

Original Investigation

Evaluation of the Compatibility of Loop Electrosurgical Excisional Procedure and Cervical Colposcopic Biopsy Results

İnal et al. Concordance between colposcopic biopsy and LEEP results

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Abstract

Objective: To evaluate the results of loop electrosurgical excisional procedures (LEEP) of 579 patients who presented to our hospital for vaginal smears between 2015 and 2020.

Material and Methods: The LEEP reports of 579 patients who presented to our gynecology clinic between January 2015 and December 2020 were retrospectively evaluated. The data were obtained from electronic patient records and the Medical Pathology Department archives.

Results: The mean age of the patients was 38.05±6.17 years. Colposcopy-guided biopsy was not taken from 102 patients. The results of the remaining 477 patients were as follows: no dysplasia (n=12; 2.5%), CIN-I (n=99; 17.1%), CIN -II (n=111; 19.2%), CIN-III (n=248; 42.8%), and cancer (n=7; 1.2%). Completed excision was performed in 87.0% of the patients using LEEP, the lesion was positive at the surgical margins in 10.9%, and the lesion could not be completely excised in 2.1%. The complication rate after LEEP was 3.1% (pelvic pain, n=5; 0.9% and bleeding, n=13; 2%). The histopathologic results of LEEP were as follows: benign (n=50; 8.6%), CIN-I (n=110; 19.0%), CIN -II (n=89; 15.4%), CIN-III (n= 280; 48.4%), cancer (n=7; 1.2%), and metaplasia (n=37; 6.4%). The concordance between colposcopic biopsy and LEEP results was observed as 85.9% for CIN-I, 71.2% for CIN-II, 98.4% for CIN-III, and 85.7% for cancer diagnoses.

Conclusion: LEEP is a simple minimally invasive method used in the treatment of CIN, with low persistence, recurrence, and complication rates and increased HPV clearance in most patients. Our results support the consistency of cervical colposcopic biopsy and LEEP results.

Keywords: Biopsy, cervical intraepithelial lesion, colposcopy, LEEP

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Introduction

Cervical cancer is the second most common malignancy worldwide after breast cancer. A woman's risk of developing cervical cancer is 0.8% in developed countries and 1.5% in developing countries. Cervical screening aims to diagnose and treat asymptomatic precancerous lesions and reduce mortality and morbidity (1). There are more than 100 subtypes of human papillomavirus (HPV) that cause precancerous lesions, about 40 of which are sexually transmitted and infect the skin and mucous membranes. HPV infections are temporary in young women under the age of 30 years and are cleared by the immune system. Therefore, HPV testing is not recommended for women aged under 30 years (2).

Cervical intraepithelial neoplasia (CIN) is a premalignant squamous lesion of the uterine cervix diagnosed through histopathologic evaluation of cervical biopsy material (3,4). Proper management of CIN is precarious because any delay in treatment increases the risk of cervical cancer, and overtreatment can cause some negative results such as preterm delivery, premature rupture of the membrane, and low birth weight (3,5). The two main management approaches for CIN are observation (cervicovaginal cytology and colposcopy) and local excision or ablation of the cervical transformation zone, hysterectomy is not considered the primary treatment (6,7).

The risk of CIN progression to invasive cancer is related to age and grade (low risk in CIN-I, high risk in CIN-II or III), with the majority of lesions regressing spontaneously in women aged under 25 years (3,6). In CIN-I under 25 years of age, management is usually in the form of observation, and the follow-up of these patients depends on the previous cytology results (2,6). Annual cervical cytology is recommended for atypical squamous cells of undetermined significance (ASC-US) and low-grade squamous intraepithelial lesions (LSIL), and annual cytology and colposcopy are recommended for high-grade squamous intraepithelial lesions (HSIL), and atypical squamous cells, cannot exclude HSIL (ASC-H) (4,8). For CIN-II under the age of 25 years, observation or treatment can be recommended according to the patient's fertility desire (6). Annual HPV testing is recommended for CIN-I lesions in women aged over 25 years, and treatment can be recommended for patients who have completed their fertility and whose follow-up will be difficult. Excision or ablation therapy is recommended for CIN-II and III (8). In pregnant women, colposcopic evaluation at the postpartum sixth week is recommended for CIN-I, and cytology and colposcopic evaluation for each trimester for CIN-II and III are recommended. An endocervical biopsy is strictly contraindicated and treatment is required only in the presence of invasive cancer (6). HPV vaccines have no therapeutic effect on CIN and they have only been shown to reduce recurrence (8).

There are two types of treatment for CIN, depending on the degree of the disease; local ablative treatment or excision. Knife cone excision and radical diathermy are traditional methods and are performed under general anesthesia, whereas excisional procedures such as local ablative methods and loop electrosurgical excisional procedures (LEEP) can be performed under local anesthesia in outpatient clinics. The transformation zone of the cervix should be fully seen and there should be no invasive and glandular disease in local ablative

treatment. Excisional treatment is mandatory in case of insufficient colposcopic findings, and invasive and glandular disease (6). Today, instead of destructive ablative methods, excisional methods with low morbidity such as laser conization and large loop excision of the transformation zone (LLETZ in the United Kingdom) or LEEP (in the United States) are preferred (6,8). Excisional methods allow the complete removal of the transformation zone of the cervix and a more accurate histopathologic examination of the tissue compared with ablative methods (8).

In this study, we aimed to evaluate the LEEP results of 579 patients who presented to our hospital for vaginal smears between 2015 and 2020.

Materials and Methods

A total of 579 patients who underwent biopsy after colposcopic examination of suspicious CIN on whom LEEP was performed were included in the study between January 2015 and December 2020. Ethical approval was obtained from the institutional review board of .. Medical Faculty (2021-3429). The data were reviewed from electronic patient records and the Medical Pathology Department archives. Informed consent was obtained from all patients included in the study at the time of their first admission to the clinic for future use. The samples obtained from LEEP were evaluated by two certified and experienced senior pathologists. The data, including the patients' age, menopausal status, smear results, colposcopic biopsy results, HPV test results before and after LEEP, surgical procedure results, histopathologic results of LEEP, complications of LEEP, follow-up time, disease course, and recurrence were recorded and analyzed. The exclusion criteria were patients who had previously been treated for CIN, inadequate colposcopic findings, and incomplete records.

The results of cervical cytology (our center or externally referred) of patients were assessed according to the Bethesda 2014 classification. The colposcopic evaluation was performed using a Carl Zeiss (Oberkochen, Germany) colposcopy device by two experienced gynecology-oncology specialists who had received colposcopy training, and biopsies were taken from the lesion and/or suspicious areas using Tischler biopsy forceps. Endocervical curettage was also routinely performed after the cervical biopsy procedure. The samples were fixed with formalin for histopathologic evaluation and sent to the Pathology department. LEEP was performed in cases of a CIN-II and CIN-III detection in colposcopic biopsy and/or with a strong CIN appearance in colposcopy or cytology even if the biopsy result was normal, or if the transformation zone could not be seen under sedative anesthesia. LEEP was performed in some patients who completed their fertility after recurrent abnormal smears without high-risk suspicion at their request. In the case of suspected endocervical disease, LEEP was performed separately for the vaginal part and the intracervical part of the cervix. The lesion and/or transformation zone was excised using a 15-25 mm round loop electrode (50-60 W). After the tissue of the suspicious or visible lesion was excised, the safe depth of field was determined as 6 mm. Bleeding control after LEEP was performed using a ball-tipped monopolar electrode. The patients were re-evaluated 3 to 6 months after the procedure for persistent disease with cytology, HPV test, colposcopy, and, if necessary, cervical biopsy and/or endocervical curettage. All procedures were conducted in accordance with the 2019 American Society for Colposcopy and Cervical Pathology Risk-Based Management Consensus Guidelines (9).

Statistical analysis

Data were analyzed using the SPSS 15.0 for Windows software package (SPSS, Chicago, IL, USA). Continuous variables are expressed as mean±standard deviation. Nominal data are expressed as the number of patients and percentages.

Results

Eighty-six of the 665 patients who were reviewed between January 201 and December 2020 were not eligible and were excluded from the study (previously treated; n=26, inadequate colposcopic findings; n=34, and incompleting patients record; n=26). The remaining 579 patients were analyzed in this retrospective study.

Table 1 lists the detailed characteristics of the patients. The mean age of the patients who underwent LEEP procedures was 38.05±6.17 and 61 patients (10.5%) were in the menopausal period. The results of cervical cytology on admission were as follows: atypical squamous cell of undetermined significance (ASCUS), n=65 (11.2%); LSIL, n=116 (20.1%); HSIL, n=316 (54.5%); ASC-H, n=64 (11.1%); and atypical glandular cells (AGC), n=18 (3.1%).

Colposcopic biopsy was not performed on 102 patients due to a strong CIN appearance in colposcopy and the transformation zone could not be seen. The remaining 477 colposcopy biopsy results were found as no dysplasia (n=12; 2.1%), CIN-I (n=99; 17.1%), CIN-II (n=111; 19.2%), CIN-III (n=248; 42.8%), and cancer (n=7; 1.2%). The HPV positivity rate was 83.2% before LEEP, and this rate decreased to 18.7% in the post-procedure follow-ups. Completed excision was performed in 87.0% of the patients who underwent LEEP; lesions were positive at the surgical margins in 10.9% and the lesions could not be completely excised in 2.1%. The procedure was repeated in eight of 12 patients whose lesions could not be completely excised, four patients had a close follow-up. The complication rate after LEEP was 3.1% (pelvic pain, n=5; 0.9% and bleeding, n=13; 2%) and four of the patients with bleeding were cauterized using monopolar cauterization, three were cauterized with silver nitrate, and hemostasis was achieved with sutures in six. When the histopathologic results after LEEP were examined, the distribution was as follows: benign outcome (n=50; 8.6%), CIN-I (n=110; 19.0%), CIN-II (n=89; 15.4%), CIN-III (n=280; 48.4%), cancer (n=7; 1.2%), and metaplasia (n=37; 6.4%). The mean follow-up period of the patients was 37.2±15.1 months, persistent disease was observed in 16 (2.8%) patients, and recurrence was observed in four (0.7%).

The concordance of the colposcopic biopsy and LEEP results of the patients is presented in Table 2. In the LEEP results of 12 patients without dysplasia in the colposcopic biopsy, metaplasia was reported in two. Of 99 patients with CIN-I detected in colposcopic biopsies, 85 had CIN-I, five had CIN-II, and three had CIN-III after LEEP. The LEEP results of 111 patients diagnosed as having CIN-II in colposcopic biopsies were reported as CIN-II in 79 patients, CIN-I in 14, and cancer in one patient. Of the 248 patients in whom preoperative CIN-III was detected on colposcopic biopsy, CIN-III was found in 244, CIN-I in one, and cancer in three patients. Seven patients were diagnosed as having cancer through colposcopic biopsies, cancer was reported again in six patients, and CIN-III was reported in one patient after LEEP. Of 102 patients without preoperative biopsies, no dysplasia was observed in 35, metaplasia was seen in 30 patients, CIN-III was found in 19 patients, CIN-I was seen in 10 patients, CIN-II was seen in five patients, and cancer observed was in three patients on histopathologic evaluation after LEEP. In terms of concordance between colposcopic biopsy and LEEP results, it was observed as 85.9% for CIN-I, 71.2% for CIN-II, 98.4% for CIN-III, and 85.7% for cancer diagnoses, and the overall concordance for all lesions was 73.2%.

Discussion

The current study presents the results of 579 women who underwent LEEP with suspicion of CIN, showing that completed excision was performed in 87.0%, the complication rate was 3.1%, the persistence rate was 2.8%, the recurrence rate was 0.7%, and the concordance between colposcopic biopsy and LEEP results was 85.9% for CIN-I, 71.2% for CIN-II, 98.4% for CIN-III, and 85.7% for cancer diagnoses. The overall concordance for all lesions was 73.2%.

LEEP, which was first tried in 1986, is now a highly effective, safe, and tolerable surgical procedure in the treatment of CIN. Studies in the literature have shown that the rate of persistence of disease is between 2-5% and the rate of recurrence is between 0.5-4% (3, 10).

The reason for these differences in rates is due to the difference in the surgical confidence intervals and therefore the depth of resection. In addition, LEEP has higher efficiency and lower complications compared with cold knife conization and can be performed under local anesthesia in outpatient clinic conditions. It is quite easy to remove lesions or the transformation zone of the cervix with the loop electrode because it is made of thin tungsten or steel wire (8). In our study, we found the persistence rate as 2.8% and the recurrence rate as 0.7%. The most prominent complication of LEEP is postoperative bleeding and pain, whose rates have been reported to vary between 2-4% and 0.5-2%, respectively (3,11-13). In our study, our complication rate was 2.2% for vaginal bleeding and 0.9% for pain. Our results are consistent with the literature.

Known risk factors for persistence and recurrence of CIN are the presence of positive surgical margins and HPV infection. In the literature, it has been reported that the majority of HPV infection after LEEP is clearances and the HPV positivity rate after surgical procedures varies between 10-25% (3,14,15). In our study, an HPV test was performed during the postoperative follow-up of the patients, and our HPV positivity after LEEP results was 18.7%, consistent with the literature.

There are no clear ratios regarding the concordance of LEEP results and colposcopic biopsy results in the literature. In previous studies, the concordance of colposcopic biopsy and LEEP results varies between 60-85% in LSIL and 80-95% in HSIL (3,16-20). In accordance with the literature, we observed that it was around 80% for LSIL and 90% for HSIL. The reason why LSIL is lower than HSIL may vary in the pathologic diagnosis of LSILs, while this variability is lower in HSIL (3). The reason for the high concordance in our study may be that colposcopic procedures were performed by two experienced and trained gynecologic oncologists, and colposcopic biopsies and LEEP were performed in the same center. The number of patients diagnosed as having CIN-II through colposcopic biopsy decreased in definitive histopathologic diagnoses after LEEP in our study. The probable cause of this situation may be the removal of the dysplastic lesion by biopsy or its spontaneous regression. The low recurrence rate and the decrease in the HPV positivity rate may also be caused by the conditions we have just mentioned.

Study limitations

The possible limitation of the study is that the study was retrospective and performed in a single tertiary center. On the other hand, a strength of our study is that cervical colposcopic biopsy and LEEP were performed by the same gynecologic oncologist. In addition, the evaluation of the samples by two pathologists who were experienced and trained in the field of oncology is another feature that makes our study strong.

Conclusion

LEEP is an easy-to-apply minimally invasive method used in the treatment of CIN, with low persistence, recurrence, and complication rates, and increased HPV clearance in most patients. Our results support the consistency of cervical colposcopic biopsy and LEEP results.

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Table 1. The characteristics of the patients				
Features		Mean ± SD	n	%
Age (years)		38.05±6.17		
Premenopause			518	89.5
Postmenopause			61	10.5
Cervical cytology results on admission	ASCUS		65	11.2
	L-SIL		116	20.1
	ASC-H		64	11.1
	H-SIL		316	54.5
	AGC		18	3.1
Colposcopic biopsy results	No dysplasia		12	2.1
	CIN-I		99	17.1
	CIN-II		111	19.2
	CIN-III		248	42.8
	Cancer		7	1.2
	No performed		102	17.6
Before LEEP HPV testing	HPV (+)		482	83.2
	HPV (-)		97	16.8
LEEP result	Completed excision		504	87.0
	No-completed excision		12	2.1
	Ambiguous appearance		63	10.9
Histopathological results of the LEEP	Benign		50	8.6
	CIN-I		110	19.0
	CIN-II		89	15.4
	CIN-III		280	48.4
	Cancer		13	2.2
	Metaplasia		37	6.4
Complications	None		561	96.9
	Pelvic pain		5	0.9
	Bleeding		13	2.2
Follow-up time (months)		37.2±15.1		
HPV testing after LEEP	HPV (-)		471	81.3
	HPV (+)		108	18.7
Disease course	No persistence		563	97.2
	Persistence		16	2.8
Recurrence	No		575	99.3
	Yes		4	0.7
ASCUS: atypical squamous cell of undetermined significance, L-SIL: low grade squamous intraepithelial lesion, ASC-H: atypical squamous cells, HSIL cannot be excluded, H-SIL: high grade squamous intraepithelial lesion, AGC: atypical glandular cells, CIN: cervical intraepithelial neoplasia, LEEP: loop electrosurgical excisional procedure, HPV: human papillomavirus				

Table 2. Concordance of colposcopic biopsy and LEEP results of the patients						
Colposcopic biopsy results (n=579) LEEP results (n=579)	No dysplasia (n=50)	CIN-I (n=110)	CIN-II (n=89)	CIN-III (n=280)	Cancer (n=13)	Metaplasia (n=37)
No Dysplasia (12) (%)	10 (83.3)	-	-	-	-	2 (16.7)
CIN-I (99) (%)	3 (3.0)	85 (85.9)	5 (5.1)	3 (3.0)	-	3 (3.0)
CIN-II (111) (%)	2 (1.8)	14 (12.6)	79 (71.2)	13 (11.7)	1 (0.9)	2 (1.8)
CIN-III (248) (%)	-	1 (0.4)	-	244 (98.4)	3 (1.2)	-
Cancer (7) (%)	-	-	-	1 (14.3)	6 (85.7)	-
No performed (102) (%)	35 (34.4)	10 (9.8)	5 (4.9)	19 (18.6)	3 (2.9)	30 (29.4)