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ORIGINAL RESEARCH

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Treatment of women with CIN3: LEEP versus hysterectomy—a retrospective study

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Abstract

Background: To compare the therapeutic effectiveness of hysterectomy and loop electrosurgical excision procedure (LEEP) in the treatment of cervical intraepithelial neoplasia grade 3 (CIN3), with a focus on recurrence rates and major complications. **Methods**: This retrospective study included patients operated between January 2017 and December 2021 with a pathological diagnosis of CIN3. Only patients diagnosed with CIN3 for the first time through cervical biopsies were included. Cases with a diagnosis other than CIN3 after LEEP or hysterectomy were excluded. A total of 100 patients were analyzed, with 50 patients undergoing LEEP (Group 1) and 50 undergoing hysterectomy (Group 2). **Results**: The median follow-up time was 49.5 months (range: 24–84 months). In Group 1, three patients experienced a recurrence of CIN3 during follow-up and underwent repeat excision procedures. In Group 2, one patient developed vaginal intraepithelial neoplasia grade 3 (VaIN3) after hysterectomy. There was no significant difference in recurrence-free survival between the two groups (p = 0.321). Smoking status was not significantly associated with recurrence (p = 0.527). **Conclusions**: Although no significant difference in recurrence rates was observed between LEEP and hysterectomy for the treatment of CIN3, the small number of recurrences limits the ability to draw definitive conclusions about the superiority of one treatment over the other. Given the well-documented low risk of cervical cancer after LEEP and its minimally invasive nature, LEEP remains the preferred treatment option for CIN3. Further large-scale studies are needed to evaluate the long-term outcomes of different treatment modalities for CIN3.

Keywords

Cervical intraepithelial neoplasia; Hysterectomy; Loop electrosurgical excision procedure

1. Introduction

To reduce cancer-related deaths, early diagnosis is crucial, and cancer screening programs should be carried out regularly [1]. Cervical cancer, which ranks fourth among the cancer types seen in women in the world, is a type of cancer that can be detected at an early stage through screening tests [2]. In 2018, an estimated 570,000 women were diagnosed with cervical cancer with approximately 311,000 women died from the disease [3]. In Turkey, the prevalence of cervical cancer is estimated to be approximately 4.5 per 100,000, making it the tenth most common type of cancer [4]. Cervical cancer screening is important in detecting cervical intraepithelial neoplasia (CIN). CIN is categorized as CIN1, CIN2 and CIN3 based on the extent of abnormal cell growth within the thickness of the cervical epithelium. CIN1 involves dysplasia in the lower one-third of the epithelium, CIN2 extends up to two-thirds, and CIN3 affects more than two-thirds up to the full thickness of the epithelial layer. CIN1 has a low risk of progression to cervical cancer and is managed with repeated testing after 1 year. CIN2 and CIN3, with a higher risk of progression to cervical cancer and are classified as high-grade neoplasias [5]. The loop electrosurgical excision procedure (LEEP) is widely used in the diagnosis and treatment of cervical neoplasias [6]. Hysterectomy is one of the most frequently performed gynecological surgeries globally, employed for both malignant and benign conditions [7]. Although hysterectomy is generally not the first-line treatment for patients with cervical intraepithelial neoplasia (CIN), it can be performed in cases where adequate follow-up is difficult, in patients with vaginal stenosis, or when benign uterine disease accompanies CIN [8]. In this retrospective study, we aimed to objectively assess the therapeutic effectiveness of hysterectomy and LEEP in the treatment of CIN3 and to compare the outcomes in terms of recurrence and major complications.

2. Materials and methods

2.1 Patients

This retrospective study included patients who underwent surgery between January 2017 and December 2021 and whose pathology results confirmed CIN3. Only patients diagnosed with CIN3 for the first time in cervical biopsies were included. Cases with a diagnosis other than CIN3 following LEEP or hysterectomy were excluded. Consequently, 100 patients were included in the study: Group 1 consisted of patients who underwent LEEP, and Group 2 consisted of patients who underwent a hysterectomy. A total of 50 (50%) patients underwent LEEP and 50 (50%) had hysterectomy. Patients who underwent hysterectomy for CIN3 reasons were followed up annually, while patients treated with LEEP were followed up every 6 months. During follow-up, patients with CIN3 and higher lesions (such as carcinoma in situ, adenocarcinoma in situ and malignancy) were considered as recurrences.

2.2 LEEP and hysterectomy

Informed consent was obtained from all patients before surgery. For patients undergoing LEEP, the excised tissue was marked at 12 o'clock and sent for histopathological examination. Endocervical curettage was performed on each patients to detect any remaining lesions in the cervix post-operation. All LEEP procedures were performed under sedoanalgesia.

Patients who underwent laparoscopic and vaginal hysterectomy were excluded from this study. All abdominal hysterectomies were performed using a Pfannenstiel incision under general anesthesia. In cases where bilateral salpingo-oophorectomy was performed in addition to hysterectomy, the decision was made after consulting with the patient and taking into account the patient's age and menopausal status. In our clinic, during a simple hysterectomy planned for benign pathologies accompanied by CIN3, patients were informed prior to surgery, and 1 cm from the upper vagina is removed to reduce the risk of recurrence.

2.3 Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics (Version 22.0. Armonk, NY, USA) for Windows. For continuous variables, standard deviation, mean and median were calculated. Mann-Whitney U test and chi-square test were used for the comparisons. Time-to-event analyses were conducted using the Kaplan-Meier method and log-rank test. Statistical significance was defined when $p < 0.05$.

3. Results

Between January 2017 and December 2021, a total of 100 women were treated for CIN3. 50 patients (50%) underwent LEEP and 50 patients (50%) had simple hysterectomy. Table 1 demonstrates the clinicopathological characteristics. Although the vaccination rate was low in both groups, it was 6% in Group 1 and 0% in Group 2. Notably, three patients in Group 1 were vaccinated after undergoing LEEP. Complications were minimal; however, one Urological complication occurred in a who underwent hysterectomy, in which the bladder was injured. The bladder was appropriately repaired by the urologist and the patient experienced no additional problems during the follow-up. Vaginal intraepithelial neoplasia grade 3 (VaIN3) developed as a recurrence in one case after hysterectomy. For this patient, an abdominal vaginal cuff resection was performed and the patient is currently under follow-up. In the Group 1, three patients experienced a recurrence of CIN3 during follow-up, and re-excision (re-LEEP) was performed in all three cases. All three patients are also currently under follow-up. Importantly, no cases of cervical cancer developed during the follow-up period in either group. In the study, the median follow-up time was 49.5 (range: 24–84) months. There was no significant difference in recurrence-free survival between the two groups ($p = 0.321$) (Fig. 1). Additionally, no significant association was found between smoking status and recurrence of CIN3 ($p = 0.527$).

4. Discussion

This study aimed to assess the clinical management, outcomes, and recurrence rates of patients treated with either LEEP or hysterectomy for CIN3 in our clinic. Although LEEP is the preferred and standard treatment for CIN3 due to its minimally invasive nature and proven effectiveness, hysterectomy is occasionally performed when LEEP is not feasible or when there are additional gynecological indications necessitating uterine removal. In our study, complications occurred in only 2% of cases following hysterectomy, a rate that may reflect the limited patient sample size. Importantly, no major complications were observed in any patients who underwent LEEP for CIN3, highlighting LEEP's safety profile as a first-line treatment for managing CIN3.

Although there was no significant difference in recurrence-free survival between the two groups ($p = 0.321$), the small number of recurrences (three in the LEEP group and one in the hysterectomy group) limits our ability to draw definitive conclusions about the superiority of one treatment over the other. Given LEEP's well-documented low risk of progression to cervical cancer after LEEP and its minimally invasive nature, LEEP remains the preferred treatment option for CIN3. Our findings highlight the importance of adhering to minimally invasive procedures when appropriate and underscore the need for larger, prospective studies to further evaluate the long-term outcomes of different treatment modalities for CIN3. In the phase 3 "Quality of life in patients with cervical cancer after open versus minimally invasive radical hysterectomy" (LACC (Locally advanced cervical cancer)) trial for cervical cancer, minimally invasive radical hysterectomy was associated with lower rates of disease-free survival and overall survival than open abdominal radical hysterectomy in women with early-stage cervical cancer [8]. Although laparoscopic hysterectomy is currently considered an acceptable method for treating CIN3, our clinic prefers an open surgical approach to CIN3 cases [9]. We evaluated CIN3 cases as a potential precursor to cervical cancer aligning our practice with the findings of the LACC study.

Multiple studies have been demonstrated that smoking is a significant risk factor for cervical cancer [10]. Smoking contributes to an increased recurrence of high-grade CIN, a pre-

TABLE 1. Patients characteristics and pathology findings (Total number of patients = 100).

	Group 1 (LEEP)	Group 2 (Hysterectomy)	*p* value
Number of patients	50	50	-
Mean age (yr)	37.6 ± 9.1	51.1 ± 8.7	<0.001*
Vaccination status			
Vaccinated	3	0	0.121
Unvaccinated	47	50	
Smoking status			
Yes	21	19	0.419
No	29	31	
Major complication	0	1	0.315
Recurrence	3	1	0.309
Recurrence free survival	94%	98%	0.321

*LEEP: loop electrosurgical excision procedure; *: p value is significant.*

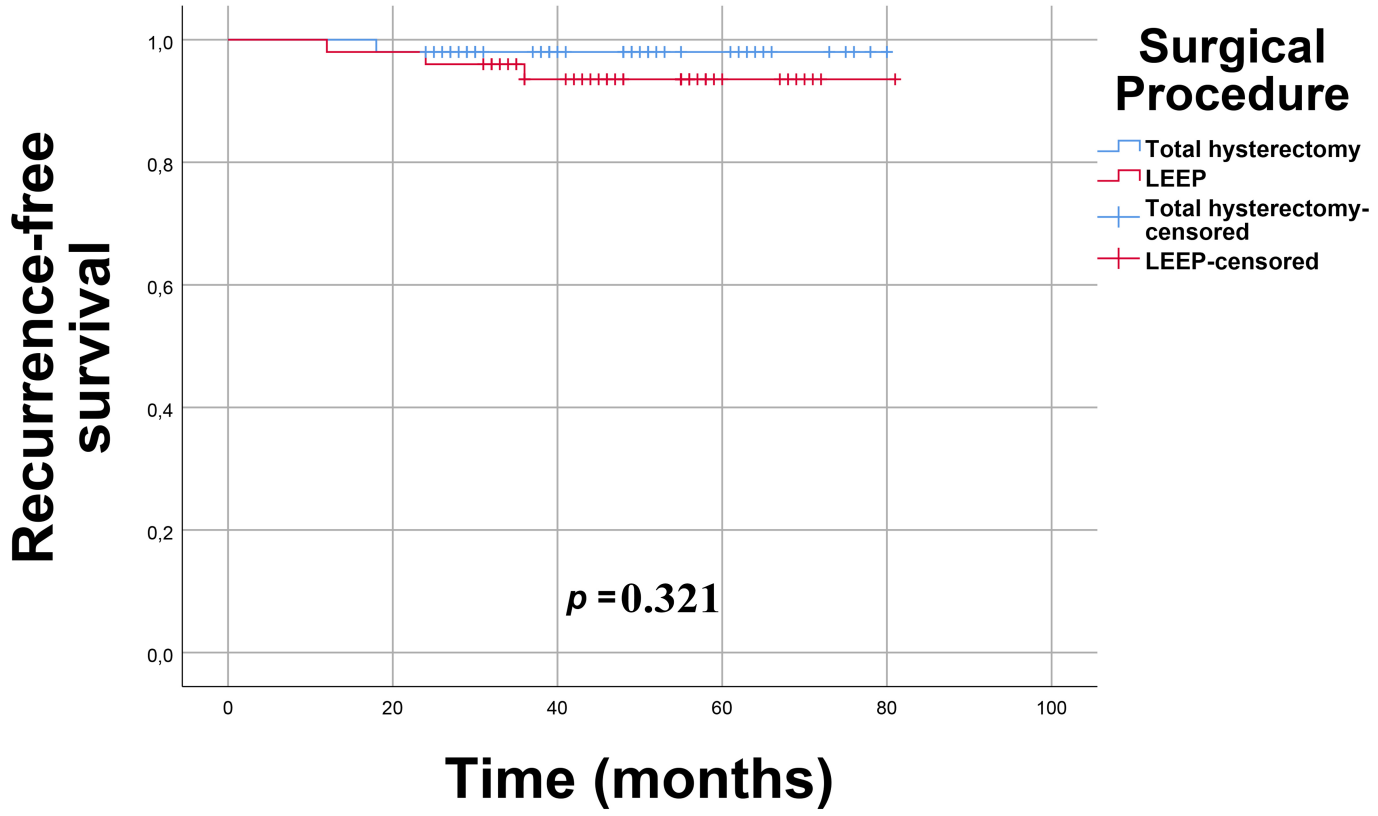

FIGURE 1. Recurrence-free survival rates with operation procedure. LEEP: loop electrosurgical excision procedure.

cursor lesions to cervical cancers, as reduces the elimination of the human papillomavirus (HPV) responsible for these lesions [11]. A recent meta-analysis also confirmed the connection between second-hand smoke exposure and cervical cancer, reinforcing the impact of tobacco exposure [12]. However, in our study, we did not find a significant association between smoking and CIN3 recurrence. HPV remains the primary cause of cervical dysplasia and cervical cancer, underscoring its role as the most common and critical factor in the development of cervical dysplasia [13]. The study by Bogani *et al.* [14] further supports that HPV vaccination can protect against the development of lower genital dysplasia, even in women who no longer have a cervix. Despite this, the vaccination rate among participants in our study was notably low, suggesting a need for increased awareness and vaccination efforts. The exclusion of malignancies in pathology results, lack of randomization, small number of patients, single-center nature, and retrospective design of the study are significant limitations of the study.

5. Conclusions

While our study found no significant difference in recurrence rates between LEEP and hysterectomy for the treatment of

CIN3, the small number of recurrences observed limits our ability to draw definitive conclusions about the superiority of one treatment over the other. Given the well-documented low risk of cervical cancer following LEEP and its minimally invasive nature, LEEP remains the preferred treatment option for CIN3. Further large-scale studies are necessary to comprehensively evaluate the long-term outcomes of different treatment modalities for CIN3.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

CYO—conception and design, analysis of data, drafting of the manuscript, writing the article. NÇ—acquisition of data, participated in drafting, analysis and interpretation of data. MS—technical and material support, acquisition of data, participated in drafting. DTA—critical revision of the manuscript, control/supervision, conception and design. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The present study was approved by the Ethical Committee of Afyonkarahisar Health Sciences University Hospital (grant no: 2024/7) and the research was continued in accordance with the Declaration of Helsinki. Consent was obtained from all patients during their hospitalization.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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