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Original Article

Cold Knife Conization Vs. Loop Electrosurgical Excision Procedure in Premalignant Cervical Lesions in a Cohort of Females in Romania

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Abstract

Cold knife conization and loop electrosurgical excision procedures (LEEP) are two methods of minimally invasive treatment used in Romania for high-grade cervical dysplasia. The purpose of this study is to identify correlations between the results of the Papanicolaou (PAP) smear and biopsy and to evaluate the positivity of resection margins in both types of conizations: cold knife conization versus LEEP. The 96 cases enrolled in this study were gathered from 'Prof. Dr. Ioan Pușcaș' City Hospital of Șimleu Silvaniei, Romania, in a time interval from 01.01.2022 to 01.01.2024. The results of our study showed that out of 20 women who underwent PAP smear for ASC-US, 4 were actually found to have high-grade squamous intraepithelial lesion (H-SIL) according to biopsy results. The estimated risk in females who underwent LEEP procedure with positive margins in the histopathological examination, in the studied population, is almost 0.5 times higher compared to those who underwent cold knife conization. Histopathological examination of cervical specimens is the gold standard method in detecting high-risk cervical lesions. Our study shows that positive deep endocervical margins are more likely to occur in loop electrosurgical excision procedures compared with cold knife conization.

Introduction

Cervical intraepithelial neoplasia is a premalignant precursor for cervical cancer. According to Bethesda system, precancerous lesions are classified into low-risk squamous intraepithelial neoplasia (CIN1 or L-SIL), moderate-risk squamous intraepithelial neoplasia (CIN2, or H-SIL), and high-risk squamous intraepithelial neoplasia (CIN3 or H-SIL) [1]. Responsible for cervical malignancies are persistant infection with Human Papillomavirus (HPV) [2,3].

According to the guidelines of American Society for Colposcopy and Cervical Pathology (ASCCP), patients with low-grade squamous intraepithelial neoplasia are constantly monitored because the regression rate with infection clearance are high, while the progression rate to moderate or high-grade squamous intraepithelial neoplasia is very low [1].

When clinicians deal with high-risk precancerous cervical lesions, when repeated screening methods show unchanged or worsening results, and when non-invasive treatment options are no longer viable, there are minimally invasive treatment methods, such as conization, to prevent the progression of pre-neoplastic cervical pathology to cervical cancer [4].

Most commonly used in Romania's public healthcare system are two techniques: cold knife conization and electrosurgical excision procedure (LEEP) [5]. These two methods offer the advantage of reaching deeper into the cervix to excise the entire pre-neoplastic transformation zone. Both methods have proven their effectiveness over time, with minimal post-procedural damage.

Both cold knife conization and LEEP are excisional procedures that remove abnormal tissue and provide cervical tissue samples for histopathological examination to determine if malignant or dysplastic cells are present. These two types of conization allow the pathologist to make assessments about resection margins. For these reasons, the two methods are preferred by most countries for moderate or high-grade squamous intraepithelial neoplasia over ablative methods [6].

Aim and objectives

This study aims to identify correlations between the results of the PAP smear and biopsy and to evaluate the positivity of resection margins in both types of conizations: cold knife procedure versus LEEP.

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Materials and methods

The study we conducted is a retrospective, observational and analytical one. The cases were gathered over a 2-year period, from January 1, 2022, to January 1, 2024. A total of 120 patients were included in this study, all from the Prof. Dr. Ioan Pușcaș City Hospital in Șimleu Silvaniei, Obstetrics and Gynecology Department.

Inclusion criteria

All reproductive-age women with repeated abnormal PAP results and with various non-invasive treatments showing continuing positive results for ASC-US, ASC-H, L-SIL, and H-SIL lesions; women with a positive result for H-SIL lesions following colposcopy with biopsy.

Exclusion criteria

Patients without the PAP cytology result requested by the gynecologist; women who, for various reasons, refused the minimally invasive treatment procedure following the histopathological result of the cervical biopsy showing moderate or high-risk squamous intraepithelial neoplasia.

The cold knife conization procedure consisted of the following steps: After a discussion between the clinician and each woman about the procedure, the woman was asked to undress from the waist down and to lie on the operating table in the gynecological position. The vulvovaginal region was disinfected. The cervix was exposed with the help of a speculum. A tampon soaked in physiological saline was introduced into the vagina to remove cervical mucus and cellular debris. An acetic acid solution and Lugol's iodine solution were applied to mark the dysplastic lesion. The anterior lip of the cervix was grasped with the help of Pozzi forceps. A hystrometer was used to enter the cervical canal and assess its length. Using a scalpel, the dysplastic area was removed with oncological safety margins. The specimen was marked at the 12 o'clock position with a surgical thread. The specimen was then removed and placed in 10% formalin for histopathological examination.

The LEEP consisted in the following steps: After a discussion between the clinician and each woman about the procedure, the woman was asked to undress from the waist down and to lie on the operating table in the gynecological position. The vulvovaginal region was disinfected. The cervix was exposed with the help of a speculum. A tampon soaked in physiological saline was introduced into the vagina to remove cervical mucus and cellular debris. An acetic acid solution and Lugol's iodine solution were applied to mark the dysplastic lesion. Using a diathermy loop connected to a monopolar cautery, the dysplastic tissue is removed with oncological safety margins. The specimen was marked at the 12 o'clock position with a surgical thread. If invasion of the lesion was suspected, additional deep excisions or slices were performed. The remaining cervical canal was dilated to prevent cervical stenosis. The specimen/speciemens were removed and placed in 10% formalin for histopathological examination.

Statistical analysis

The data collected from each patient were introduced into Microsoft Excel 2016, and with the help of the Statistical Package for the Social Sciences, Version 26 (SPSS 26) the results were obtained. This study utilized frequency tables, figures, and crosstabulation tables. Quantitative and qualitative data were grouped into nominal and categorical variables. For correlations and differences between the variables, the Chi-Square test, Pearson Correlation Coefficient, and Eta Coefficient were applied. To determine which of the two invasive treatment methods has a higher rate of positive resection margins, relative risk was calculated. The statistical significance of the research was established at a p-value less than 0.005, with a 95% confidence interval.

Results

The study conducted included 120 women aged between 21 years, which was considered the lower limit, and 68 years, which was the upper limit. The mean age is 44 years, median age 45 years old with a standard deviation of 8.832. Most women were aged between 41 and 50 years old, followed by 31-40 age group. Individuals at extreme ages, below 30 years old and above 61 years old, were less represented in the studied group.

43.3% from all females included in our study had repeated cytological results H-SIL and 25% cytolocical results of ASC-US (Table 1).

Table 1. *PAP smear results*

PAP smear results			
		Frequency	**Percent**
Valid	AGC	2	1.7
	H-SIL	52	43.3
	L-SIL	16	13.3
	ASC-H	30	25.0
	ASC-US	20	16.7
	Total	120	100.0

Table 2. *Biopsy results*

Biopsy results			
		Frequency	**Percent**
Valid	Cervicitis (chronic or acute)	60	50.0
	AGC	2	1.7
	H-SIL	42	35.0
	L-SIL	8	6.7
	NU	8	6.7
	Total	120	100.0

50% of all women had a positive result on biopsy for chronic or acute cervicitis, while only 35% of females were diagnosed with H-SIL lesions by biopsy (Table 2).

Out of the 20 females with PAP smear results for ASC-US, 4 were found to have H-SIL according to biopsy results, while the remaining 16 were diagnosed with chronic or acute cervicitis. Out of 30 patients with ASC-H cytological lesions, 16 were diagnosed with chronic or acute cervicitis on biopsy, 4 showed no lesions in the biopsy results, and 6 were diagnosed with H-SIL lesions according to the biopsy results (Table 3). These results were statistically significant, $p = 0.001$.

Table 3. *Crosstabultation between PAP smear results and biopsy results*

Crosstabulation between PAP smear results and biopsy results								
			Biopsy results					Total
			No lesion	L-SIL	H-SIL	AGC	Cervicitis	
PAP smear results	ASC-US	Count	0	0	4	0	16	20
		% of Total	0.0%	0.0%	3.3%	0.0%	13.3%	16.7%
	ASC-H	Count	4	2	6	0	18	30
		% of Total	3.3%	1.7%	5.0%	0.0%	15.0%	25.0%
	L-SIL	Count	2	0	0	0	14	16
		% of Total	1.7%	0.0%	0.0%	0.0%	11.7%	13.3%
	H-SIL	Count	2	6	32	2	10	52
		% of Total	1.7%	5.0%	26.7%	1.7%	8.3%	43.3%
	AGC	Count	0	0	0	0	2	2
		% of Total	0.0%	0.0%	0.0%	0.0%	1.7%	1.7%
Total		Count	8	8	42	2	60	120
		% of Total	6.7%	6.7%	35.0%	1.7%	50.0%	100.0%

Table 4. *Crosstabulation between the type of conization and positive margins of the specimen sent for histopathological exam*

Crosstabulation between the type of conization and positive margins of the specimen sent for histopathological exam					
			Procedure		Total
			Cold knife	LEEP	
Positive margins	NO	Count	20	19	39
		% within positive margins	51.3%	48.7%	100.0%
		% within procedure	100.0%	86.4%	92.9%
	YES	Count	0	3	3
		% within positive margins	0.0%	100.0%	100.0%
		% within procedure	0.0%	13.6%	7.1%
Total		Count	20	22	42
		% within positive margins	47.6%	52.4%	100.0%
		% within procedure	100.0%	100.0%	100.0%

Positive resection margins of the specimen sent for histopathological exam were determined in 13.6% of all cases in the LEEP procedure. No positive margins were determined by histological exams on cold knife specimens (Table 4). However, this results are not statistically significant p value being 0.087.

However, the estimated risk in individuals who underwent LEEP procedure with positive margins in the histopathological examination, in the studied population, is almost 0.5 times higher compared to those who underwent cold knife conization (Table 5).

Table 5. *Risk estimate*

Risk Estimate			
	Value	95% Confidence Interval	
		Lower	Upper
For cohort procedure = LEEP	0.487	0.353	0.672
N of Valid Cases	42	-	-

Discussion

With the help of the PAP test, conventional cytology or liquid-based cytology, women at high risk for high-grade premalignant cervical lesions or even invasive cancer can be identified. As a result, when cervical dysplastic lesions are repeatedly diagnosed through existing screening methods such as cytology, HPV detection, or, in some cases, the CINtec PLUS method, and when

medical treatments do not have favorable results and the lesion continues to be diagnosed by cytological examinations or the CINtec PLUS test is positive, it is recommended use colposcopy with biopsy for a precised diagnose. This is an essential test for women with abnormal cytology, used to accurately locate the lesions to obtain a definitive diagnostic, a result on biopsy, and to determine the correct treatment [7].

Our research showed a mean age of 44 years old, a median age of 45 years, with the lower age limit of 21 years and an upper age limit of 68 years old. In line with our results, a study conducted by Enechukwu, et al. showed that the mean age of the participants included in their study was approximately 43 years [8]. The results of a study conducted by Martinez-Ruiz also align with our findings, demonstrating that women included in their study had a mean age of 49 years [9]. Other study showed a higher mean age among studied population like 54,47 [10].

Regarding the variances in the mean age across the worldwide studies, we observed that the average age varies depending on the geographic area where the research was conducted. It is evident that preneoplastic lesions do not spare either young women or those in middle or older age groups. This indicates that cervical cancer screening should begin as early as 21 years old and continue until the age of 65.

A study conducted by Simone, et al. showed that out of 42 cases with discordant results between cytological and histological examinations, 18 patients were diagnosed by histopathological exam, after biopsy with L-SIL [11]. A study conducted in Turkey showed that 164 patients were under-diagnosed by cytology, with the histopathological exam revealing H-SIL lesions in 47.6% [12]. Two patients (1.7%) in our studied group, with a positive cytology result for H-SIL lesions, had a normal biopsy result, and ten patients (8.3%) had a biopsy result indicating chronic or acute cervicitis.

Considered by some clinicians as a historical treatment method, cold knife conization is still a technique successfully used in European countries for the minimally invasive treatment of squamous intraepithelial lesions. A study conducted in Italy in 2024 shows that the prevalence of positive endocervical margins following cold knife conization is significantly lower compared to CO2 laser technique (22.7% vs. 58.8%) [13]. Positive margins in our study were found only in the loop electrosurgical procedure and none in cold knife conization, suggesting that the scalpel is easier to be manipulated by the surgeon, allowing for better assessment of the lesion. The scalpel can be used for a larger excision of the specimen, thereby reducing the incidence of positive histological margins.

Conclusions

PAP cytology is used as a method of screening for detecting cervical lesions. When high-grade cervical lesions are detected consistently through multiple methods of screening, a biopsy is indicated. Histopathological exam of cervical specimens is the gold standard method in detection high-risk cervical lesions. The loop electrosurgical procedure is more frequently utilized in the treatment of squamous intraepithelial neoplasia compared to the cold knife procedure. However, our study shows that positive deep endocervical margins are more likely to occur in loop electrosurgical procedure compared with cold knife conization.

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