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Independent Predictive Factors for Positive Margins after Conization of Cervical HSIL in Women of Childbearing Age and the Necessity of Secondary Surgery

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Abstract: This study aims to analyze the high-risk factors for positive surgical margins after loop electrosurgical excision procedure (LEEP) and the necessity of secondary surgery in women of childbearing age (20-40 years) with high-grade squamous intraepithelial lesions (HSIL). Through retrospective analysis of 526 HSIL patients who underwent LEEP at the Third Affiliated Hospital of Sun Yat-sen University from 2015 to 2019, the positive margin rate was found to be 22.43%. Multivariate analysis indicated that TCT result of HSIL (OR = 3.414, 95%CI = 1.793-6.500, P < 0.001) and lesions involving ≥5 points (OR = 8.567, 95%CI = 4.439-16.533, P < 0.001) were independent risk factors for positive margins. Among 34 patients who underwent secondary surgery within six months after initial conization, 32 had positive margins, and the residual disease rate among them was only 21.88% (7/32), indicating that positive margins do not necessarily lead to residual lesions. Therefore, the decision for secondary surgery in patients with positive margins should be individualized based on factors such as age, fertility needs, lesion characteristics, complications, and personal preferences, rather than reflexively performing secondary surgery.

Keywords: women of childbearing age; cervical high-grade squamous intraepithelial lesion; loop electrosurgical excision procedure; positive margin; predictive factors; secondary surgery

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1. Introduction

Cervical cancer is one of the most common malignant tumors among women worldwide, posing a serious threat to their health. In 2018, there were over 569,000 new cases of cervical cancer globally and more than 311,000 deaths, with 85% of cases occurring in developing countries [1]. In China, cervical cancer ranks as the second most common malignant tumor in women, just after breast cancer. In 2020, the number of new cases and deaths from cervical cancer in China reached 109,000 and 59,000, accounting for 18.2% and 17.3% of the global total, respectively [2,3]. Even more concerning is the increasing incidence and mortality rates of cervical cancer in China over the past 20 years, along with a trend toward younger onset [4]. According to research statistics, approximately 40% of cervical cancer patients are of childbearing age, making the prevention and control of cervical cancer particularly critical [5].

High-grade squamous intraepithelial lesion (HSIL) is a significant precancerous lesion of cervical cancer, and timely diagnosis and treatment are essential for preventing cervical cancer [6]. Loop electrosurgical excision procedure (LEEP) is one of the primary

approaches used to treat HSIL [7]. However, positive margins after surgery remain a clinical concern as they may increase the risk of residual lesions and recurrence [6,7]. There is currently no unified standard for whether patients with positive margins need to undergo secondary surgery [8].

This study aims to analyze the high-risk factors for positive margins after conization for HSIL in women of childbearing age and explore the necessity of secondary surgery for patients with positive margins, providing a basis for clinical decision-making.

2. Materials and Methods

2.1. Research Subjects

This study selected female patients of childbearing age who underwent conization at the Third Affiliated Hospital of Sun Yat-sen University from 2015 to 2019. The age range was 20 to 40 years old, and a total of 526 patients with histological diagnosis of HSIL were included. The inclusion criteria were as follows: undergoing conization for treatment; histopathological confirmation of cervical high-grade squamous intraepithelial lesion; aged between 20 and 40 years; having complete clinical data; and being able to meet study requirements and complete follow-up. The exclusion criteria included: postoperative diagnosis of cervical invasive cancer; personal history of other malignant tumors; history of radiotherapy or chemotherapy; history of treatment for mental illness or cognitive impairment; history of hysterectomy, cervical cauterization, or other surgical treatments that led to cervical defects; incomplete clinical data; and cases lost to follow-up. This study was approved by the hospital's ethics committee, and all subjects provided written informed consent on a completely voluntary basis.

2.2. Research Methods

All patients' clinical data were collected through the hospital's electronic medical record system, including age, HPV infection status, TCT results, extent of lesions, glandular involvement, and other factors. The cervical tissue removed after surgery was routinely sent for pathological examination, and the margin status was recorded. Thirty-four patients who underwent initial cervical conization received supplementary surgery — either secondary cervical conization or total hysterectomy with or without bilateral salpingectomy — within six months. The decision was based on pathological results and patient preferences, such as the presence of positive margins or concurrent gynecological conditions, and the pathological results after secondary surgery were recorded.

2.3. Pathological Determination

Positive cervical conization margin was defined as visible lesions at the margin after cervical conization or a margin-to-lesion distance of less than 1 mm [9,10]. The extent of lesion involvement was reflected by the number of points involved in the specimen after cervical conization, such as 1-12 points counted as 12 position numbers. Residual lesion referred to CIN 2 or more severe pathological findings confirmed within six months after the initial cervical conization.

Positive margins were classified into outer, inner, and basal types. The outer margin referred to the edge near the vaginal end, the inner margin to the area close to the internal os and uterine segment, and the basal margin to regions excluding both the cervical surface and the inner and outer margins [11]. In this study, positive margins included positive inner margins, outer margins, and basal margins, without further subdivision for analysis.

2.4. Statistical Analysis

SPSS version 25.0 was used for statistical analysis, and all statistical tests were two-sided. Measurement data were described using mean and standard deviation, while categorical data were summarized as frequencies and percentages. Group comparisons

for categorical data were conducted using the χ^2 test, and those for continuous variables using the independent samples t-test. The analysis of factors affecting positive margins used a multivariate Logistic regression model to calculate related risk factors. In this study, $P < 0.05$ was considered statistically significant.

3. Results

3.1. Margin Status after Initial Conization in HSIL Patients

Of the 526 patients in this study, 118 had positive margins and 408 had negative margins, with a positive margin rate of 22.43%. Among the positive margin cases, 89 had inner margins positive and outer margins negative, 18 had inner margins negative and outer margins positive, and 11 had both inner and outer margins positive. The proportion of positive inner margins was 77.1% (89/118), the proportion of positive outer margins was 15.3% (18/118), and the proportion of both positive inner and outer margins was 9.3% (11/118).

3.2. Analysis of High-Risk Factors for Positive Margins

3.2.1. Univariate Analysis

Univariate analysis of factors including age, HPV infection status, TCT results, glandular involvement, and number of points involved showed that age, TCT results, glandular involvement, and the number of points involved were significantly associated with positive margins ($P < 0.05$) as shown in Table 1.

Table 1. Univariate Analysis of Margin Status after Conization in Patients with HSIL.

Variable	Positive Margin Group (n = 118)	Negative Margin Group (n = 408)	χ^2/t	P
Age (years)	34.58 ± 3.26	32.17 ± 4.85	2.9	0.000*
TCT Result			37.799	0.000*
≤LSIL	46 (52.27)	230 (84.25)		
HSIL	42 (47.73)	43 (15.75)		
Glandular Involvement			47.01	0.000*
Yes	104 (88.14)	217 (53.19)		
No	14 (11.86)	191 (46.81)		
Number of Involved Points			131.181	0.000*
<5	24 (21.82)	303 (80.16)		
≥5	86 (78.18)	75 (19.84)		

3.2.2. Multivariate Analysis

Factors with statistical significance in the univariate analysis were included in the multivariate Logistic regression analysis (Table 2). The results showed that Having a TCT result of HSIL (with ≤LSIL as the reference group) (OR = 3.414, 95%CI = 1.793-6.500, P < 0.001) and lesions involving ≥5 points (with <5 as reference) (OR = 8.567, 95%CI = 4.439-16.533, P < 0.001) were independent risk factors for positive margins after cervical conization.

Table 2. Multivariate Logistic Regression Analysis of Positive Margins after Conization in Patients with HSIL.

Influencing Factor	β	Wals	P	OR	95%CI
Age	0.012	0.159	0.690	1.012	0.954-1.075
TCT (compared to ≤LSIL)	1.228	13.959	0.000*	3.414	1.793-6.500
Glandular involvement (compared to no involvement)	0.826	3.701	0.054	2.283	0.985-5.294

Number of involved points (compared to <5)	2.148	40.991	0.000*	8.567	4.439-16.533

3.3. Residual Lesions after Secondary Surgery

Among the 34 patients who underwent secondary surgery (secondary conization or total hysterectomy) within six months after conization, 32 underwent secondary surgery due to positive margins. As shown in Table 3, the residual lesion rate among patients with positive margins was 21.88% (7/32). In contrast, the two patients with negative margins who underwent secondary surgery had no residual lesions. Two patients with negative margins underwent secondary surgery, and no residual lesions were found.

Table 3. The Relationship between the Status of the Cutting Edge after Initial Cervical Conization and Residual Lesion after the Second Surgery.

Status of Cutting Edge After Initial Conization	Pathology After Second Surgery	
	Residual (n)	No Residual (n)
Negative	0	2
Positive	7	25
Total	7	27

4. Discussion

This study found that in women of childbearing age with HSIL, the positive margin rate after conization was 22.43%, falling within the previously reported range of 15% to 40% [12,13]. Multivariate analysis showed that TCT result of HSIL and lesions involving ≥5 points were independent risk factors for positive margins, indicating that preoperative TCT results and the extent of lesions have important value in predicting margin status [14].

TCT examination is an important means of cervical cancer screening that can reflect the degree of abnormality of cervical epithelial cells. This study found that patients with TCT results of HSIL had a 3.414-fold increased risk of positive margins compared to patients with TCT results of LSIL or lower. This may be attributed to HSIL lesions being more extensive and penetrating deeper into the cervical epithelium [12]. Therefore, for patients with preoperative TCT results of HSIL, physicians should pay more attention to margin management during surgery and expand the excision range if necessary to reduce the positive margin rate [11].

The number of points involved serves as a key indicator of lesion extent. This study showed that patients with lesions involving ≥5 points had an 8.567-fold increased risk of positive margins compared to patients with lesions involving <5 points [15]. This suggests that more extensive lesion involvement is associated with a higher risk of positive margins after conization. For patients with extensive lesions, preoperative assessment of the lesion should be thorough, and a reasonable surgical plan should be developed, including consideration of staged excision or deeper excision when appropriate to reduce the positive margin rate.

Notably, this study found that only 21.88% of patients with positive margins had residual lesions, meaning that nearly 80% of patients with positive margins actually had no residual lesions. This finding is consistent with previous research results, with multiple studies showing that the residual lesion rate in patients with positive margins is between 10%-30% [16]. This may be related to the following factors: on one hand, thermal damage during electrosurgery may destroy the lesion tissue; on the other hand, the body's immune system may clear the remaining lesion cells after surgery.

There is still a lack of consensus regarding the clinical management of patients with positive margins, particularly concerning the necessity of secondary surgical intervention. The traditional view is that positive margins are a high-risk factor for residual lesions and recurrence, suggesting secondary surgery. However, the results of this study indicate that

positive margins do not necessarily lead to residual lesions, and routine secondary surgery may lead to overtreatment. This is particularly important for women of childbearing age, as overtreatment may adversely affect fertility.

Furthermore, the potential impact of LEEP on the reproductive function of women of childbearing age needs to be considered.Studies have demonstrated that LEEP may elevate the risk of adverse pregnancy outcomes, including but not limited to preterm birth, miscarriage, and premature rupture of membranes [17]. In a meta-analysis including 36,954 patients and 1,794,174 controls from 4 prospective cohort studies and 22 retrospective studies, LEEP was found to increase the risk of preterm birth [18]. Most current studies confirm that LEEP increases the incidence of adverse pregnancy outcomes such as miscarriage and premature rupture of membranes, and secondary conization raises further concerns regarding fertility preservation in women of childbearing age. Given that positive margins do not necessarily indicate residual lesions, the appropriateness of routinely performing secondary surgery based solely on margin status should be carefully evaluated [19,20].

Therefore, for women of childbearing age with positive margins, the decision for secondary surgery should comprehensively consider patient age, fertility desires, lesion severity, and the capacity for consistent follow-up, and be individualized [21]. For younger patients with fertility needs, if the lesion is mild, close follow-up rather than immediate secondary surgery can be considered. For older patients without fertility needs or with more severe lesions, secondary surgery may be considered [22].

Moreover, negative margins do not guarantee the absence of disease, as residual or recurrent lesions may still occur even in patients with initially negative margins. This highlights the necessity of continued surveillance regardless of surgical margin status. Therefore, regardless of margin status, regular follow-up monitoring after surgery is necessary to ensure timely detection of potential recurrence.

This study's retrospective nature and the use of a single-center patient cohort may introduce selection bias and limit generalizability. The impact of specific margin locations (endocervical, ectocervical, or basal) was not analyzed separately, which may obscure the differential prognostic value associated with each site, and the 6-month follow-up period limits assessment of long-term recurrence.

5. Conclusion

This study investigated independent predictors of positive margins following cervical conization for HSIL in reproductive-age women (20-40 years) and evaluated the necessity of secondary surgery. Through retrospective analysis of 526 patients undergoing LEEP at a tertiary hospital (2015-2019), multivariate logistic regression identified HSIL on preoperative TCT (OR = 3.414, 95%CI: 1.793-6.500; $P < 0.001$) and lesions involving ≥5 points (OR = 8.567, 95%CI: 4.439-16.533; $P < 0.001$) as independent risk factors. Critically, only 21.88% (7/32) of margin-positive cases exhibited residual lesions after secondary surgery, challenging the routine use of reoperation. These findings underscore that clinical decisions should integrate fertility preservation goals, lesion characteristics, and patient preferences rather than margin status alone.

Future multicenter prospective studies should confirm the predictive value of preoperative TCT results and lesion extent, while incorporating HPV genotyping and molecular biomarkers (e.g., p16/Ki-67) to enhance risk stratification. Optimizing individualized management algorithms remains essential for balancing oncological safety and reproductive health outcomes in this population.

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