

#### ORIGINAL RESEARCH

# The Effect of Cervical Cold-Knife Conization (CKC) on HPV Infection in Patients with High-Grade Cervical Intraepithelial Neoplasia: A Retrospective Study

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Purpose: Investigation of HPV infection treatment in women undergoing cervical cold-knife conization for advanced cervical intraepithelial neoplasia.

Patients and Methods: A retrospective analysis was conducted on patients who underwent cervical cold-knife conization for cervical intraepithelial neoplasia grade II-III at Beijing Obstetrics and Gynecology Hospital from January 2017 to December 2018. The HPV infection status of the patients at 6 months, 1 year, and 2 years after surgery was collected. We use chi square analysis and binary logistic regression to evaluate various factors such as age, number of pregnancies, number of cesarean sections, number of vaginal deliveries, HPV type, size of surgical specimens (diameter and height), and the influence of specimen edge on HPV infection. Results: A total of 334 patients were included in the analysis. The patients are mainly infected with HPV 16/58/52. Age is a influencing factor for HPV recovery 12 months after CKC surgery (P=0.002). Based on the diagnosis of HPV one year after CKC, the recovery rate of HPV58 patients is significantly lower than HPV16. Age is a influencing factor for the recovery of HPV

Conclusion: The treatment of HPV infection by CKC is related to the patient's age and HPV subtype but not to number of pregnancies, number of pregnancies, number of vaginal deliveries, size of surgical specimens, and marginal conditions. The rate of HPV negative conversion is relatively high 24 months after the patient does not undergo surgery, but there is currently a lack of data on cervical lesions that match HPV results.

Keywords: cold-knife conization, HPV infection, recovery rate, high-grade cervical intraepithelial neoplasia

#### Introduction

Cervical cancer is the fourth most common cancer among women worldwide. In 2018, 57,000 new cases of cervical cancer occurred and caused 311,000 deaths. Persistent HPV infection is the main driving factor for the occurrence of cervical cancer.<sup>2</sup> The United States Preventive Services Working Group, the American Society for Colposcopy and Cervical Pathology, and the American College of Obstetrics and Gynecology all recommend cytological screening or HPV combined with Pap testing based on patient age to detect cervical precancerous lesions as soon as possible.<sup>2</sup> At present, there is still no effective treatment for the persistence of HPV. Preventing health problems caused by HPV infection can only by injecting HPV vaccines, or frequent cervical HPV testing to detect diseases in advance.<sup>3</sup>

For patients who are HPV 16 or 18 positive during the HPV testing process, those who have been positive for one type of HPV for more than a year, or those with cervical cytology testing indicating LSIL or above, vaginal examination

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and pathological examination are required. If the patient is diagnosed with CINII or more advanced lesions, further treatment such as loop electrosurgical excision procedure (LEEP), cryotherapy (low grade CINs), laser therapy, and conization is required based on age and reproductive needs.<sup>4</sup>

Cervical cold-knife conization (CKC) is a surgical method of removing the conical part of the cervix to eliminate the transformation zone of cervical lesions. When the pathological examination of the colposcopy indicates that cervical intraepithelial neoplasia (CIN) has persisted for more than 2 years or progressed to CIN 3, CKC is needed to treat cervical lesions and prevent the occurrence of cervical cancer. CKC can promote the recovery of HPV by removing a portion of cervical tissue and reducing the HPV-DNA load. It can be observed in clinical practice that CKC has a certain therapeutic effect on HPV, however, there are still patients who have doubts about the recovery of HPV after CKC surgery, and there is no comprehensive statistical data available to provide patients.

The aim of this study is to evaluate the relationship between CKC and the recovery rate of HPV patients, as well as the influencing factors. This result helps to provide a basis for HPV evaluation and treatment plans for postoperative CKC patients.

#### **Materials and Methods**

#### **Patients**

In this retrospective study, we collected 899 patients who underwent cervical cold knife conization at Beijing Obstetrics and Gynecology Hospital from January 1, 2017 to December 31, 2018 due to pathological results of colposcopy biopsy CINII-CINIII.

Inclusion criteria: 1. Patients with pathological confirmation of CINII-CINIII under colposcopy; 2. Preoperative HPV positive and clear typing results. 3. The patient underwent cervical cold knife conization; 4. Informed consent of the patient.

Exclusion criteria: 1. The patient undergoes total hysterectomy for any reason (uterine fibroids, other malignant tumors, etc.) within 2 years after surgery; 2. The patient underwent cervical conization again within two years after surgery due to any reason (long-term HPV infection, difficulty in follow-up, psychological stress, etc.); 3. The patient becomes pregnant within 2 years after surgery; 4. The patient who have undergone cervical surgery before this cervical cold knife conization surgery.

We collected HPV test results from all patients who met the standards at 6/12/24 months after surgery. Persistent infection of a certain type of HPV is considered when a patient is infected with the same type of HPV before surgery and still infected with the same type of HPV after surgery. Due to the current medical guidelines requiring patients with persistent high-risk HPV infection 12 months after surgery to undergo colposcopy again, some patients have undergone a second cervical surgery treatment. We divided the patients into two groups based on their HPV prognosis at 12 months after surgery, and separately listed the data of patients with persistent HPV infection for 24 months. Only when the type detected during preoperative HPV typing testing is consistent with the type detected during postoperative HPV typing testing, patients are considered to have sustained HPV infection. The impact of cervical cold knife conization on each HPV subtype of patients was analyzed. Patient consent was waived due to the retrospective nature of this study. We confirmed that the privacy of participants would be kept in strict confidence. The study was carried out in accordance with the ethical standards laid down in the Declaration of Helsinki, and was approved by the ethics committees of Beijing Obstetrics and Gynecology Hospital, Capital Medical University (No:2023-KY-021-01).

#### Test Method

#### **HPV** Testing

Cervical scrape specimens were gently collected from the squamocolumnar junction of the cervix using a sampling brush. The genotype of HPV was determined using a 23-HPV Genotyping Real-time PCR Kit (Hybribio, China) which detects 15 high-risk types (HPV 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82) according to the manufacturer's instructions.

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#### Cervical Liquid-Based Cytology Tests

Cells were collected from the ectocervix and the cervical canal using a cervical canal brush, and the cells attached to the small brush were eluted in vials containing cell preservation solution and sent to the pathology department (Beijing Obstetrics and Gynecology Hospital, Capital Medical University, China). The laboratory physician provided the final report.

## **Observation Parameters**

We collected and analyzed the age, number of pregnancies, number of deliveries completed through cesarean section, number of natural deliveries, preoperative HPV results, ThinPrep cytologic test (TCT) results, diameter and cone height of the cervical resection section in surgical records, and postoperative pathological indications of the incision margin.

## Statistical Method

All statistical analyses were conducted using SPSS version 26.0 and Excel. The grade data was described by frequency and composition ratio. We used ANOVA to analyze the possible influencing factors of patients in the cured and non-cured groups, and binary logistic analysis was performed on the possible influencing factors of patients with HPV16, 52, and 58. The statistical significance is set to 0.05.

#### Results

465 out of 799 patients were excluded (21 patients had negative preoperative HPV testing, 79 patients did not undergo HPV testing or had unknown HPV test results, 116 patients had unclear HPV infection types, 36 patients underwent CKC surgery again within 2 years, 39 patients underwent hysterectomy or larger surgery due to various reasons, and 152 patients did not have follow-up data from our hospital. There are 334 patients included in this study. As patients may be infected with multiple HPV subtypes, we calculated the infection rates of different subtypes and their proportion to the number of infections of all types. Among all patients, 73.7% (n=246) had only one high-risk type of HPV, 20.4% (n=68) had two high-risk types of HPV, 3.6% (n=12) had three types, and 2.4% (n=8) had four or more types of HPV. We presented the proportion of different HPV infection types and the proportion of each HPV infection type to all HPV infection types. The two infection rates of each HPV subtype are shown in Table 1 shows the infection rates.

Among patients with multiple HPV subtypes, HPV16 combined with 31 infection was the most common (n=19), followed by 52 (n=12). We present the specific HPV infection types of all patients with multiple HPV types in Table 2.

Table	I Infaction	Rate and	Proportion	of Different	Types of HPV
Table	<b>i</b> infection	Kate and	Frobortion	or Dillerent	Types of mrv

Types of HPV	Number (n=334)	Proportion of Population (%)	Proportion of Infection Types (%)	Types of HPV	Number (n=334)	Proportion of Population (%)	Proportion of Infection Types (%)
6	1	0.3%	0.2%	55	1	0.3%	0.2%
11	3	0.9%	0.7%	56	6	1.8%	1.3%
16	231	69.5%	51.8%	58	44	13.2%	9.8%
18	22	6.6%	4.9%	59	5	1.5%	1.1%
31	17	6.0%	4.5%	61	1	0.3%	0.2%
33	17	5.1%	3.8%	64	1	0.3%	0.2%
35	6	1.8%	1.3%	66	5	1.5%	1.1%
39	5	1.5%	1.1%	67	1	0.3%	0.2%
42	2	0.6%	0.4%	68	5	1.5%	1.1%
43	1	0.3%	0.2%	74	1	0.3%	0.2%
45	7	2.1%	1.6%	81	3	0.9%	0.7%
51	13	3.9%	2.9%	82	6	1.8%	1.3%
52	39	11.7%	8.7%	83	1	0.3%	0.2%
53	6	1.8%	1.3%				

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Table 2 Number of Patients with Multiple HPV Infections

HPV Types	Number	HPV Types	Number
HPV16/31/33/35/52/58	I	HPV16/66	2
HPV16/52/58/59/68	I	HPV16/61	1
HPV31/33/52/58/67	1	HPV16/59	2
HPV16/56/68/82	I	HPV56/58	1
HPV16/39/51/68	1	HPV39/58	1
HPV16/43/59/66	1	HPV33/58	1
HPV16/31/58/59	1	HPV16/58	4
HPV16/31/52/58	1	HPV53/56	1
HPV16/66/81	1	HPV16/56	I
HPV16/52/81	1	HPV55/58	I
HPV/16/58/66	1	HPV16/53	2
HPV16/53/58	1	HPV35/52	I
HPV51/52/58	1	HPV33/52	I
HPV16/51/58	1	HPV16/52	8
HPV16/45/58	1	HPV33/51	I
HPV16/52/56	1	HPV16/51	6
HPV16/42/53	1	HPV45/58	I
HPV16/18/45	1	HPV18/45	3
HPV16/35/39	1	HPV42/52	I
HPV16/18/39	1	HPV31/39	I
HPV16/83	1	HPV16/33	3
HPV45/82	1	HPV31/58	I
HPV18/82	1	HPV18/31	I
HPV16/82	1	HPV16/31	16
HPV52/81	1	HPV11/16	3
HPV64/74	1	HPV6/16	I
HPV16/68	2		

According to whether the HPV infection subtypes at 12 months after cervical conization were the same as before surgery, the patients were divided into a cured group and an untreated group. The patients were divided into an HPV untreated group (n=26) and an HPV cured group (n=308). The basic data of the patients are shown in Table 3. The age of patients in the cured group (37.38) was significantly lower than that in the untreated group (42.15) (P=0.002). The number of HPV infection types (P=0.057), number of pregnancies (P=0.717), number of vaginal deliveries (P=0.201),

Table 3 Basic Data of HPV Positive 12 Months After Surgery Group (n=26) and HPV Negative 12 Months After Surgery Group (n=308)

Influence Factor		HPV Negative 12 Months After Surgery (n=308)	HPV Positive 12 Months After Surgery (n=26)	P
Age				0.002
	>60	3 (0.9%)	2 (7.7%)	
	50–60	15 (4.8%)	5 (19.2%)	
	40–50	69 (22.4%)	5 (19.2%)	
	30-40	155 (50.3%)	11 (42.3%)	
	≤30	66 (21.4%)	3 (11.5%)	

(Continued)

Table 3 (Continued).

Influence Factor		HPV Negative	HPV Positive	Р
		12 Months After	12 Months After	
		Surgery (n=308)	Surgery (n=26)	
Number of types of HPV infections				0.057
Trained of types of the time calculation	1	231 (75.0%)	15 (57.7%)	0.007
	2	61 (19.8%)	7 (27.0%)	
	≥3	16 (5.20%)	4 (15.4%)	
Number of pregnancy		(5.25/5)	. (13.173)	0.717
. tumber of programe,	0	31 (10.1%)	2 (7.7%)	
		56 (18.2%)	3 (11.5%)	
	2	83 (27.0%)	6 (23.1%)	
	3	65 (21.1%)	8 (30.7%)	
	4	44 (14.3%)	3 (11.5%)	
	≥5	29 (9.4%)	4 (15.4%)	
Number of vaginal deliveries	-3	27 (7.170)	1 (13.170)	0.246
Transpor of tagillal deliveries	0	56 (18.2%)	6 (23.1%)	J.Z-10
	ı	189 (61.4%)	11 (42.3%)	
	2	58 (18.8%)	8 (30.8%)	
	3	5 (1.6%)	I (3.8%)	
Number of cesarean sections	3	3 (1.0%)	1 (3.6%)	0.181
Number of cesarean sections	0	234 (76.0%)	19 (73 19/)	0.101
	l i	68 (22.1%)	19 (73.1%) 5 (19.2%)	
	2	1 '	, ,	
The ments of TCT	2	6 (1.9%)	2 (7.7%)	0.681
The result of TCT		07 (20 29()	4 (22 19)	0.681
	Normal or	87 (28.2%)	6 (23.1%)	
	Inflammatory	(0 (22 49/)	7 (24 0%)	
	AUS-CS	69 (22.4%)	7 (26.9%)	
	AUS-H	17 (5.5%)	0 (0%)	
	LSIL	64 (20.8%)	4 (15.4%)	
	HSIL	70 (22.7%)	8 (30.8%)	
	AGC	2 (0.6%)	0 (0%)	
Specimen condition		04 (07 000)	F (10.000)	
Sample size	Not mentioned in	86 (27.9%)	5 (19.2%)	
	the surgical			
	records			
Specimen diameter				0.883
	<3	58 (18.8%)	6 (23.1%)	
	3–4	148 (48.1%)	13 (50.0%)	
	≥4	16 (5.2%)	2 (7.7%)	
Specimen height				0.880
	<2	22 (7.1%)	3 (11.5%)	
	2	101 (32.8%)	9 (34.6%)	
	2.5	96 (31.2%)	9 (34.6%)	
	3	3 (1.0%)	0 (0%)	
Pathological status of surgical specimen e				0.697
	Positive	31 (10.1%)	2 (7.7%)	
	Negative	277 (89.9%)	24 (92.3%)	

number of cesarean sections (P=0.488), TCT results (P=0.387), diameter of surgical pathological specimens (P=0.883), cone height (P=0.880), and edge positivity (P=0.697) were not related to the HPV cure rate.

We compared the differences in HPV infection between patients 12 and 24 months after surgery, with 11 patients recovering from HPV infection and 2 patients relapsing. The statistical data is shown in Table 4. Two patients with recurrent HPV, aged 38/36 years, were both infected with HPV16. The preoperative TCT was LSIL and Normal, and the size of the intraoperative specimen was not recorded. There was no residual pathological margin after surgery, and the subtypes of recurrent HPV were HPV16/66, respectively. Due to the small number of patients who recovered for the first time within 24 months and experienced HPV recurrence, further analysis was not conducted.

The specific situation of different types of HPV recovery in patients is shown in Table 5.The number of people infected with each type of HPV is: HPV16 (n=231), HPV18 (n=22), HPV33 (n=17), 52 (n=39), 58 (n=44), others (n=10). Considering the small number of HPV59/61/67/68 infections, this article only analyzes the HPV subtypes of over 10 patients infected with HPV in Table 6. The results showed that the recovery rate of HPV58 was lower than that of HPV16 at 12 and 24 months after cervical conization (P=0.006 at 12 months and P=0.025 at 24 months).

We analyzed the incidence rate 12-month after the surgery according to different HPV types, and used binary logistic regression to analyze the factors affecting the recovery of the three types of HPV with the highest incidence rate, HPV16, HPV52, and HPV58. The results showed that the recovery of the three types of HPV was unrelated to all factors in the statistics, as shown in Table 7.

Table 4 Status of Patients Who Have Recovered from the First HPV Typing in 24 Months

Age	Number of Types of HPV Infections	Number of Pregnancy	Number of Vaginal Deliveries	Number of Cesarean Sections	тст	Specimen Diameter*Specimen Height	Pathological Status of Surgical Specimen Edge	HPV Subtypes Not Recover 12 Months After Surgery
41	11/16	2	0	0	HSIL	Not mentioned	Negative	16
27	16/52	0	0	0	HSIL	Not mentioned	Negative	16
44	31/33/52/58/67	3	2	0	Normal	3*2.5	Negative	58/67
56	16	5	1	0	Normal	3*2.5	Negative	16
29	16	3	1	0	Normal	3*2.5	Negative	16
46	16	3	2	0	Normal	3*2	Negative	16
53	52	6	2	0	HSIL	3*2	Negative	52
36	16/61	2	1	I	HSIL	3*2	Negative	61
32	58	3	1	1	AUS-	3*2	Negative	58
					CS			
37	42/52	0	0	0	AUS-	3*1.5	Negative	52
					CS			
42	58	2	Ţ	I	LSIL	2*2.5	Negative	58

Table 5 Healing Status of Different HPV Types

Type of HPV	HPV Negative 12 Months After Surgery	HPV Positive 12 Months After Surgery	Cure Rate (%)	HPV Negative 24 Months After Surgery	HPV Positive 24 Months After Surgery	Cure Rate (%)
16	222	9	96.1%	227	4	98.2%
18	21	1	95.5%	21	1	95.5%
33	16	1	94.1%	16	1	94.1%
52	36	3	92.3%	38	1	97.4%
58	37	7	84.1%	40	4	90.9%

Table 6 Comparison of Cure Rates for Different HPV Subtypes at 12 and 24 Months After Surgery

	HPV Positive 24 Months After Surgery							
HPV Positive 12 Months after Surgery		HPV 16	HPV 18	HPV 33	HPV 52	HPV 58		
	HPV 16		0.368	0.301	0.544	0.025		
	HPV 18	0.603		0.688	0.549	0.456		
	HPV 33	0.514	0.688		0.519	0.57		
	HPV 52	0.214	0.543	0.647		0.22		
	HPV 58	0.006	0.178	0.218	0.217			

**Table 7** Comparison Between the HPV Positive 12 Months After Surgery Group and HPV Negative 12 Months After Surgery Group of HPV 16, 52, and 58

Influence Factor	HPV16 (n=231)			HPV52 (n=39)			HPV58 (n=44)		
	HPV Negative 12 Months After Surgery (n=222)	HPV Positive 12 Months After Surgery (n=9)	P	HPV Negative 12 Months After Surgery (n=36)	HPV Positive 12 Months After Surgery (n=3)	P	HPV Negative 12 Months After Surgery (n=37)	HPV Positive 12 Months After Surgery (n=7)	P
Age	36.69±7.43	39.3±8.45	0.204	36.63±7.02	41.33±8.34	0.998	36.51±9.26	40.86±10.15	0.325
Number of types			0.996			0.996			0.295
of HPV infections									
1	159	7		18	2		20	4	
2	46	2		11	1		9	1	
≥3	18	0		7	0		8	2	
Number of			0.348			0.999			0.211
pregnancy									
0	25	0		3	1		4	0	
1	44	1		8	1		6	1	
2	59	2		9	0		10	1	
3	47	2		10	0		10	4	
4	29	2		4	0		6	0	
≥5	19	1		2	1		1	1	
Number of vaginal deliveries			0.240			0.998			0.174
0	46	2		4	2		6	1.	
ı	132	4		29	0		23	4	
2	40	3		3	li		8	2	
3	5	0		0	0		0	0	
Number of			0.181			0.999			0.378
cesarean sections									
0	170	7		27	3		26	5	
1	49	1		9	0		10	2	
2	5	1		0	0		1	0	
TCT			0.128			0.996			0.407
Normal or Inflammatory	77	5		7	0		6	1	
AUS-CS	47	2		8	1		5	2	

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Table 7 (Continued).

Influence Factor	HPV16 (n=231)			HPV52 (n=39)			HPV58 (n=44)		
	HPV Negative 12 Months After Surgery (n=222)	HPV Positive 12 Months After Surgery (n=9)	P	HPV Negative 12 Months After Surgery (n=36)	HPV Positive 12 Months After Surgery (n=3)	P	HPV Negative 12 Months After Surgery (n=37)	HPV Positive 12 Months After Surgery (n=7)	P
AUS-H	10	0		3	0		4	0	
LSIL	39	0		9	0		13	2	
HSIL	49	2		9	2		9	2	
AGC	1	0		0	0		0	0	
Surgical specimen condition									
Not mentioned in	58	3		15	0		9	1	
the surgical									
records									
Specimen			0.596			0.997			0.129
diameter									
<3	42	1		5	0		6	2	
<4	116	4		14	3		16	4	
≥4	6	1		2	0		6	0	
Specimen height			0.549			0.995			0.696
<2	17	0		2	1		4	1	
2	74	3		10	1		13	1	
2.5	72	3		8	1		11	4	
3	2	0		1	0		0	0	
Pathological status			0.643			0.999			1.000
of surgical									
specimen edge									
Positive	25	1		4	0		1	0	
Negative	198	8		32	3		36	7	

## **Discussion**

There is currently no reliable drug treatment for HPV virus, and it is possible to cure HPV infection through cervical photodynamic therapy, local cryotherapy, and surgical treatment. Cervical conization is a diagnostic and therapeutic method for CIN, which can directly reduce the HPV-DNA load by removing HPV infected lesions, thereby promoting the recovery of patients with HPV infection. Park reported that the high level of cervical HR-HPV is the main reason why some patients still have persistent lesions after cervical conization. Due to the fact that only visible lesions were removed during the surgery, postoperative HPV may still remain positive, ultimately leading to the patient's hysterectomy.

Patient age is considered an important factor in the duration of HPV infection. In a 2005 study, the proportion of persistent HPV infection gradually increased with age. <sup>10</sup> A study in 2017 suggested that the incidence rate of high-risk HPV in elderly women was lower than that in young people, <sup>11</sup> but the clearance rate of HPV after cervical conization decreased with age. In our study, similar to previous studies, the age of the untreated group was significantly higher than that of the cured group.

The type of HPV infection is an important factor in patient prognosis, <sup>12</sup> and among cervical cancer patients, the prognosis of HPV18 infected patients is worse than that of HPV16 infected patients. <sup>13</sup> Statistics show that the incidence rate of HPV58 in Chinese women is the second of all HPV types. <sup>14</sup> For the prognosis of HPV after surgery, our study suggests that the cure rate of HPV58 is significantly lower than that of other HPV types. Chen et al's study suggests that

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HPV58 infection is a risk factor for patients with poorly differentiated cervical cancer, <sup>15</sup> which may be due to the particularity of HPV58 protein structure. Some scholars have suggested that for patients with HPV58 positive, Colposcopy examination should be more frequent. <sup>16</sup>

A study has shown that over 50% of all CIN patients have multiple subtypes of HPV.<sup>17</sup> This study only focuses on CINII-CINIII patients who require cervical cold knife conization. In our study, the number of patients with multiple HPVs reached 20%. There are studies suggesting that infection with different types of HPV makes it easier for patients to acquire another type of HPV (such as HPV16 and HPV52).<sup>18</sup> In this study, the number of HPV16 combined with 31 and 52 infections exceeded 10. Simultaneous infection of different types of HPV may lead to more severe cervical lesions. In the study by Spinillo et al,<sup>19</sup> the proportion of CIN3+in patients with HPV16 and HPV18 co infection was higher than the probability of HPV16 alone. However, in our study, the number of infection types was not related to the prognosis of HPV itself, indicating that the promoting effect of different HPVs can only occur on the basis of a certain HPV load. CKC surgery can directly reduce the virus load, and the HPV treatment effect on patients with multiple HPV infections is the same as that of patients with a single HPV infection.

The pathological margin condition after cone resection is usually considered one of the reasons for treatment failure of cervical cancer precancerous lesions.<sup>20</sup> Studies have found that age, menopausal status, and abnormal cytological testing are common risk factors for positive margins.<sup>21</sup> However, in our study, abnormal cytological testing and pathological margins were not associated with HPV infection status. Debaudrap et al<sup>22</sup> did a meta-analyses, showed that in the treatment of cervical precancerous lesions in HIV infected women, the failure rate of treatment with positive margins (47.2%, 95% CI 22.0–74.0) was significantly higher than that of patients with negative margins (19.4%, 95% CI 11.8–30.2). This may indicate that HPV infection is related to the body's autoimmune status, but due to the inability to monitor the patient's autoimmune status, there is currently a lack of objective indicators to determine the relationship between autoimmune status and HPV infection.

Persistent long-term HPV infection is considered one of the influencing factors for cervical precancerous lesions, and the HPV viral load is closely related to the risk of high-grade cervical lesions.<sup>23</sup> In 2001, a cohort study in Brazil suggested that the duration of HPV infection was related to the incidence rate of cervical precancerous lesions.<sup>24</sup> In 2016, a study<sup>25</sup> showed that 54% of patients with persistent high-risk HPV infection had persistent vaginal and cervical lesions, while only 32.3% of patients with low-risk HPV infection had lesions, suggesting that further treatment is needed for persistent high-risk HPV infection after CKC. Byun et al<sup>26</sup> analyzed the HPV infection status of 172 CIN2, CIN3, and CIS patients after cold knife conization. It was mentioned in the analysis that 29.3% of all postoperative HPV infected patients were persistently infected with the same HPV subtype. In this experiment, our results showed that the postoperative recovery rate of HPV58 was significantly lower than that of the highest prevalent HPV16 at 12 and 24 months after surgery, and there was no significant difference compared to other high-risk HPV types. This suggests that for Chinese patients, Further research on the characteristics of HPV58 related infections is necessary. Due to the focus of this experiment on studying the recovery of HPV after CKC surgery and not paying attention to the condition of cervical lesions in patients, further statistical analysis of relevant data is needed.

## **Conclusion**

Based on the HPV test results one year after surgery, the age of patients in the HPV negative 12 months after surgery group was significantly lower than that in the HPV positive 12 months after surgery group. The number of HPV infection types, pregnancy frequency, vaginal delivery frequency, cesarean section frequency, TCT results, diameter and cone height of surgical pathological specimens were not related to the HPV cure rate. At 12 and 24 months after surgery, the recovery rate of HPV58 patients is significantly lower than HPV 16. Analyzing HPV16/52/58 infected patients separately, the above factors are not related to the cure rate of HPV.

## **Abbreviations**

CKC, cervical cold-knife conization; CIN, cervical intraepithelial neoplasia; HPV, human papilloma virus; TCT, ThinPrep cytologic test; LEEP, Loop electrosurgical excision procedure.

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#### **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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