ORIGINAL RESEARCH

DOI: 10.5336/jcog.2022-93046

Prognostic Value of Endocervical Curettage at the Time of Colposcopic Assessment of the Uterine Cervix: Cross-Sectional Analytical Research

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ABSTRACT Objective: This study aimed to investigate the necessity and diagnostic value of endocervical curettage (ECC) in cervical preneoplastic and neoplastic lesions. **Material and Methods:** A total of 296 patients who were admitted to the gynecologic oncology outpatient clinic at a single tertiary care center and who simultaneously underwent colposcopic biopsy and ECC between 2018 and 2020 were included in the study. Hematoxylin-Eosin (H&E), p16, and ki-67-stained preparations obtained from biopsy and curettage samples of the patients were analyzed by light microscope. Demographic data of the patients were obtained from the hospital system. Results were statistically and comparatively analyzed. **Results:** Cervical premalignant/malignant lesion was detected in 125 out of 296 patients and premalignant/malignant lesion was detected in 42 patients on ECC. Out of these 42 patients, 19 were diagnosed by ECC material alone. It was striking that all of the 5 HPV-18- positive patients were diagnosed with ECC material. When conization materials of CIN 2-3 patients were assessed with ECC results, it was observed that adenocarcinoma and glandular involvement were remarkably significant in ECC-positive patients. **Conclusion:** Our study involves important findings in the determination of the role of ECC in diagnosing cervical premalignant lesions. ECC simultaneously performed with colposcopic biopsy for appropriate women increases the diagnosticity of colposcopic biopsy procedure and gives information about glandular involvement. Moreover, it can decrease the risk of recurrence and minimize surgical margins.

Keywords: Endocervical curettage; colposcopic biopsy; HPV

Nowadays, endocervical curettage (ECC) is increasingly accompanying colposcopic biopsies in patients with suspected findings on a cervical screening test.[1-3] ECC's rate of finding CIN 2 ranges from 1-15% in the literature. It is known that an ECC is a good option especially for elderly women as it is hard to see squamocolumnar junction although there is a contraindication in pregnancy.[4] However, no cut-off value determining in which ages ECC is performed has been defined in the guidelines up to now.[5] Nevertheless, various studies in the literature report that ECC must be performed with multiple samplings in order to increase the possibility to find cervical cancers.[4,6,7]

Our study aimed to find out the diagnostic value of ECC that is routinely used in the detection of cervical preneoplastic lesions at our hospital.

MATERIAL AND METHODS

In our study, research involving direct intervention on humans or animals, no treatment methods or tools were used. Data scanning was performed retrospectively. This study was approved by the Ethics Committee in Konya Training and Research Hospital, Türkiye (date: July 2, 2020, no: 48929119/774). A total of 296 patients who were admitted to the gynecologic oncology outpatient clinic at a single tertiary care center and who simultaneously underwent col-

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Peer review under responsibility of Journal of Clinical Obstetrics & Gynecology.

Received: 14 Sep 2022 ***Received in revised form:*** 01 Dec 2022 ***Accepted:*** 20 Dec 2022 ***Available online:*** 22 Dec 2022

poscopic biopsy and ECC between 2018 and 2020 were included in the study. ECC and colposcopic biopsy were performed for screening in patients with suspected malignancy. H&E (Hematoxylin & Eosin), p16, and ki-67-stained preparations obtained from biopsy and curettage samples of the patients were analyzed by light microscope. Demographic data of the patients were obtained from the hospital system. Colposcopic biopsy and human papilloma virus (HPV) subtype results of all patients were recorded. Diagene® HC2 HPV DNA test kits were used in HPV screening tests (Qiagen GmbH, Hilden, Germany). HPV DNA; PCR was performed with LCD Array HPV 3.5 kit (Chipron GmbH, Germany). More than 100 subtypes of HPV have been defined. Therefore, high-risk common types have been specified, and some of the high-risk HPV types are classified as "other."

The results were statistically and comparatively analyzed. The methodology of this study is a descriptive-analytical method and data were analyzed using the statistical software SPSS 21 [SPSS v.21.0 software package program (SPSS Inc, Armonk, NY, US)].

Since the variables in the study were categorical, the normal distribution was not investigated. The only numerical variable of the study is age, but its normal distribution was not investigated, since it is not a dependent but an independent variable.

Arithmetic mean±standard deviation in summarizing numerical data; numbers and percentages were used to summarize categorical data. Statistical significance was accepted as $p<0.05$ in all analyses.

Our study was made in accordance with the Declaration of Helsinki principles and institutional ethical, and legal permissions were obtained.

RESULTS

Premalignant/malignant lesion [low-grade squamous intraepithelial lesion, high-grade squamous intraepithelial lesion (HSIL), and carcinoma], was detected in 42%, of 125 out of 296 patients who were admitted to the gynecologic oncology outpatient clinic and who underwent ECC and colposcopic biopsy. The mean age of 296 patients was 45.4±9.3 (Table 1). While a lesion was detected in the ECC material of 42 out of these 125 (33%) patients, no lesion was detected in the ECC material of 83 (%66) patients. Out of 42 patients who were diagnosed in ECC material, 19 (45%) had the lesion only in ECC material and 23 (%54) had the lesion in both biopsy and curettage materials (Table 2).

While the mean age of 42 patients in whom a lesion was detected on ECC was 45.4, the mean age of the patients who were diagnosed by colposcopic biopsy alone but in whom no lesion was detected on ECC was 42.6. The rate of ECC-positive patients between the ages of 40 and 50 (17/42) was 40% and the

TABLE 1: Age of the patients.

	n	Age (mean±SD)
Cervical lesion positive	125	43±9.4
ECC positive	42	45.7±11.01
ECC negative	83	42.6±8
Cervical lesion negative	171	42.6±10
All	296	45.4±9.3

SD: Standard deviation; ECC: Endocervical curettage.

TABLE 2: Relationship of ECC and colposcopic biopsy results of patients diagnosed with cervical premalignant/malignant lesions.

	Biopsy				
	ECC positive		ECC negative		
	n	%	n	%	
Colposcopic biopsy positive	23	21	83	78	106
Colposcopic biopsy negative	19	10	171	90	190
	42	14	254	85	296

ECC: Endocervical curettage.

rate of those between the ages of 30 and 40 (11/42) was 26% (Table 3).

According to HPV results, while the rate of HPV positivity in patients with a lesion in curettage material was 36/42 (85%), it was 68/83 (81%) in patients who were diagnosed by colposcopic biopsy alone but in whom no lesion was detected in curettage materials. When HPV types were evaluated in the groups who were diagnosed and who were not diagnosed in ECC material dominance superiority of HPV 16 was observed in both groups. However, it was striking that all 5 HPV-18 positive patients were diagnosed in ECC material. No significant difference was observed among other HPV types in neither of the groups (p>0.05) (Table 4).

TABLE 3: ECC results and age distribution of CIN I/LSIL and CIN 2-3/HSIL patients.

	LSIL		HSIL	
Age	n	%	n	%
20-30	3	3.5	0	0.0
31-40	32	37.2	15	41.7
41-50	30	34.9	16	44.4
51-60	19	22.1	3	8.3
61-70	2	2.3	2	5.6

ECC: Endocervical curettage; LSIL: Low-grade squamous intraepithelial lesion; HSIL: High-grade squamous intraepithelial lesion.

TABLE 4: Relationship of HPV types with ECC results.

	ECC			
	Negative		Positive	
HPV type	n	%	n	%
16	30	36.1	14	33.3
18	-	0.0	5	11.9
56	1	1.2	2	4.7
31	9	10.8	4	9.5
33	-	0.0	1	2.3
39	1	1.2	1	2.3
51	8	9.6	1	2.3
35	3	3.6	1	2.3
45	3	3.6	-	0.0
52	3	3.6	1	2.3
68	2	2.4	-	0.0
70	1	1.2	-	0.0
59	1	1.2	-	0.0
Other subtypes	6	7.2	6	14.2
Negative	15	18.0	6	14.2

HPV: Human papilloma virus; ECC: Endocervical curettage.

TABLE 5: Relationship of ECC positive and negative patients with glandular involvement in conization materials.

Conization results	Conization results of ECC-positive patients (n=12)	Conization results of ECC-negative patients (n=25)
Adenocarcinoma	4/12 (34%)	-
Glandular involvement	3/12 (25%)	1/25 (4%)
HSIL	4/12 (34%)	18/25 (72%)
LSIL	1/12 (8%)	4/25 (16%)

ECC: Endocervical curettage; LSIL: Low-grade squamous intraepithelial lesion; HSIL: High-grade squamous intraepithelial lesion.

TABLE 6: Presence of lesion on conization in patients in whom a lesion was monitored on ECC.

Conization results	ECC positive HSIL	ECC negative HSIL	Total
HSIL on conization	13	20	33
LSIL on conization	1	5	6
HSIL+adenocarcinoma	2	-	2
No finding on conization	None	None	0

ECC: Endocervical curettage; LSIL: Low-grade squamous intraepithelial lesion; HSIL: High-grade squamous intraepithelial lesion.

In addition, when conization materials of the patients diagnosed with HSIL after colposcopic biopsy and ECC were assessed with ECC results, it was observed that adenocarcinoma and glandular involvement were remarkably significant in ECC-positive patients (Table 5).

When the conization results of patients with lesions in ECC were compared with patients without lesions in ECC, no significant difference was found in the presence of lesion in the conization material (Table 6).

DISCUSSION

According to the results of our study, performing ECC during colposcopic assessment in order to detect premalignant/malignant cervical lesions increases the sensitivity of colposcopic biopsies. Nineteen out of 125 patients in our series could be diagnosed by ECC alone. ECC's rate of finding the lesions was quite high in our study and this rate is 5.4% (26/181) in a current study in the literature.[6]

Although no cut-off value for age to undergo ECC was determined in the literature, some studies

suggest the age above 45 for ECC. In our study, although ECC-positive patients were mostly between the ages of 40 and 50 (17/42) (40%), patients between the ages of 30 and 40 had a considerable rate (11/42) (26%). This result suggests that patients older than 30 should routinely undergo ECC.[8-10] The results of our study also showed that routine ECC should be performed above the age of 30.

In our study, all HPV 18 positive patients were diagnosed on ECC and the association of HPV 18 with glandular involvement at increasing rates is consistent with the association of ECC with glandular involvement.[11] If we review the most encountered type of HPV, HPV 16, we see that the positive and negative rates of ECC at HPV 16 are almost equal. Although differences with other types were noticed in our results, our data is limited to comment.

According to our results, the positivity rate of cervical premalignant lesions with endocervical involvement on ECC was high. This result suggests performing the conization extensive enough to include the whole endocervical canal for patients in whom a lesion is detected on ECC and comprehensive and supportive studies on this issue are needed.

ECC significantly increases the sensitivity in cervical premalignant or malignant lesions, which supports routine ECC, however, it is contradicted in pregnancy and painful in young women. These are the limiting factors for this sampling.

Studies are reporting that ECC prevents the recurrence of the lesion. However, we have found no difference between ECC-positive and ECC-negative patients in terms of the presence of a lesion in conization materials, which does not support this hypothesis. The low number of patients who underwent conization may cause this result to be different.

CONCLUSION

Our study involves important findings in the determination of the role of ECC in diagnosing cervical premalignant lesions. ECC simultaneously performed with colposcopic biopsy-appropriate women increases the diagnosticity of the colposcopic biopsy procedure and gives information about glandular involvement. Moreover, it can decrease the risk of recurrence and minimize surgical margins.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Fatih Yılmaz, Melike Geyik Bayman;* ***Design:*** *Melike Geyik Bayman, Ayşe Nur Uğur Kılınç;* ***Control/Supervision:*** *Yaşar Ünlü, Fatih Yılmaz, Ayşe Nur Uğur Kılınç;* ***Data Collection and/or Processing:*** *Fatih Yılmaz, Melike Geyik Bayman, Ayşe Nur Uğur Kılınç;* ***Analysis and/or Interpretation:*** *Ayşe Nur Uğur Kılınç, Elif Nur Yıldırım Öztürk;* ***Literature Review:*** *Ayşe Nur Uğur Kılınç, Fatih Yılmaz;* ***Writing the Article:*** *Ayşe Nur Uğur Kılınç, Fatih Yılmaz, Melike Geyik Bayman;* ***Critical Review:*** *Fatih Yılmaz, Melike Geyik Bayman, Yaşar Ünlü;* ***References and Fundings:*** *Yaşar Ünlü;* ***Materials:*** *Fatih Yılmaz, Melike Geyik Bayman, Ayşe Nur Uğur Kılınç.*

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