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Outcomes following conization and factors on HPV regression among young females in Wuxi

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Abstract

Purpose It is crucial to prioritize the detection of precancerous lesions in clinical practice, especially in young women who have not yet made decisions about family planning. Herein, we conducted a retrospective study to track HPV regression among young females who underwent conization in the past five years and identify predictors of persistent HPV infection.

Methods We involved 400 women under the age of 35, who underwent colposcopy-guided biopsy after primary infection with high-risk HPV at the affiliated Hospital of Jiangnan University and were histologically confirmed with LSIL/HSIL between June 2018 and December 2022. Follow-up data was collected at 3 months, 6 months, 12 months and 24 months postoperatively. Clinical characteristics, including age, BMI, marital status, gravidity, contraception method, sexual history, HPV infection duration, HPV vaccination status, preoperative HPV, and cytology status, were analyzed by SPSS 20.0 software.

Results A total of 400 patients aged 18 to 35 were included, with 354 (88.5%) undergoing cervical biopsy and 92 (23%) undergoing cervical conization. There were no significant differences in age, BMI, marital status, pregnancy history, and HPV vaccination between patients with persistent HPV infection and those with HPV regression after conization. However, the timing of first sexual activity and the use of condom contraception had a statistically significant impact on HPV status.

Conclusions Duration of sexual life may play a significant role in the development of cervical precancerous, showing a positive correlation. Condoms for contraception can promote HPV regression by creating a physical barrier that blocks the transmission of HPV. Regular follow-up intervals following cervical conization are of greater significance than HPV vaccination.

Keywords Conization, HPV regression, Contraception method, HPV vaccination

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Introduction

Cervical cancer remains one of the most prevalent malignancies affecting women worldwide, ranking as the fourth most common cancer among females, with an alarmingly high incidence and mortality rate, particularly in developing countries [1]. The global burden of cervical cancer is disproportionately high in low- and middle-income countries (LMICs), where screening and vaccination programs are often limited [2]. According to the World Health Organization (WHO), persistent infection with high-risk human papillomavirus (Hr-HPV) is the leading cause of cervical cancer and its precancerous lesions [3]. Among the numerous HPV genotypes, HPV-16 and HPV-18 are responsible for approximately 70% of cervical cancer cases [4]. The natural history of HPV infection suggests that while the majority of infections resolve spontaneously within 1–2 years due to host immune responses, persistent Hr-HPV infection significantly increases the risk of cervical intraepithelial neoplasia (CIN) and progression to invasive cancer over a span of 7–15 years [5].

Vaccination against HPV has been recognized as an essential primary prevention measure for cervical cancer. The introduction of prophylactic HPV vaccines has significantly reduced the incidence of HPV-related diseases in developed countries with high vaccination coverage [6]. However, in China, HPV vaccination rates remain suboptimal, particularly among young females, due to factors such as lack of awareness, accessibility, and cost concerns [7]. Limited vaccination coverage poses a significant barrier to maximizing the potential impact of primary prevention efforts. In addition, despite vaccination efforts, a significant proportion of women have already acquired HPV before receiving the vaccine, highlighting the importance of secondary prevention strategies.

Secondary prevention strategies, including screening methods such as Hr-HPV testing and liquid-based cytology (TCT), remain critical for identifying precancerous lesions and preventing their progression to cervical cancer [8]. Screening programs are particularly relevant in the context of young women who may acquire HPV infection shortly after their first sexual encounter. It is estimated that nearly 85–90% of sexually active adults will be infected with HPV at some point in their lifetime, although most will clear the infection without clinical consequences [9]. However, for a subset of individuals with persistent infection, the risk of cervical lesion development remains substantial. Clinical guidelines emphasize the importance of regular cervical screening in detecting and managing CIN before it progresses to invasive cancer [10].

In cases where precancerous cervical lesions are detected, conservative surgical interventions such as cervical conization are commonly employed for both diagnostic and therapeutic purposes. Conization is a standard procedure for excising high-grade cervical lesions while preserving reproductive function, making it a preferred option for young women who have yet to complete their family planning [11]. Despite its effectiveness, conization does not eliminate the risk of persistent HPV infection, residual lesions, or recurrence of CIN, particularly in cases where high-risk HPV strains persist postoperatively [12]. Studies suggest that factors such as patient age, lesion severity, immune status, and HPV type influence the likelihood of viral persistence and lesion recurrence [13].

Further research is needed to evaluate the long-term outcomes of young women following conization. Identifying predictors of HPV regression or persistence is crucial for optimizing post-treatment management strategies, guiding follow-up protocols, and minimizing the risk of cervical cancer development. Additionally, understanding the role of behavioral and biological factors, such as sexual activity, immune response, and contraceptive methods, in HPV regression may provide insight into developing comprehensive prevention and management strategies.

In this retrospective study, we assessed HPV regression among young females in Wuxi who underwent conization over the past five years. Patient characteristics, HPV status before and after conization, and potential risk factors associated with persistent HPV infection were analyzed. Our findings contributed to a deeper understanding of post-conization HPV outcomes and inform future clinical recommendations for managing cervical health in young women.

Materials and methods

Study design and population

This retrospective study involved 400 women under the age of 35 who underwent colposcopy-guided biopsy after primary infection with high-risk HPV at the affiliated Hospital of Jiangnan University and were histologically confirmed with LSIL/HSIL between June 2018 and December 2022.

Inclusion and exclusion criteria

We included women diagnosed with LSIL (Low-grade squamous intraepithelial lesion) / HSIL (High-grade squamous intraepithelial lesion) who underwent cervical biopsy or conization. Exclusion criteria included women with invasive pathology, positive surgical margins post-conization, immunosuppressive conditions, previous cervical procedures, or incomplete follow-up data.

Data collection and follow-up

Clinical and demographic data were collected from electronic medical records and patient interviews. The

collected variables included age (years), BMI (kg/m²), marital status, gravidity, parity, duration of sexual life (total months of sexual activity), contraceptive method, HPV vaccination status, HPV status, cytology results, cervical biopsy findings under colposcopy, and pathology results post-conization/LEEP (Loop Eelectrosurgical Excision Procedure). Follow-up evaluations were performed at 3, 6, 12, and 24 months after the initial conization procedure.

HPV status was determined using polymerase chain reaction (PCR)-based HPV DNA testing, and cytological evaluations were performed using liquid-based cytology.

Follow-up strategy and outcome

Follow-up evaluations were performed according to the outlined time intervals (3, 6, 12, and 24 months after conization). Endocervical curettage (ECC) was routinely carried out during colposcopy in our clinic unless the patient was pregnant. Any abnormal screening results necessitated colposcopy-guided biopsy and/or ECC for further histological diagnosis, in accordance with ASCCP (American Colposcopy and Cervical Pathology Society) guidelines and expert consensus on cervical precancerous lesions. If the initial result was negative, HPV and cytology screening were conducted at 12 and 24 months after conization.

The primary outcome was HPV regression, defined as the clearance of Hr-HPV infection post-conization. Persistent infection was defined as Hr-HPV positivity at any follow-up visit beyond 12 months postoperatively. Secondary outcomes included recurrence of CIN and risk factors influencing HPV persistence.

Statistical analysis

Statistical analyses were conducted using IBM SPSS20.0 (Statistic Package for Social Science) Statistics software. The normality test through Shapiro-Wilk indicated that the included data conform to the normal distribution. The categorical variables (marriage, gravidity, parity, contraception method, HPV vaccination, HPV status, cytology, cervical biopsy, pathology after conization/LEEP) were compared using the Pearson χ^2 test, and continuous variables (age, BMI, duration of sexual life) were compared using the Student's t-test. Univariate ANOVA analysis and Multivariate time-dependent COX regression analysis was employed to identify the influencing factors of HPV regression. Statistical significance was set at $p < 0.05$.

Ethical considerations

This study received approval from the Ethics Committee of the affiliated Hospital of Jiangnan University and adhered to the principles of the Declaration of Helsinki. Informed consent was obtained from all participants prior to study enrollment.

Results

A total of 400 patients aged 18 to 35 were included in the analysis, with 354 (88.5%) undergoing cervical biopsy and 92 (23%) undergoing cervical conization between the ages of 26 and 35. The mean BMI of the participants was 24.35 ± 4.91 kg/m², with a marriage rate of 56%. The duration of sexual activity ranged from 10 to 120 months, with a median duration of 38 months. Condom use as contraception was chosen by 86 patients (21.5%).

130 patients (32.5%) tested positive for HPV16/18, initially. According to HPV testing, the top five HPV types with the highest comprehensive infection rates were HPV16, HPV52, HPV58, HPV53, and HPV39, with infection rates of 24.9%, 17.3%, 13.92%, 11.97%, and 9.28%, respectively. The infection rate of HPV18 was 7.6%. Out of the total 400 patients, 168 (42%) had received vaccination against HPV. In the cytology assessment, 190 cases (47.5%) were classified as ASC-US, 82 cases (20.5%) as LSIL, and 26 cases (6.5%) as ≥HSIL. Among the colposcopic cervical biopsy cases, 96 (27.2%) were HSIL + and the majority were ≤LSIL (72.8%). Following cervical conization, pathology results showed that 28 patients had ≤LSIL (30.4%), while 65.3% had HSIL, and there were four cases of cervical cancer (4.3%) (Table 1).

After conization, 28 cases of HSIL regressed to ≤LSIL, while 2 cases were upgraded to microinvasive cervical cancer, all of which were associated with HPV16/18 infection. The remaining 60 cases of HSIL persisted (Table 2).

According to endocervical curettage (ECC), the rate of missed HSIL was 0.5% (1 out of 189 patients) in benign cervical lesions and 4.3% (3 out of 69 patients) in LISL cases, compared to cervical biopsy. Moreover, a majority of ECC patients showed no malignant lesions (60.4%). Therefore, ECC plays a more significant role in reducing missed diagnoses during cervical biopsies, particularly for unsatisfactory colposcopy (Table 3).

During the follow-up, HPV clearance in the first year was approximately 82%, which decreased over time as the proportion of HPV re-infection increased. However, the type of infection post-conization did not completely align with pre-conization findings. The proportion of TCT abnormalities increased over time, with ASC-US being the predominant type. No recurrence of cervical lesions was found in patients undergoing repeated cervical biopsy (Table 4).

After conization, age, BMI, marital status, pregnancy history and HPV vaccination had no significant correlation with HPV regression. However, the timing of first sexual activity and the use of condom contraception had a statistically significant impact on HPV status (Table 5).

Table 1 General information of included population

parameters	Classification	P50 / *N* (%)
Age(years)	≤ 25	21 (18,25) / 42 (10.5)
	26–30	27 (26,30) / 148 (37)
	31–35	33 (31,35) / 210 (52.5)
BMI (kg/m^2)		24.35 ± 4.91
Marriage	Married	224 (56)
	Unmarried	176 (44)
Gravidity		2.45 ± 1.26
Parity		1.14 ± 0.66
Duration of sexual life (month)		38 (10, 120)
HPV vaccination	Vaccinated	168 (42)
	Unvaccinated	232 (58)
Contraceptive method	Intrauterine ring	62 (15.5)
	Condom	86 (21.5)
	Oral contraceptive	24 (6.0)
	No contraception	228 (57)
HPV status	HPV16/18	130 (32.5)
	Other Hr-HPV (Non16/18)	260 (65.0)
	Negative/unknown	10 (2.5)
cytology	NILM	102 (25.5)
	ASC-US	190 (47.5)
	LSIL	82 (20.5)
	≥HSIL	26 (6.5)
cervical biopsy under colposcope	≤LSIL	258 (72.8)
	HSIL	94 (26.6)
	Cervical Cancer	2 (0.6)
Pathology after conization/LEEP (*N* = 92)	≤LSIL	28 (30.4)
	HSIL	60 (65.3)
	Cervical Cancer	4 (4.3)

Table 2 Pathology comparison of biopsy and Conization/LEEP

Pathology		Biopsy			*N*
		LSIL	HSIL	Cervical cancer	
conization	Normal	0	2	0	2
	LSIL	0	26	0	26
	HSIL	0	60	0	60
	Cervical cancer	0	2	2	4
N		0	90	2	92

Table 3 Pathology comparison of biopsy and ECC

Pathology		Biopsy			*N*
		Normal	LSIL	HSIL+	
ECC	Normal	166	61	58	285(80.5%)
	LSIL	22	5	27	54(15.3%)
	HSIL	1	3	11	15(4.2%)
N		189(53.4%)	69(19.2%)	96(27.1%)	354

After two years follow-up, 112 were still HPV positive while 288 turned negative (72%). There was no significant difference in age, BMI, marital status, number of pregnancies and deliveries, vaccination, type of HPV infection, and contraceptive method between the two groups. However, the duration of sexual history was a significant factor affecting the regression of HPV, statistically. Conization was beneficial for the clearance of HPV, which showed a statistically significant difference in our study (Table 6).

Table 4 HPV and TCT status in follow-ups

Follow-up time	Parameters	Results	*N* = 92
First follow-up (3 months post-operation)	HPV+	16	17.39%
	TCT ≥ ASCUS	0	0%
Second follow-up (6 months post-operation)	HPV+	20	21.74%
	TCT ≥ ASCUS	3	3.26%
Third follow-up (12 months post-operation)	HPV+	14	15.22%
	TCT ≥ ASCUS	5	5.43%
Fourth follow-up (24 months post-operation)	HPV+	13	14.13%
	TCT ≥ ASCUS	6	6.52%

Table 5 Comparative analysis of HPV status in two years after conization

Parameters	HPV+ *N* = 13 (%)	HPV- *N* = 79 (%)	t/χ2	*P*
Age(years)	34 (26,35)	30 (20,33)	-1.76	> 0.05
BMI (kg/m^2)	24.78 ± 2.91	24.67 ± 3.24	0.08	> 0.05
Marriage				
Married	4 (30.8)	37 (46.84)	0.46	> 0.05
Unmarried	9 (69.2)	42 (53.16)		
Gravidity	2.35 ± 0.98	2.51 ± 1.05	0.09	> 0.05
Parity	1.23 ± 0.15	1.74 ± 0.66	0.25	> 0.05
Duration of sexual life (month)	38 (15, 120)	29 (10, 100)	5.78	0.03
HPV vaccination				
Vaccinated	3 (23.07)	34 (43.04)	8.19	> 0.05
Unvaccinated	10 (76.92)	45(56.96)		
Contraceptive method				
Intrauterine ring	1(7.70)	5(6.33)	1.63	> 0.05
Condom	1 (7.70)	15(18.99)	7.14	0.02
Acyeterion	2 (15.38)	10(12.66)	0.97	> 0.05
None	9(69.23)	49(62.03)	0.24	> 0.05

Discussion

The clinical relevance of HPV persistence and cervical lesions

Cervical cancer remains the fourth most prevalent malignancy among women globally, with persistent high-risk HPV infection as the primary risk factor [3]. Cervical intraepithelial neoplasia follows a multi-stage process, where LSIL often regresses, while HSIL poses a significant risk for cervical cancer if untreated [9]. The 2014 WHO classification simplified CIN grading into LSIL and HSIL [14]. Conization is the preferred intervention for HSIL, as it removes affected tissue and facilitates HPV clearance. However, persistent HPV infection post-conization increases recurrence risk, necessitating long-term surveillance [10].

Table 6 Comparative analysis of HPV status in two years Follow-up

prameters	HPV+ *N* = 112 (%)	HPV- *N* = 288 (%)	F/t	*P*
Age(years)	28 (18, 35)	26 (20, 35)	0.04	> 0.05
BMI (kg/m^2)	24.39 ± 2.46	25.12 ± 1.98	1.13	> 0.05
Marriage				
Married	36 (32.1)	188 (65.3)	2.46	> 0.05
Unmarried	76 (67.9)	100 (34.7)		
Gravidity	2.31 ± 0.67	2.01 ± 0.95	1.64	> 0.05
Parity	1.25 ± 0.19	1.77 ± 0.61	1.35	> 0.05
Duration of sexual life (month)	58 (12, 120)	27 (10, 96)	5.78	0.01
HPV vaccination				
Vaccinated	50 (44.6)	118 (43.04)	1.19	> 0.05
Unvaccinated	62 (55.4)	170 (56.96)		
Contraceptive method				
Intrauterine ring	29 (25.9)	33(11.5)	1.63	> 0.05
Condom	13 (11.6)	73(25.3)	6.76	> 0.05
Acyeterion	11 (9.8)	13(4.5)	1.21	> 0.05
None	59 (52.7)	169(58.7)	2.07	> 0.05
LEEP/conization				
Yes	13(11.6)	79(27.4)	3.96	0.04
no	99(88.4)	209(72.6)	0.58	> 0.05

HPV clearance rates and factors influencing regression

Studies report HPV clearance rates of 78.2%, 89.74%, 96.10%, and 98.72% at 6, 12, 18, and 24 months post-conization [11]. Our study observed a slightly lower clearance rate, (78.26%, 84.78%, 85.87% at 6, 12, and 24 months), possibly due to sampling errors or reinfection in sexually active individuals. While most HPV infections resolve within 8–10 months, some persist, underscoring the need for targeted preventive measures [15].

Impact of HPV vaccination on regression and reinfection

We did not observe a statistically significant effect of vaccination, possibly due to a small sample size and low vaccine coverage. Despite this, prior research emphasizes vaccination's role in preventing initial HPV infection and reducing high-risk HPV-related lesions [6]. Many vaccinated individuals may have already been exposed to HPV before vaccination. Prior studies emphasize that prophylactic vaccines are most effective before sexual debut, highlighting the importance of early vaccination programs [11]. Further large-scale studies are needed to confirm the vaccine's long-term efficacy in post-conization patients.

Sexual history, condom use, and their association with HPV persistence

The duration of sexual history was significantly associated with HPV persistence. Longer sexual activity correlates with prolonged infection, increasing the risk of high-grade lesions, possibly due to repeated exposure or reinfection. This aligns with research linking HPV persistence to sexual behavior and partner dynamics. Condom use was identified as a protective factor, reinforcing its role in reducing viral transmission and reinfection risk. These findings align with studies suggesting condom use lowers HPV acquisition and persistence rates [16–20].

Comparison with global studies

Our HPV clearance rate was lower than those reported in European and North American cohorts. Studies in Western populations report HPV clearance rates up to 98% at 24 months post-conization, compared to our observed rate of 72% [21, 22]. Regional differences in HPV genotype distribution sexual behavior, and healthcare access may contribute. These disparities highlight the need for tailored post-treatment monitoring protocols across populations.

Limitations and future directions

This study has several limitations, including its retrospective design and lack of precise data on the time of initial HPV infection. Additionally, information on sexual partners, which could influence HPV transmission dynamics, was not available for all patients. Furthermore, the sample size was relatively small, limiting the generalizability of our findings. Future research should incorporate a multi-center study and prospective follow-up studies to further investigate the long-term outcomes of HPV regression and reinfection prevention strategies.

Conclusion

Conization remains an effective treatment for HSIL and contributes to HPV clearance. However, persistent HPV infection post-conization remains a concern, particularly in women with longer sexual histories. Elderly individuals among young females were at a higher risk of developing high-grade precancerous lesions due to prolonged HPV infection. The duration of sexual life plays a significant role in the development of cervical precancerous lesions, showing a positive correlation. Condom use was found to be a protective factor against reinfection, likely due to its ability to create a physical barrier that blocks HPV transmission. Conversely, HPV vaccination did not show a significant protective effect in this study, potentially due to limited sample size and vaccination coverage. Regular follow-up intervals following cervical conization are of greater significance than HPV vaccination in preventing recurrent lesions. Further research is needed to explore strategies for improving HPV clearance and preventing recurrence post-treatment.

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Author contributions
M.S: Conceptualization, Data curation, Formal analysis, and Writing - original draft; B.X: Data curation, Formal analysis, and Methodology; J.Y: Formal analysis, Investigation and Methodology; Y.W: Conceptualization, Project administration and Writing - review & editing. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study received approval from the Ethics Committee of the affiliated Hospital of Jiangnan University (LS2022328), and adhered to the principles of the Declaration of Helsinki. Informed consent was obtained from all participants prior to study enrollment.

Consent for publication
All authors read and approved the final manuscript.

Competing interests
The authors declare no competing interests.

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