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Analysis of high-risk HPV infection and cervical HPV in 10670 women

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Abstract: Objective To analyze the infection of cervical high-risk HPV (HR-HPV), study the correlation of cervical HR-HPV infection and help the clinical cervical cancer screening. Methods Statistics from January 2019 to December 2020 in the gynecological outpatient department of 10670 women of cervical HPV infection, among which 731 patients with cervical HR-HPV infection underwent colposcopy + cervical biopsy, analyzed the relationship between cervical HR-HPV infection and cervical pathology results, clear the association between cervical HR-HPV infection and cervical lesions. Results 10670 female HR-HPV patients, with the highest number of 20.00% (347/1738), and the top 5 single infections were 16,52,58,53 and 51.HR-HPV infected patients were divided into four categories according to type 16,18, other 13 and multiple infections, and the other 13 types accounted for the most proportion, with 59.09% (1027/1738).The 347 patients with multiple infection had the highest rate of other type 13 coinfection, accounting for 60.23% (209/347).A total of 1738 patients with HR-HPV infection were divided into five groups according to their age, and the number of women aged 41 to 50 was the largest (29.34%), second by> 50 years (28.48%), with HPV16 and 18 infections mainly from 41 to 50 and> 50 years, as were other 13 high-risk HPV infections.HR-HPV infection at different ages was statistically significant ($\chi 2=61.419$, $P=0.000<0.05$).In 731 patients with HR-HPV infection undergoing cervical biopsy in our hospital, pathological cervical low-grade intraepithelial lesions were mainly other type 13 infections, accounting for 58.17% (356/612); cervical high-grade intraepithelial lesions were mainly type 16 infections (including single type 16,16 and other type 13 infections), accounting for 67.23% (80/119).The distribution of HR-HPV type in the pathological diagnosis of cervical biopsy was statistically significant ($\chi 2=126.830$, $P=0.000<0.05$).Conclusion HR-HPV infection can increase the incidence of cervical precancerous lesions and cervical cancer is mainly type HPV16.

1. Introduction

Cervical cancer, one of the most common malignancies in women [1]. cervical carcinomaIncidence and mortality in developing countries is two times the developed countries, WHO has clear cervical cancer is preventable tumor, prevention means namely early detection and

treatment, so need to strengthen HPV vaccination, cervical cancer screening, diagnosis and treatment, launched a global push to eliminate cervical cancer, expected by 2050 will reduce new cases of cervical cancer by 40%, the number of deaths reduced by 5 million [2]. Chinese women are paying more and more attention to their own health status, HPV vaccine (China is mainly bivalent, four valent, nine valent) in the market in short supply, prevention is important, but cervical cancer screening can not be ignored. At present, the main methods of screening in China are: HPV detection, TCT (thin-layer liquid-based cytology) detection. In early prevention, HPV detection plays a very important position. Different types of HPV have differences in the pathogenicity of cervical epithelium. Continuous HR-HPV infection increases the risk of cervical precancerous lesions and cervical cancer, especially HPV16, type 18. Shan Wei, Zhang Tao and others analyzed female HPV infection in mainland China and found that 60.54% and HPV18 were 11.74% [3]. The 2019 guidelines of the American Society of Colposcopy and Cervical Pathology (ASCCP) proposed that HPV alone is better than cytology alone, and HPV alone has lower cost. They still considered HPV16 and 18 have the highest risk of CIN and cervical cancer, and were directly referred for colposcopy [4], Cervical biopsy was performed immediately after finding a suspicious lesion. This study mainly investigated the association between cervical HR-HPV infection and cervical lesions.

2. Data and methods

2.1 General Information

The test results of 10,670 women with HPV test in the gynecological outpatient department of the Affiliated Hospital of Shaanxi Zhongda from January 2019 to December 2020 were analyzed, including 1738 with HR-HPV infection, 731 with HR-HPV infection and colposcopy and cervical biopsy in our hospital, and the relationship between HR-HPV infection and cervical biopsy results was retrospectively analyzed. The patients were between 20 and 85 years old, and the mean age was 42.33 years.

2.2 Clinical data

(1) HPV collection and testing: cervical epithelial detached cell samples were routinely collected with a disposable cervical cell collector, Preserved in a sample tube, Send it to the laboratory for testing, Using the nucleic acid thermotemperature amplification method, Using 21 HPV typing detection techniques (PCR-membrane hybridization), Including 15 high-risk subtypes (16,18,31,33, 35, 39,45,51,52,53,56,58,59,66,68) and six low-risk subtypes (6,11,42,43,44, CP8304), The detection results were read according to the instructions of human papillomavirus (HPV) typing detection kit (PCR-membrane hybridization method) of Chaozhou Kaipu Biochemistry Co., LTD. (2) Colposcopy and cervical biopsy: routine exposure to the cervix, with cotton ball to wipe cervical secretions, using jinke electronic colposcopy, adjust to the appropriate multiple of cervical abnormal, fully cotton dipped in acetic acid, wet cervix 30s~1min, dynamic observation in the cervical changes, suspicious biopsy, fixed specimens, pathology test.

2.3 Pathological diagnostic criteria

Pathologists routinely produce, stain, read films, and according to the 4th edition of WHO [4] interpretation. The pathological diagnosis was classified into: chronic cervicitis <cervical low grade intraepithelial lesions (LSIL) <cervical high grade intraepithelial lesions (HSIL) <cervical cancer (CC). In this study, there were more than two pathological diagnoses for the same pathological results, unified with the highest level as the diagnostic standard.

2.4 Statistical methods

SPSS19.0, count data are expressed as examples and percentage, using $\chi 2$ test, $P < 0.05$ indicates statistical significance.

3. Results

3.1 HPV detection

Among 10670 women undergoing HPV detection, the positive rate was 17.57% (1875/10670). The positive rate of HR-HPV infection (single HR-HPV infection, multiple HR-HPV infection, HR-HPV infection with low-risk HPV infection) was 16.29% (1738/10670), and the positive rate of low-risk HPV infection (single low-risk HPV infection, multiple low-risk HPV infection) was 1.28% (137/10670).

3.1.1 Distribution of HR-HPV infection

Table 1: Order of HR-HPV infection

HPV type	Example number	percentage (%)
multiple	347	20.00
16	284	16.34
52	229	13.18
58	170	9.78
53	138	7.94
51	99	5.70
39	90	5.18
18	80	4.60
68	60	3.45
31	55	3.16
33	49	2.82
56	43	2.47
66	42	2.42
59	32	1.84
45	13	0.75
35	7	0.40
amount to	1738	100

Table 2: Distribution of HR-HPV infection

HR-HPV type	Example number	positive rate (%)	HR-HPV infection proportion (%)
16	284	2.66	16.34
18	80	0.75	4.60
Other type 13	1027	9.63	59.09
multiplicities of infection	347	3.25	19.97
Note: ① other type 13 is a single high-risk HPV infection except type 16,18 ② two types or more types are multiple infections			

1738 HR-HPV infected patients (including single infections and multiple infections) had the largest number of multiple infections, accounting for 20.00% (347/1738). The top 5 of single infections were types 16, 52, 50, 58, 53, 51, which are shown in Table 1. HR-HPV infected patients were divided into four categories according to types 16,18, other 13 and multiple infections, with the proportion: other 13 (59.09%)> multiple infections (19.97%)> 16(16.34%)>18 (4.60%), as shown in Table 2.

3.1.2 Distribution of HR-HPV multiple infections

Among 1738 HR-HPV patients, 347 multiple infections were detected, and the proportion was: other 13 (60.23%)> 16 and other 1 type 13 (28.82%)> 18 and other 13 (8.65%)> 16,18 or 16,18 and other 13 (2.31%), shown in Table 3.

Table 3: Distribution of multiple infections with HR-HPV

HR-HPV type	Example number	HR-HPV infect proportion (%)	The proportion of HR-HPV multiple infections is (%)
16*	100	5.75	28.82
18*	30	1.73	8.65
16,18, or 16,18 *	8	0.46	2.31
*	209	12.03	60.23
Note: ① 16 * with type 16 with other 13 infections ② 18 * with type 18 with other 13 infection ③ 16,18 * with type 16,18 co-infection or type 16,18 with other 13 infection ④ * with other 13 co-infection			

3.2 HR-HPV infection at different ages

1738 patients with HR-HPV infection were divided into 5 groups according to their age, with the largest number of HR-HPV infection among women aged 41-50 years, accounting for 29.34% (510/1738), followed by> 50 years, accounting for 28.48% (495/1738).Specific analysis is as follows: type 16 mainly> 50 years, 18 mainly 41-50, other 13 infections 41-50,16 and other 13> 50,18 and 13> 50 years, 16,18 or 16,18 with 41-50 years, other 13 infections> 50 years.HR-HPV infection at different ages was statistically significant ($\chi 2=61.419$, $P=0.000 <0.05$), as shown in Table 4.

Table 4: The HR-HPV infection at different ages [Example (%)]

age (year)	HR-HPV Total number of cases	16	18	Other type 13	16*	18*	16,18 or 16, 18*	*
≤20	11(0.63)	2(0.70)	0(0.00)	8(0.78)	1(1.00)	0(0.00)	0(0.00)	0(0.00)
21~30	267(15.36)	42(14.79)	6(7.50)	167(16.26)	16(16.00)	1(3.33)	2(25.00)	33(15.79)
31~40	455(26.18)	75(26.41)	18(22.50)	287(27.95)	20(20.00)	7(23.33)	2(25.00)	46(22.01)
41~50	510(29.34)	80(28.17)	30(37.50)	323(31.45)	17(17.00)	10(33.33)	3(37.50)	47(22.49)
>50	495(28.48)	85(29.93)	26(32.50)	242(23.56)	46(46.00)	12(40.00)	1(12.5)	83(39.71)
amount to	1738	284	80	1027	100	30	8	209

3.3 Analysis of HR-HPV type and cervical biopsy results

1738 H R-HPV infected patients underwent colposcopy + cervical biopsy in our hospital, and cervical low-grade intraepithelial lesions were mainly other 13 infections, accounting for 58.17% (356/612). Pathological diagnosis = cervical high-grade intraepithelial lesions were dominated by single type 16,48.54% (50/103), single type 18,2.91% (3/103), type 16,15,13% (16/103), type 18,

type 13 (3/103), 16,18, type 18 or type 16 and 18,0% (0/0). Pathological diagnosis = cervical cancer is a single type 16,68.75% (11/16), single type 18,0% (0/16), type 16 and 13 (3/16), type 13,13,12.5% (2/16), 16,18 or 16 and 18,0% (0/0).The distribution of HR-HPV type in the pathological diagnosis of cervical biopsy was statistically significant ($\chi 2=126.830$, $P=0.000 <0.05$), as shown in Table 5.

Table 5: Analysis of H R-HPV type and cervical biopsy results [Case (%)]

HR-HPV type	pathologic diagnosis				
	chronic cervicitis	Low-grade intraepithelial lesions of the cervix	High-grade intraepithelial lesions of the cervical cervix	cervical carcinoma	amount to
16	56(13.83)	27(13.04)	50(48.54)	11(68.75)	144
18	26(6.42)	9(4.35)	3(2.91)	0(0.00)	38
Other type 13	237(58.52)	119(57.49)	25(24.27)	0(0.00)	381
16*	25(6.17)	13(6.28)	16(15.53)	3(18.75)	57
18*	9(2.22)	7(3.38)	3(2.91)	2(12.50)	21
16,18, or 16,18 *	8(2.00)	2(0.97)	0(0.00)	0(0.00)	10
*	44(10.86)	30(14.49)	6(5.83)	0(0.00)	80
amount to	405	207	103	16	731

4. Discussion

Cervical cancer, as a malignant disease, causes a healthy and economic burden on individuals and society. In recent years, its incidence rate increases year by year, and it has the trend of younger age[5-8]. According to the global female cancer statistics in 2020, cervical cancer in most countries ranked second, and first in 23 countries, 36 countries, Chinese women cervical cancer is 110000,18.2%, 59000 deaths, 17.3%, global incidence, mortality, our country are significantly lower than the world average, it shows that the positive prevention achieved significant results [9]. HPV infection for more than 1 year is called HPV infection [10], but Continuous HR-HPV infection, especially HPV16,18, is closely related with cervical precancerous lesions and cervical cancer. With the continuous improvement of medical level, the prognosis of cervical cancer has been significantly improved, and the mortality rate is also decreasing year by year. The occurrence and development of cervical cancer is finally formed from quantitative change to qualitative change, so to improve the screening program, improve the screening technology, strengthen the screening efforts, active prevention, early diagnosis and early treatment, can effectively delay and block the occurrence and development of cervical cancer.

Among the 10670 women in this study, 1875 were HPV positive (17.57%) and 1738 were HR-HPV infected (16.29%), with the highest rate of other 13 infections (59.09%), which is reported in the literature [11-14] Basically consistent; followed by multiple infections (19.97%), and the cervical pathogenicity of multiple infections is controversial, and some scholars believe that multiple infections increase the risk of persistent HPV infection, precancerous lesions and cancer [15-16]; Some scholars believe that multiple infections do not make the cervical lesions develop sexually [17-19]. This study is closer to the second view, suggesting that HPV multiple infection with cervical cancer is not sufficiently necessary.HR-HPV multiple infections still have the highest proportion of other type 13 coinfections (60.23%), and no literature similar to the classification of HR-HPV multiple infections in this paper was found, so it cannot be compared. This study shows that other type 13 infections accounted for a large proportion of HR-HPV infection, but their pathogenicity to the cervix is weak. The author believes that high-risk HPV infection type 13 except types 16 and 18

should be strictly followed-up. At present, domestic and foreign studies still show that type 16 and 18 infection are the most pathogenic to the cervix, especially type 16 [20-30]. The 1738 cases of HR-HPV patients were divided into 5 groups according to age, with the largest number of women aged 41 to 50 (29.34%) and> 50 years (28.48%). Specific analysis shows that not only the HPV16 and 18 type infections were mainly concentrated in 41 to 50 and> 50 years, but other 13 high-risk HPV infections, which may be related to polysexual partners, contraceptives, immune deficiency, excessive labor, close birth, smoking, drug use and so on.HR-HPV infection at different ages was statistically significant ($\chi 2$=61.419, P=0.000 <0.05). A large number of studies explore the relationship between age and HR-HPV infection rate, and all believe that different age stages and HR-HPV infection rate, most of the literature shows that HR-HPV infection rate increases with age, while individual literature shows that HR-HPV infection rate decreases with age [31-39], This study did not show a clear increasing or decreasing trend, which may be related to a small sample size to determine the relationship between different age stages and HR-HPV infection. A total of 731 patients with HR-HPV infection underwent colposcopy cervical biopsy in our hospital, and the pathological diagnosis of low grade intraepithelial lesions was other type 13 infections, accounting for 58.17% (356/612); the lesions were type 16 infections (including single type 16,16 and other type 13 infections), accounting for 67.23% (80/119). The distribution of HR-HPV type in the pathological diagnosis of cervical biopsy was statistically significant ($\chi 2$=126.830, P=0.000 <0.05). In this study, type HPV16 infection had a greater impact on high-grade and above cervical lesions, and HPV16 was more closely related to cervical lesions than H P V type 18, which basically shared the arguments of Xu Huihui, Zhou Qin, Wang Li et al [40-51], Patients with HPV16 infection should be vigilant and closely follow-up, and undergo colposcopy + cervical biopsy and cervical taper to clarify the lesions if necessary.

In conclusion, HR-HPV infection is closely related with cervical lesions, and HPV16 type is the most pathogenic to the cervix, followed by HPV18, while other HR-HPV infections except HPV16, 18 have a lower chance of developing cervical cancer. HPV testing has low technical requirements for professionals, belongs to automatic testing technology, avoids the subjectivity of doctors' reading, and its sensitivity is a better clinical testing method, can be used not only for cervical cancer screening, but also suitable for the follow-up after combined treatment of cervical cancer. HPV testing training has low requirements and simple operation, which is an effective means of cervical cancer screening, which can be regarded as an ideal choice for cervical cancer screening in economically backward areas of China. However, the detection rate of HPV test combined with cytology test is higher and more accurate. In order to reduce the missed diagnosis rate, joint screening should be the preferred screening program in the clinic [52]. HPV vaccine is the main method to prevent HPV infection. HPV vaccine is reported to significantly reduce the rate of HPV infection and cervical cancer, and even reduce the incidence of genital warts, the relative rate of premature and small gestational ages, or have other potential broader benefits [53-54]. In recent years, the rapid development of traditional Chinese medicine, its unique diagnosis and treatment methods have achieved good results in the treatment of some diseases, has been recognized by the majority of patients, Ding Zhanping, children use traditional Chinese medicine to treat HPV infection, the curative effect has been recognized [55], We can study it in depth in this aspect. Active prevention, regular screening, early detection and early treatment, has a great contribution to the health of the majority of women.

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