-excision (CIN 3)	CIN 3 followed by NILM	30

ASC-US, atypical squamous cells of undetermined significance; NILM, negative for intraepithelial lesion or malignancy; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells, cannot exclude HSIL; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; YAG, yttrium-aluminum-garnet.

the appropriate intervals and methods have not been fully elucidated (2).

For the first 4 years after surgery, close observation is considered necessary, but the number of patient follow-up visits decreased over time. In our hospital, ~50% of cases in were followed-up for 48 months. When no cytological abnormality was identified, the follow-up was often interrupted. As only 50% of cases returned, the proportion of recurrent cases was higher. Even if the HPV test is negative, follow-up for 20 years after conization is recommended in the ACOG guidelines (2,3). Continuous observation of all cases for 48 months is difficult. In order to prevent abnormal cytology or CIN 3 recurrence, margin ablation is important, particularly in coin resection cases. Margin ablation is important in the prevention of recurrence after conization, and it is possible to reduce the follow-up visits after surgery in such cases (20,21).

Katki *et al* reported that, among ASC-US patients who tested positive for high-risk HPV, CIN 2 was diagnosed in 18%, CIN 3 in 6.8%, and cervical cancer in 0.41% of the cases (12). However, in patients who tested negative for high-risk HPV, CIN 2 was diagnosed in 1.1%, and CIN 3 in 0.43% of the patients in previous studies (12,22). High-risk HPV tests are used for risk stratification and they may be a reasonable alternative to post-treatment Pap smear cytology based on sensitivity and specificity. However, these sensitivity and specificity values are likely not applicable in a post-treatment surveillance setting, in which the prevalence of high-risk HPV is significantly higher compared with the screening phase (5,23). In the post-treatment setting, it is important to distinguish between a newly detected HPV genotype or recurrent detection of a lesion-associated HPV genotype, as it has been reported that most HPV infections are cleared 12 months after surgery, whereas very few

are cleared after this interval (24). Thus, the interpretation of the role of high-risk HPV tests for post-treatment surveillance may be difficult.

Abnormal cytology worse than LSIL suggests recurrence of CIN 3. Cytology may predict the presence and grade of dysplasia. Approximately one-fifth of patients who had abnormal postoperative cytology develop recurrence. Worse than LSIL cases are particularly likely to develop recurrence. Recurrence of CIN 3 was identified in 6 cases (4.2% of all patients); this recurrence rate was somewhat higher compared with the reported margin-negative cases (14,15). CIN 3 recurrent cases were observed within 12 months and after 42 months following conization. For early detection of recurrence, cervical smears should be performed within at least 12 months after surgery.

Although several options for post-treatment surveillance have been proposed, the current recommendations by the ACOG and the American Society of Colposcopy and Cervical Pathology suggest that, after treatment, women may require follow-up with a combination of cytology, colposcopy and the high-risk HPV test (2-4). A Cochrane Database Systematic Review found no evidence from randomized controlled trials to update decisions on the optimal surveillance strategy following treatment for CIN (2). If surveillance cytology shows ASC-US, immediate colposcopy is recommended based on the results of the present study.

Approximately one-fifth of the conization cases had CIN 3 as a postoperative cytological abnormality worse than ASC-US. Approximately one-fifth of patients with abnormal cytological findings after conization had recurrence. Worse than LSIL cases are more likely to develop recurrence. Cytological abnormalities and CIN 3 recurrence require close postoperative follow-up. As regards the risk stratification of women following treatment for CIN, if surveillance cytology shows ASC-US, immediate colposcopy is recommended, along with long-term follow-up.

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