Evaluation of Endocervical Canal in Women With Minimal Cervical Cytological Abnormalities

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■ **Abstract**

Objective. This study aimed to examine the endocervical canal curettage (ECC) results of patients with atypical squamous cells of undetermined significance (ASC-US) or low-grade intraepithelial lesion (LSIL) and secondarily to explore the features of patients who are at greatest risk for endocervical involvement.

Materials and Methods. This is a retrospective analysis of 846 women who underwent ECC with ASC-US or LSIL on cervical cytology between January 2003 and April 2011. Records of demographic data and colposcopic impression were evaluated. Histopathological results of biopsies and ECC were classified into 2 categories as less than cervical intraepithelial lesion 2 (CIN 2) and CIN 2+ lesions for comparison. Multivariate analysis was performed using binary logistic regression analysis to identify predictors of ECC results.

Results. CIN 1 lesions were detected in 8.9% of patients, and the rates of CIN 2 or 3 and invasive/microinvasive cancers in ECC were 3.8% and 0.7%, respectively. Cervical intraepithelial lesion 2 or worse lesions were detected in 1.6% (7/419) of the patients with normal colposcopic findings. There was no statistically significant difference in the rate of CIN 2+ lesion in endocervical canal between the patients with or without satisfactory colposcopic examination (4.4% vs 4.1% $p = .69$). A total of 1.7% of the patients who did not have cervical biopsy and also 1.1% of the patients who had less than CIN 2 biopsy results were diagnosed with CIN 2+ lesion by ECC despite the satisfactory colposcopy. Only a positive biopsy result for dysplasia was found to be an independent factor for the detection of a dysplastic lesion in endocervical canal (odds ratio = 0.06; 95% CI = 0.01–0.35; $p = .02$).

Conclusions. Endocervical canal curettage had minimal diagnostic utility for the detection of CIN 2 or worse lesions in women with ASC-US or LSIL smear result and normal colposcopic findings. In addition to this, the presence or absence of CIN 2+ lesions diagnosed by means of endocervical curettage was independent of a satisfactory or unsatisfactory colposcopic examination. ■

Key Words: endocervical curettage, ASC-US, LSIL, cervical intraepithelial lesion

Consensus guidelines developed by the American Society for Colposcopy and Cervical Pathology advise endocervical sampling for women referred with low-grade cytological findings when no lesion is identified on colposcopic examination or when the colposcopic examination is unsatisfactory and has high-grade cytological findings [1]. Endocervical sampling is considered "acceptable" in the context of a satisfactory colposcopic examination and an identified lesion. Although it is generally agreed on that endocervical curettage (ECC) should not be performed in certain populations (adolescents, immunocompromised patients, and pregnant women), debate remains about who should need an ECC [2]. Some investigators prefer to perform ECC in

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every woman undergoing colposcopy regardless of age or cytological results, even if the entire transformation zone can be visualized, to avoid missing cases of preinvasive lesions and invasive cervical cancer in the canal [3–5]. Others believe that ECC is an overused procedure, which has minimal diagnostic utility, suggesting it to be used only in selected cases as an adjunct to colposcopy [6–10]. The prevalence of occult endocervical lesions reported as 25% to 30% in patients with high-grade squamous intraepithelial lesions and endocervical assessment should be performed as a part of colposcopic management of high-grade squamous intraepithelial lesions [7, 11, 12]. However routine endocervical canal evaluation during colposcopic examination is still controversial in low-grade cervical cytological result.

Aside from the discomfort to the patient, ECC can be problematic owing to its potential morbidity (such as hypotensive attack and syncope) and high cost. In addition, pathological interpretation can be difficult owing to the inadequacy of specimen collection and poorly oriented specimens without a stroma. In addition, at the time of the procedure, the presence of an ectocervical lesion might contaminate the ECC specimen, resulting in more extensive treatment of a suspected endocervical lesion that does not exist.

We aimed to examine the ECC results of patients with mildly abnormal cytological result and secondarily to explore the features of patients who are at greatest risk for endocervical involvement.

MATERIALS AND METHODS

We conducted a retrospective study that included women with low-grade cervical cytological result evaluated between January 2003 and April 2011 at the colposcopy unit of 2 clinical centers, Haseki Teaching and Research Hospital and Kanuni Sultan Suleyman Teaching and Research Hospital. The medical records of 1,944 women referred to the colposcopy service owing to atypical squamous cells of undetermined significance (ASC-US) or low-grade intraepithelial lesion (LSIL) were reviewed, and patients who underwent ECC procedure were analyzed for this study. Records from the colposcopic examination database to abstract the colposcopic impression and whether the examination was satisfactory were evaluated. In addition, demographic characteristics of women were obtained including gravidity, parity, use of contraception, and menopausal status.

The colposcopic examinations were performed by gynecologic oncologists. Colposcopic examination was performed after the application of 5% acetic acid solution to the cervix. The examination was considered satisfactory when the entire squamocolumnar junction and the margin of any visible lesion could be visualized with the colposcope. A colposcopic result was considered positive when a flat or slightly elevated, mostly well-demarcated, acetowhite lesion, punctuation pattern or mosaic pattern were found after acetic acid application. Colposcopically directed cervical biopsy specimens were obtained from any lesion suspicious for cervical intraepithelial lesion (CIN). Colposcopy was defined "unsatisfactory" if squamocolumnar junction was not visible during the examination. Endocervical curettage was performed according to the clinicians' judgment, often in cases where the transformation zone or proximal extent of a cervical lesion was not adequately visualized. Endocervical curettage was performed with an endocervical curette according to routine local practice and processed as a histopathological specimen. Clinical management was based on the clinical center pathologists' histological diagnosis. If the specimen is reported as insufficient for diagnosis/no-endocervical sampling, repeated diagnostic procedure was performed for obtaining sufficient material for evaluation. The patients with sufficient endocervical sampling were analyzed in this study. Histopathological data were classified into 2 categories, less than CIN 2 (including cervicitis, atrophy, cervical polyp, metaplasia, and CIN 1) and CIN 2+ lesions.

All statistical analyses were performed using SPSS 15.0 version for Windows (SPSS, Chicago, IL). We calculated χ^2 statistics with p values to compare the clinicopathological features of the patients with and without endocervical canal dysplasia. A multivariate analysis was performed using binary logistic regression analysis to identify predictors of ECC results.

RESULTS

A total of 846 women who underwent ECC were analyzed for this study. The rate of ECC for women who referred to the colposcopy service owing to ASC-US or LSIL was detected as 43.5%. The median age was 42 years (21–75 years), and most of the patients were premenopausal (n = 663, 78.4%). Table 1 summarizes the demographic and clinical characteristics of the patients.

Satisfactory colposcopic examination was found in 49.5% (n = 419) of the patients, and 78.5% of the patients underwent biopsy. Table 2 summarizes the clinicopathological features of the patients. Cervical

Table 1. Demographic and Clinical Characteristics of the Patients

Age, median (range)	42 (21–75)
Gravidity, *n* (%)	
0	46 (5.4)
1–3	427 (50.5)
>4	373 (44.1)
Parity, *n* (%)	
0	89 (10.5)
1–3	570 (67.4)
>4	187 (22.1)
Menopause, *n* (%)	183 (21.6)
Current smoker, *n* (%)	269 (31.8)
Age at first coitus, mean (SD), y	20.2 (4.3)
Total no. sexual partner, *n* (%)	
1	804 (95.1)
>1	42 (4.9)
Smear results, *n* (%)	
ASC-US	446 (52.7)
LSIL	400 (47.3)

ASCUS, atypical squamous cells of undetermined significance; LSIL, low-grade intraepithelial lesion.

intraepithelial lesion 2+ lesions in the endocervical canal were detected in 4.4% (n = 38) of the patients. Cervical intraepithelial lesion 1 lesions were detected in 75 of patients (8.9%) and the rates of CIN 2/3/CIS and invasive/microinvasive cancers in ECC were 3.8% (n = 32) and 0.7% (n = 6), respectively.

Table 3 shows the clinicopathological features of the patients with and without CIN 2+ lesions in the endocervical canal. Cervical intraepithelial lesion 2+ lesions were detected in 1.6% (7/419) of the patients with normal colposcopic findings. Cervical intraepithelial lesion 2+ lesions were detected in 4.7% (20/419) of the patients with satisfactory colposcopic examination and 4.2% (18/427) of the patients with unsatisfactory colposcopy. There was no statistically significant difference in endocervical canal dysplasia between the patients with and without satisfactory colposcopic examination (p = .69). Of the patients with less than CIN 2 biopsy results, 1.6% (7/419) had CIN 2 or higher-grade lesions.

Table 2. Clinicopathological Features of the Patients

	n (%)
Satisfactory colposcopy	419 (49.5)
Colposcopic findings	
Normal	494 (58.3)
Abnormal	352 (41.7)
No. patients who had biopsy	664 (78.5)
Cervical biopsy results	
Normal	343 (40.5)
CIN 1	216 (25.6)
CIN 2	30 (3.5)
CIN 3/CIS	69 (8.2)
Invasive/microinvasive cancer	6 (0.7)
No biopsy	182 (21.5)
ECC result	
Normal	733 (86.7)
CIN 1	75 (8.9)
CIN 2 or 3/CIS	32 (3.8)
Invasive/microinvasive cancer	6 (0.7)

CIN, cervical intraepithelial neoplasia; CIS, carcinoma in situ; ECC endocervical canal curettage.

Table 3. Comparision of the Clinicopathological Features of the Patients With or Without CIN 2+ Lesions of the Endocervical Canal

	<CIN 2	CIN 2+	
	(n = 808), *n* (%)	(n = 38), *n* (%)	p[a]
Age, y			.17[b]
21–30	124 (15.3)	3 (7.9)	
31–40	244 (30.2)	14 (36.8)	
41–50	331 (41.0)	12 (31.6)	
>50	109 (13.5)	9 (23.7)	
Current smoker	84 (32.1)	4 (26.7)	.66
Premenopause	170 (21.0)	13 (34.2)	.06
Smear results			.18
ASC-US	422 (52.2)	24 (63.2)	
LSIL	386 (47.8)	14 (36.8)	
Satisfactory Colposcopy			.69
Yes	399 (49.4)	20 (52.6)	
No	409 (50.6)	18 (47.4)	
Colposcopic findings			.0001
Normal	487 (60.3)	7 (18.4)	
Abnormal	321 (39.7)	31 (81.6)	
Biopsy result			.0001
<CIN 2	552 (68.4)	7 (18.4)	
CIN 2+	79 (9.7)	26 (68.4)	
No biopsy	177 (21.9)	5 (13.2)	

CIN, cervical intraepithelial neoplasia; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade intraepithelial lesion.
[a] p < .05 was considered significant.
[b] χ^2 test for trend.

Endocervical curettage results in patients with or without satisfactory colposcopic examination were summarized in Table 4. Of the patients who had normal colposcopic findings with satisfactory colposcopic examination, 15 (6.3%) had CIN 1 or worse lesion in the endocervical canal, 4 of those were found as CIN 2+. It is noteworthy that, only 6 of the patients who did not have cervical biopsy were diagnosed with squamous cervical dysplasia by ECC despite the satisfactory colposcopy; CIN 2+ lesions were detected in one of them. Of the patients with less than CIN 2 lesions in the biopsy results, 23 were diagnosed with squamous cervical dysplasia by ECC despite the satisfactory colposcopy and 3 of them were detected with CIN 2+.

Multivariate analysis of the factors which can be related with CIN 2+ lesions in endocervical canal in patients with minimal cytological abnormalities is shown at Table 5. Only positive biopsy results for dysplasia was found to be an independent factor for the

Table 4. Endocervical Curettage Results According to Colposcopic Examination and Performance of Biopsy in Patients With or Without Satisfactory Colposcopic Examination

	ECC results			
	Normal	CIN 1	CIN 2/3	Invasive cancer
Satisfactory colposcopy	367	32	16	4
Colposcopic findings, *n* (%)				
Normal	223 (93.7)	11 (4.6)	4 (1.7)	0 (0.0)
Abnormal	144 (79.6)	21 (11.6)	12 (6.6)	4 (2.2)
Cervical biopsy, *n* (%)				
<CIN 2	267 (92.0)	20 (6.9)	3 (1.1)	0 (0.0)
CIN 2+	47 (67.1)	7 (10.0)	12 (17.1)	4 (5.8)
Not performed	53 (89.8)	5 (8.5)	1 (1.7)	0 (0.0)
Unsatisfactory colposcopy	366	43	16	2
Colposcopic findings, *n* (%)				
Normal	237 (92.6)	16 (6.2)	3 (1.2)	0 (0.0)
Abnormal	129 (75.4)	27 (15.8)	13 (7.6)	2 (1.2)
Cervical biopsy, *n* (%)				
<CIN 2	235 (87.3)	30 (11.2)	4 (1.5)	0 (0.0)
CIN 2+	24 (68.6)	1 (2.8)	8 (22.8)	2 (5.8)
Not performed	107 (80.4)	22 (16.5)	4 (3.1)	0 (0.0)

ECC, endocervical canal curettage; CIN, cervical intraepithelial neoplasia.

detection of CIN 2+ lesion in endocervical canal (odds ratio = 0.06; 95% CI = 0.01–0.35; $p = .02$).

DISCUSSION

The evaluation of endocervical canal in patients with cytological abnormalities is important for the identification of the existence of a lesion, which is relatively invisible by colposcopic examination. Clinicians are highly variable in their choice of ECC as a procedure. The main factors associated with the clinicians' decision to perform an ECC are older age, increasing severity of cytological result and colposcopic findings, and an inadequate colposcopic impression [9]. Our findings indicated that the rate of endocervical canal abnormalities were not significantly different between the groups according to age and menopausal status. Inadequate colposcopic examination was found in 50.5% of the patients involved in this study. This ratio was previously reported to range from 5% to 45.9% [13–18]. The higher rate that we reported can be explained by the selection of the cohort, which includes only the patients who underwent ECC.

Solomon et al. [9] reported the diagnostic yield of ECC as part of the colposcopic procedure in the multicenter, randomized trial of management strategies for women with mildly abnormal cytological result (ASCUS-LSIL Triage Study). Cervical intraepithelial lesion 2+ lesions were defined as end point in the latest study, and 3.7% of ECCs yielded a positive result compared with 21.7% of colposcopically directed biopsies. The overall sensitivity of colposcopically directed biopsy was 72.5%, whereas the corresponding rate was 12.2% for ECC in the latest report. The value of ECC as a diagnostic tool is questionable and raises concern that an endocervical lesion could go undetected for the low sensitivity rate.

The recent data suggest that CIN 1 uncommonly progresses to CIN 2 or 3, at least within the first 24

Table 5. Multivariate Analyses of the Factors That Can Be Related With CIN 2+ Lesions in Endocervical Canal in Minimal Cytological Abnormalities

	OR	95% CI	p^a
Age, y			
21–30	Reference		
31–40	1.88	0.86–4.91	.68
41–40	2.51	0.14–4.23	.52
>50	2.84	0.45–2.44	.18
Smoking			
No	Reference		
Yes	2.24	0.59–8.45	.23
Menopause status			
Premenopause	Reference		
Postmenopause	0.49	0.09–2.56	.40
Smear results			
ASC-US	Reference		
LSIL	2.17	0.71–6.44	.49
Satisfactory colposcopy			
Yes	Reference		
No	1.27	0.34–4.69	.71
Colposcopic findings			
Normal	Reference		
Abnormal	0.96	0.16–5.76	.96
Biopsy result			
Negative	Reference		
Positive	0.06	0.01–0.35	.02

CIN, cervical intraepithelial lesion; OR, odds ratio; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade intraepithelial lesion.
[a] $p < .05$ was considered significant.

months [19]; in case of CIN 1 preceded by ASC-US or LSIL, a strict follow-up with either HPV DNA testing every 12 months or repeated cervical cytological examination every 6 to 12 months is recommended [20]. Colposcopic examination and treatment are necessary in case of the persistence or progression of the abnormalities. The studies focused on minimal cytological abnormalities of the cervix reported CIN 2+ lesion in endocervical canal with a range of 0.8% to 4% [9, 21]. Of the 846 patients with LSIL or ASC-US included in our study, 13.4% had overall endocervical canal dysplasia and 4.5% had CIN 2 or worse lesions. Overall endocervical squamous dysplasia and CIN 2+ rates were found to be 12.4% and 4.7%, respectively, in satisfactory colposcopy in the present study. The rate of endocervical canal dysplasia has been reported to range from 1.4% to 17.9% in cervical cytological abnormalities [13–18, 22].

Available guideline for the use of ECC in low-grade cervical cytological result stated that it is "preferred" for nonpregnant women in whom no lesion is identified and in those with a satisfactory colposcopy but is "acceptable" when colposcopic impression is an abnormal strategy regardless of a satisfactory colposcopy [1]. It is also still questionable what technique is appropriate in the satisfactory examination with normal colposcopic findings with minimal cytological abnormality. It has been reported that the patients with any grade of cervical smear abnormalities with unsatisfactory colposcopic examination have a higher prevalence of coexisting endocervical lesions than those with satisfactory colposcopy (31% vs 17%) [9]. The largest study searching for endocervical canal evaluation in patients with satisfactory examination with normal colposcopic findings in minimal cytological abnormalities was conducted by Williams et. Al [22]. They reported the incidence of squamous dysplasia of the endocervical canal as 0.63% in 159 women who had a satisfactory and normal colposcopic examination result and cervical cytological results of ASC-US, ASC-US favor SIL, or LSIL. The authors concluded that endocervical canal curettage might be safely avoided in such patients. In the present study, 238 patients were identified with satisfactory colposcopy and normal colposcopic impression, and 6.3% of them had CIN 1 or worse lesion in the endocervical canal, whereas 1.7% of them were diagnosed with CIN 2+. Moreover, the patients with satisfactory colposcopy who did not need cervical biopsy were diagnosed with squamous cervical dysplasia by ECC with a rate of 10.2%, and 1.7% of them were CIN 2+ lesions. Abnormal ECC results in normal colposcopic findings can be explained by inaccurate identification of the entire transformation zone, making inadvertent contamination owing to an unrecognized or very small lesion near the cervical os from which biopsy could not be taken.

Squamous dysplasia of the endocervical canal was found to be statistically significantly more common in patients with abnormal colposcopic findings and positive biopsy results for dysplasia in our cohort. Multivariate analyses, which were performed for describing the patients who were at greatest risk for endocervical canal abnormalities, demonstrated that positive biopsy result for cervical dysplasia is an independent factor for endocervical canal involvement for patients with ASC-US or LSIL cytology. We suggest that women who met study criteria with positive biopsy results for cervical dysplasia, in whom the ECC is omitted, might be suitable for evaluation of the endocervical canal.

This study is limited by its retrospective nature and by the performance of the colposcopic examination by multiple colposcopists and selective evaluation of endocervical canal by ECC procedure in certain cases. However, all colposcopies were uniformly performed at gynecologic oncology units by expert colposcopists, and the study included one of the largest numbers of patients with low-grade cytological result. We consider that ideally, our findings should be confirmed by prospective studies that can be designed in such a way that all women with ASC-US or LSIL consecutively undergo endocervical evaluation regardless of adequacy of colposcopy and colposcopic impression with bigger sample sizes for the determination of true incidence.

In conclusion, probably, ECC had minimal diagnostic utility for the detection of CIN 2 or worse lesions in women with ASC-US or LSIL cytology and normal colposcopic findings. In addition to this, the presence or absence of CIN 2+ lesions diagnosed by means of endocervical curettage was independent of a satisfactory or unsatisfactory colposcopic examination. The only independent risk factor for CIN 2+ lesions in endocervical canal was positive biopsy results for cervical dysplasia.

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