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Predicting the risk of high-grade precancerous cervical lesions based on high-risk HPV typing in Changsha China

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Abstract

Background Persistent infection with high-risk human papillomavirus (HPV) is a significant risk factor for cervical cancer. HPV typing and cytology are conducted in women of appropriate age to assess the risk of cervical lesions and to guide the need for further diagnostic procedures such as colposcopy, cervical biopsy, or treatment. This article explores methods to predict the risks of high-grade precancerous cervical lesions based on high-risk HPV typing.

Methods We conducted a retrospective analysis of HPV typing data from 158,565 women, including 19,707 who underwent ThinPrep cytologic testing (TCT), 7,539 who had colposcopy examinations, and 4,762 who had biopsies. We evaluated the sensitivity, specificity, and risk parameters of high-grade lesions associated with high-risk HPV types.

Results (1) The overall prevalence of HPV infection was 17.89%, with the most prevalent types being HPV52 (4.44%), HPV58 (2.10%), HPV53 (1.96%), HPV81 (1.85%), HPV42 (1.75%), and HPV16 (1.44%). (2) The sensitivity and specificity of detecting high-grade lesions in TCT, colposcopy, and biopsy, based on high-risk HPV typing, demonstrated a strong linear correlation with the infection rate of each type. (3) HPV16 was confirmed to have a higher risk of CIN2 + in biopsies using a self-defined risk parameter. (4) The top five HPV types with the highest PPVs and pathogenicity risks in biopsies were HPV45, HPV16, HPV58, HPV33, and HPV18.

Conclusion In Changsha, China, HPV52, HPV58, and HPV53 were the most prevalent and contributed significantly to high-grade lesions. After adjusting for infection rates, a self-defined risk parameter was proposed as a measure of the intrinsic risks of high-grade lesions associated with high-risk HPV types. Focused monitoring of prevalent high-risk HPV types such as HPV45, HPV16, HPV58, HPV33, and HPV18, which show the highest pathogenicity risks, is recommended in our region.

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Keywords HPV typing, TCT, Colposcopy, Biopsy, Cervical lesions, Pathogenicity risk

Introduction

Infection with high-risk human papillomavirus (HPV) is a major risk factor for cervical cancer [1, 2]. About 99.7% of cervical cancer cases are caused by persistent high-risk HPV infections [3], with HPV16/18 infections contributing to 70-75% of cervical cancer cases worldwide [4] and 40-60% of precancerous lesions [5]. Nevertheless, clinical epidemiologic studies have also reported that approximately 5% of cervical cancers are not associated with persistent HPV infection [6], and in particular, some cervical adenocarcinomas are not associated with HPV infection [7]. Cervical cancer could be prevented by screening for and treating cervical precancer, defined as high-grade squamous intraepithelial lesions of the cervix. High-grade lesions can progress to cervical cancer if not treated [8]. HPV DNA testing has become a primary screening tool for cervical cancer due to its advantages of higher sensitivity and cost-effectiveness compared to the Thinprep Cytologic Test (TCT) [9]. The combination of HPV typing and TCT has been reported to have the highest sensitivity and positive predictive value [10].

More than 200 distinct HPV types have been identified that persist within the human population [11–13], of which approximately 30 types can be transmitted through sexual contact [14]. HPV infections that can occur in human genitalia are categorized as high-risk, low-risk, and unspecified. Low-risk or non-oncogenic HPV types include types 6, 11, 42, 43, and 44, while high-risk or oncogenic HPV types include types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 [3]. Most HPV infections are transient and will be cleared within a couple of years, about 10–20% of infections persist latently and about 1–2% may lead to ultimately invasive cancer [15, 16].

In this study, women of the appropriate age in Changsha had been screened to identify high-grade lesions, treatment was typically recommended for women with histologically confirmed high-grade lesions (CIN2+).

Materials and methods

Ethical approval and inclusion criteria

All clinical observation cases were obtained from the free examination of women of the appropriate age from the Changsha Health and Livelihood Program in 2023. This study was approved by the Medical Ethics Review Committee of Changsha Maternal and Child Health Hospital (EC-20240308-12). All participants had signed the informed consent form before the examination. Inclusion criteria: the study population consisted of women aged 35–64 years residing in Changsha City, with a history of sexual intercourse, who voluntarily underwent gynecological examination. Those with any of the following conditions were excluded: (1) menstruation; (2) acute inflammation of the reproductive tract, sexual intercourse or vaginal douching, and vaginal medication within 48 h before sampling; (3) a history of cervical cancer; (4) other genital malignancies.

Sample collection and detection

Patients emptied their bladders, assumed the cystotomy position, underwent gynecological examination, and samples were collected in the cervical transformation zone using a disposable sterile cervical sampler. The samples were transported in a sealed cooler or foam box with ice over a period of no more than 5 days. HPV qualitative testing was performed for 23 HPV types (high-risk 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, and low-risk 6, 11, 42, 43, 81). According to the Chinese cervical cancer screening guidelines [17], colposcopy was performed directly for the positive cases of HPV16/18; and TCT was performed for the positive cases of the other high-risk types; and then colposcopy was performed if TCT found any intraepithelial lesions or malignant lesions.

Diagnosis criteria

TCT cytology: no intraepithelial lesions or malignant lesions (NILM), normal or inflammatory cells; atypical squamous epithelial cells of uncertain significance (ASC-US); atypical squamous epithelial cells, not excluding high-grade squamous intraepithelial lesions (ASC-H); low-grade squamous intraepithelial lesions (LSIL); high-grade squamous intraepithelial lesions (HSIL); squamous cell carcinoma (SCC); atypical glandular cell (AGC); atypical glandular cell, tending to neoplasia (AGC-FN); adenocarcinoma in situ (AIS) and adenocarcinoma (ADCA). HSIL + refers to HSIL plus other potential carcinoma.

Colposcopy: normal or benign, abnormal. Abnormal colposcopy including low-grade lesions, high-grade lesions, suspected invasive carcinoma, cancer, etc.

Cervical biopsy: normal group, low-grade lesions (CIN1), high-grade lesions (CIN2/CIN3), adenocarcinoma in situ, minimally invasive carcinoma, and invasive carcinoma. CIN2 + refers to high-grade lesions (CIN2/CIN3) plus other potential carcinoma.

Nucleic acid extraction and qPCR assay

Nucleic acids were extracted using the Nucleic Acid Extraction or Purification Kit (Magnetic Bead Method,

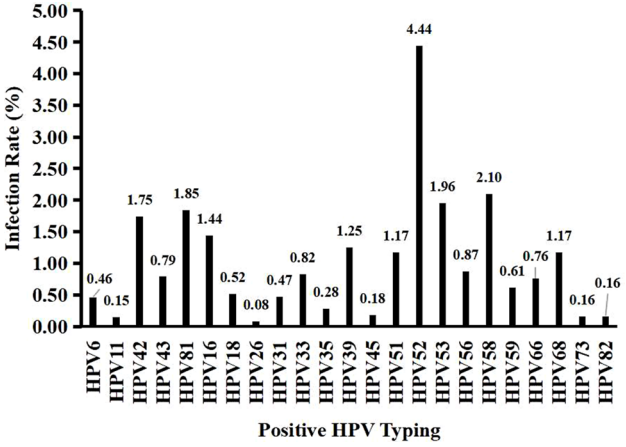

Fig. 1 Infection rates of the 23 HPV types in 158,565 cases

Sansure Biotech Inc). The Human Papilloma Virus (HPV) Nucleic Acid Typing Kit (PCR using the Fluorescent Probe Method, Sansure Biotech Inc) was used for qualitative testing of 23 HPV types. Fluorescent quantitative PCR amplification was performed using a SLAN-96P PCR amplifier (Shanghai Hongshi Medical Technology Co. Ltd.). The negative result should be consistent with no amplification curve (No Ct) or Ct value > 39. The positive cutoff value of Ct was determined to be 39.

Data analysis

The infection rate or positive rate is calculated as the number of positive cases divided by the number of all cases in the test. The infection rate (I_i) of HPV type i is calculated as the number of cases that test positive for type i (Ni) divided by the total number of cases (N): $I_i = N_i / N$.

The following parameters were calculated to assess the risk of HSIL+, high-grade lesions and CIN2+:

Sensitivity = No. of cases with lesions detected in the positive cases of each HPV type / No. of cases with lesions detected in all cases of the test.

Specificity = No. of cases with no lesion detected in the negative cases of each HPV type / No. of cases with no lesion detected in all cases of the test.

Odds Ratio (OR) = the ratio of lesion detected over non-lesion detected in the positive cases of each HPV type / the ratio of lesion detected over non-lesion detected in the negative cases of each HPV type.

Positive Predictive Value (PPV) = No. of cases with lesions detected in the positive cases of each HPV type / No. of cases of all positive cases of each HPV type.

Pathogenicity Risk = Sensitivity / Positive Rate = % of cases with lesions detected in the positive cases for each HPV type / % of cases with lesions detected in all cases of the test.

Chi-square test and Pearson correlation were performed using R script.

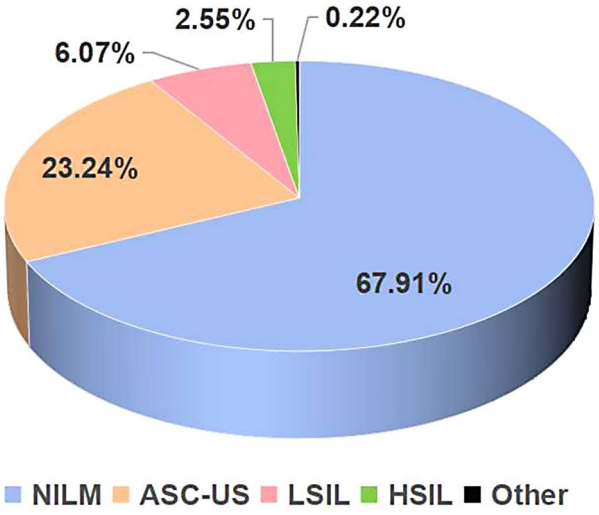

Fig. 2 TCT results of 19,707 cases positive for non-16/18 high-risk HPV typing

Results

HPV typing and prevalence

A total of 158,565 cases with Human Papillomavirus (HPV) typing results were analyzed, of which 28,367 tested positive for at least one of the 23 types. This resulted in an overall infection rate of 17.89%. The prevalence of infection for each of the 23 types is illustrated in Fig. 1. The most common types with infection rates of 1% or higher were HPV52 (4.439%), HPV58 (2.101%), HPV53 (1.958%), HPV81 (1.847%), HPV42 (1.746%), HPV16 (1.444%), HPV39 (1.251%), HPV68 (1.175%), and HPV51 (1.174%). Notably, the high-risk HPV18, which is a significant concern, ranked 15th with an infection rate of 0.52%.

Sensitivity and specificity of HSIL + detected by TCT in non-16/18 high-risk HPV positive cases

A total of 19,707 non-16/18 high-risk human papillomavirus (HPV) positive cases underwent TCT. As depicted in Fig. 2, among these cases, 67.9% were Negative for Intraepithelial Lesion or Malignancy (NILM), 23.2% were Atypical Squamous Cells of Undetermined Significance (ASC-US), 6.1% were Low-grade Squamous Intraepithelial Lesions (LSIL), 2.6% were High-grade Squamous Intraepithelial Lesions (HSIL), and 0.22% were others, including Atypical Glandular Cells (AGC; 27 cases), Squamous Cell Carcinoma (SCC; 9 cases), AGC-Favor Neoplastic (AGC-FN; 4 cases), Atypical Squamous Cells - cannot exclude High-grade SIL (ASC-H; 3 cases), and Adenosquamous Carcinoma (ADCA; 1 case). Colposcopy was recommended for a total of 6,326 (32.1%) cases with ASC-US and above. Additionally, 3,054 cases positive for HPV16/18 were directly referred for colposcopy.

The TCT results of 19,707 cases positive for 16 non-16/18 high-risk types are presented in Table 1. There were

Table 1 TCT results of 19,707 cases positive for 16 non-16/18 high-risk HPV types

Type	# Positive	Non-HSIL+	HSIL+	Positive Rate	Sensitivity	Specificity	Odds Ratio	PPV	x^2P value
HPV52	6611	6400	211	33.55%	38.57%	66.60%	1.25	3.19%	0.01
HPV58	3096	2913	183	15.71%	33.46%	84.80%	2.80	5.91%	0.00
HPV53	2904	2866	38	14.74%	6.95%	85.04%	0.42	1.31%	0.00
HPV39	1849	1826	23	9.38%	4.20%	90.47%	0.42	1.24%	0.00
HPV68	1740	1721	19	8.83%	3.47%	91.02%	0.36	1.09%	0.00
HPV51	1723	1681	42	8.74%	7.68%	91.23%	0.86	2.44%	0.41
HPV56	1273	1254	19	6.46%	3.47%	93.46%	0.51	1.49%	0.01
HPV33	1190	1124	66	6.04%	12.07%	94.13%	2.20	5.55%	0.00
HPV66	1114	1098	16	5.65%	2.93%	94.27%	0.50	1.44%	0.01
HPV59	893	875	18	4.53%	3.29%	95.43%	0.71	2.02%	0.19
HPV31	686	651	35	3.48%	6.40%	96.60%	1.94	5.10%	0.00
HPV35	392	382	10	1.99%	1.83%	98.01%	0.92	2.55%	0.91
HPV45	257	246	11	1.30%	2.01%	98.72%	1.58	4.28%	0.20
HPV82	229	218	11	1.16%	2.01%	98.86%	1.78	4.80%	0.09
HPV73	223	219	4	1.13%	0.73%	98.86%	0.64	1.79%	0.49
HPV26	108	102	6	0.55%	1.10%	99.47%	2.20	5.56%	0.14

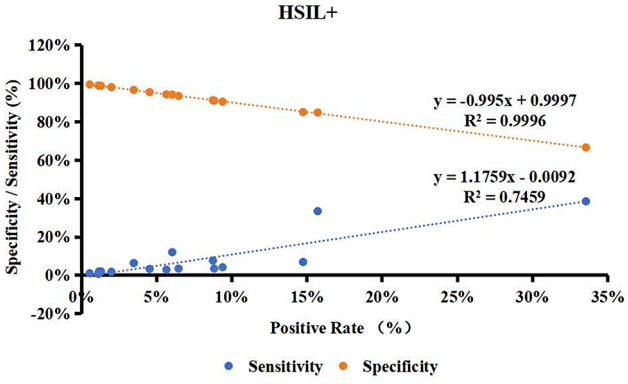

Fig. 3 The sensitivity and specificity of detecting HSIL + by TCT in relation to the prevalence of non-16/18 high-risk types

three types with sensitivity of detecting HSIL + exceeding 10%: HPV52 (38.57%), HPV58 (33.46%), and HPV33 (12.07%). There was a strong correlation between OR and PPV, with Pearson correlation $r = 0.9881$. 9 HPV types showed statistically significant x^2 p value < 0.05. Among them, HPV58, HPV33, HPV31 and HPV52 had the highest OR and PPV.

Figure 3 illustrates the sensitivity and specificity of detecting HSIL + in TCT relative to the prevalence of each non-16/18 high-risk type. The sensitivity demonstrated a strong positive linear correlation with the infection rate of each HPV type: $\text{Sensitivity}_i = 1.1759 * \text{Positive Rate}_i - 0.0092$, $R^2 = 0.75$, Pearson correlation $r = 0.86$ and p value = 1.63E-5. Conversely, the specificity exhibited a strong negative linear correlation with the infection rate of each type: $\text{Specificity}_i = -0.995 * \text{Positive Rate}_i + 0.9997$, $R^2 = 0.9996$, Pearson correlation $r = -0.9998$ and p value = 2.76E-25. This implies that the likelihood of detecting HSIL + in TCT from the positive high-risk HPV types is primarily associated with the prevalence of infection of that type.

Colposcopy findings in high-risk HPV positive cases

A total of 7539 cases underwent colposcopy, of which 4,249 (56.36%) had low-grade lesions (CIN 1), 2,479 (32.88%) had high-grade lesions and above (CIN2+), and another 811 (10.76%) had no lesions detected. There were 2,449 (32.5%) cases that did not have TCT testing, originating from HPV16/18 positives. There were 5,090 (67.5%) cases that had TCT testing done, originating from the positives of non-16/18 high-risk types.

The colposcopy results of 7,539 cases positive for 18 high-risk HPV types are shown in Table 2. There are four types with sensitivity detecting high-grade lesions above 10%: HPV52 (28.48%), HPV16 (21.10%), HPV58 (13.51%) and HPV53 (13.43%). HPV16 ranked 2nd in sensitivity but HPV18 ranked 8th. There was a weak correlation between OR and PPV, with Pearson correlation $r = 0.6676$. Only five HPV types showed statistically significant x^2 p value < 0.05. HPV68, HPV53 and HPV58 had the highest PPV. HPV16/18 ranked 4th and 5th in PPV but 5th and 3rd in OR.

Figure 4 displays the sensitivity and specificity in colposcopy detecting high-grade lesions in relation to the prevalence of each high-risk type. The sensitivity showed a strong positive linear correlation with the infection rate of each type. $\text{Sensitivity}_i = 0.9385 * \text{Positive Rate}_i + 0.0024$, $R^2 = 0.9831$, Pearson correlation $r = 0.9915$ and p value = 1.30E-15. The specificity showed a strong negative linear correlation with the infection rate of each type. $\text{Specificity}_i = -1.0313 * \text{Positive Rate}_i + 1.0014$, $R^2 = 0.9966$, Pearson correlation $r = -0.9983$ and p value = 4.01E-21. This suggests that the risk of detecting high grade lesions

Table 2 Colposcopy results of 7,539 cases positive for 18 high-risk HPV types

Type	# Positive	Non- High-grade	High-grade lesion	Positive Rate	Sensitivity	Specificity	Odds Ratio	PPV	x^2 *P* value
HPV52	2131	1425	706	28.27%	28.48%	71.84%	1.15	33.13%	0.795
HPV16	1839	1316	523	24.39%	21.10%	73.99%	0.56	28.44%	0.000
HPV58	1145	810	335	15.19%	13.51%	83.99%	0.69	29.26%	0.005
HPV53	910	577	333	12.07%	13.43%	88.60%	1.78	36.59%	0.012
HPV18	654	487	167	8.67%	6.74%	90.38%	0.92	25.54%	0.000
HPV51	557	380	177	7.39%	7.14%	92.49%	1.22	31.78%	0.596
HPV39	514	339	175	6.82%	7.06%	93.30%	1.29	34.05%	0.594
HPV68	480	301	179	6.37%	7.22%	94.05%	1.36	37.29%	0.038
HPV33	460	323	137	6.10%	5.53%	93.62%	0.85	29.78%	0.159
HPV56	455	309	146	6.04%	5.89%	93.89%	1.57	32.09%	0.748
HPV66	360	238	122	4.78%	4.92%	95.30%	1.30	33.89%	0.720
HPV59	284	181	103	3.77%	4.15%	96.42%	1.26	36.27%	0.241
HPV31	247	167	80	3.28%	3.23%	96.70%	0.84	32.39%	0.921
HPV35	132	84	48	1.75%	1.94%	98.34%	1.58	36.36%	0.444
HPV45	98	61	37	1.30%	1.49%	98.79%	0.67	37.76%	0.355
HPV82	86	59	27	1.14%	1.09%	98.83%	0.80	31.40%	0.857
HPV73	70	46	24	0.93%	0.97%	99.09%	1.31	34.29%	0.902
HPV26	46	27	19	0.61%	0.77%	99.63%	2.08	41.30%	0.288

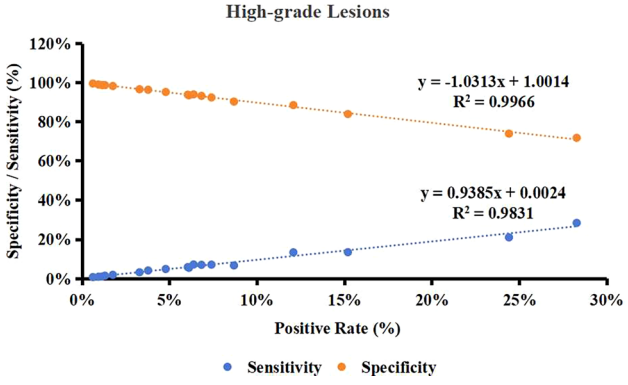

Fig. 4 The sensitivity and specificity of detecting high-grade lesions by colposcopy in relation to the prevalence of high-risk types

by colposcopy for each HPV type is mainly related to the infection rate of that type.

Biopsy results in high-risk HPV positive cases

A total of 4,762 cases underwent cervical biopsy, of which 2,194 (46.07%) were normal, 1569 (32.95%) were CIN1, 809 (16.99%) were CIN2+, including 744 CIN2/CIN3 and 65 Cancer, and 190 (3.99%) had other benign abnormalities such as inflammation.

Table 3 lists 4,762 cases of cervical biopsy results divided to Non-CIN2 + and CIN2 + for the positives of 18 high-risk HPV types. There are three types with sensitivity detecting CIN2 + above 20%: HPV52 (27.81%), HPV16 (38.81%), HPV58 (23.11%). There was a strong correlation between Odds Ratio and PPV with Pearson correlation $r = 0.9854$. Ten HPV types showed statistically significant x^2 p value < 0.05, and the top four with highest OR and PPV were HPV45,HPV16,HPV58, and HPV33. HPV18 ranked 5th in both OR and PPV.

Figure 5 displays the sensitivity and specificity in biopsy detecting CIN2 + in relation to the prevalence of each high-risk type. The sensitivity showed a strong positive correlation with the positive rate of each type. Sensitivity $_i$ = 1.2393*Positive Rate $_i$ – 0.0208, $R^2 = 0.8597$, Pearson correlation $r = 0.9272$ and p value = 3.14E-08. The specificity showed a strong negative correlation with the positive rate of each type. Specificity $_i$ = -0.951*Positive Rate $_i$ + 0.9957, $R^2 = 0.9885$, Pearson correlation r = -0.9942 and p value = 6.11E-17. This suggests that the risk of detecting CIN2 + in biopsy for each HPV type is mainly related to the infection rate of that type.

Variation in pathogenicity risk among high-risk HPV types

The self-defined pathogenicity risk demonstrated perfect correlation with PPV for HSIL + in TCT, high-grade lesions in colposcopy, and CIN2 + in biopsy, featuring a Pearson correlation coefficient (r) greater than 0.999998 and a p-value less than 2.65E-40. However, the pathogenicity risk for high-grade lesions observed in colposcopy correlated poorly with HSIL + in TCT and CIN2 + in biopsy, with Pearson correlation coefficients of -0.2303 and – 0.2112, respectively. In contrast, the pathogenicity risk for HSIL + in TCT showed a good correlation with CIN2 + in biopsy, with a Pearson correlation coefficient of 0.7545 and a p-value below 0.05.

Figure 6 depicts the pathogenicity risks of high-grade lesions for high-risk HPV types detected through TCT, colposcopy, and biopsy. The average risk of HSIL + for the 16 non-16/18 HPV types identified by TCT was 1.12, with a 95% confidence interval (CI) of 0.81–1.44. For

Table 3 Biopsy results of 4,762 cases positive for 18 high-risk HPV types

Type	# Positive	Non- CIN2+	CIN2+	Positive Rate	Sensitivity	Specificity	Odds Ratio	PPV	x^2 *P* value
HPV52	1344	1119	225	28.22%	27.81%	71.69%	0.98	16.74%	0.808
HPV16	1226	912	314	25.75%	38.81%	76.93%	2.12	25.61%	0.000
HPV58	775	588	187	16.27%	23.11%	85.13%	1.72	24.13%	0.000
HPV53	541	509	32	11.36%	3.96%	87.12%	0.28	5.91%	0.000
HPV18	445	400	45	9.34%	5.56%	89.88%	0.52	10.11%	0.000
HPV51	361	325	36	7.58%	4.45%	91.78%	0.52	9.97%	0.000
HPV39	318	293	25	6.68%	3.09%	92.59%	0.40	7.86%	0.000
HPV33	314	243	71	6.59%	8.78%	93.85%	1.47	22.61%	0.008
HPV56	295	272	23	6.19%	2.84%	93.12%	0.40	7.80%	0.000
HPV68	290	264	26	6.09%	3.21%	93.32%	0.46	8.97%	0.000
HPV66	218	199	19	4.58%	2.35%	94.97%	0.45	8.72%	0.001
HPV59	171	151	20	3.59%	2.47%	96.18%	0.64	11.70%	0.076
HPV31	158	122	36	3.32%	4.45%	96.91%	1.46	22.78%	0.062
HPV35	81	68	13	1.70%	1.61%	98.28%	0.93	16.05%	0.938
HPV82	56	45	11	1.18%	1.36%	98.86%	1.20	19.64%	0.724
HPV45	56	39	17	1.18%	2.10%	99.01%	2.15	30.36%	0.012
HPV73	40	33	7	0.84%	0.87%	99.17%	1.04	17.50%	1.000
HPV26	25	22	3	0.52%	0.37%	99.44%	0.67	12.00%	0.690

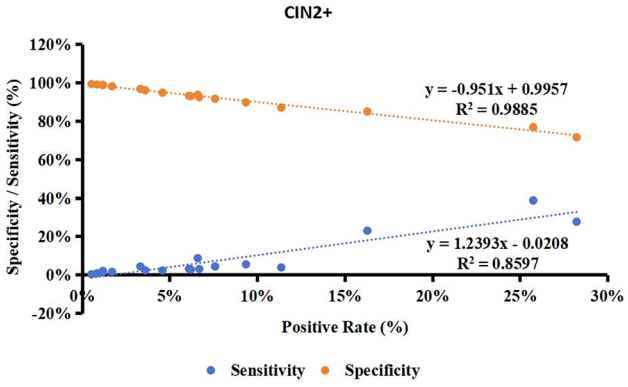

Fig. 5 The sensitivity and specificity of detecting CIN2 + by biopsy in relation to the prevalence of high-risk types

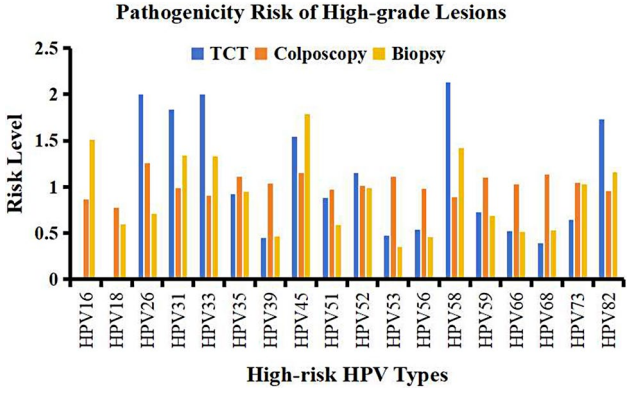

Fig. 6 Pathogenicity risk of high-grade lesions for high-risk HPV types detected by TCT, colposcopy and biopsy

high-grade lesions identified by colposcopy, the average risk was 1.02, with a 95% CI of 0.96–1.07. The average risk of CIN2 + for the 18 high-risk HPV types was 0.91, with a 95% CI of 0.70–1.12. For HPV types 16/18 detecting high-grade lesions in colposcopy, the risk levels were 0.86 and 0.78, respectively, both falling below the 95% CI. In biopsies, the risk levels for CIN2 + associated with HPV16/18 were 1.51 and 0.60, respectively, with HPV16 exceeding and HPV18 falling below the 95% CI.

Among the HPV types from biopsy results in Table 3 showing statistically significant results (p-value < 0.05), the top five HPV types with the highest PPV and pathogenicity risks were HPV45, HPV16, HPV58, HPV33, and HPV18.

Discussion

Comparing with the results of 17 high-risk and 10 low-risk typing in Shanghai, China, reported in 2022 [18], the total prevalence (17.89%) of HPV typing (18 high risk and 5 low risk) in Changsha was very close to that in Shanghai (18.81%). The top 5 high-risk HPV types in Changsha were the same as those in Shanghai but the ordering was slightly different. HPV16 (1.44%) in Changsha ranked 4th, while HPV16 (2.34%) in Shanghai ranked 2nd, and the infection rate of the top 3 types in Changsha was slightly higher than that in Shanghai. It appears that variations in the prevalence of HPV types might be attributed to geographic, temporal, vaccination and sampling differences. The decreasing rates of HPV16/18 infection over time might be due to the widespread adoption of HPV vaccination [19], unfortunately we didn't have the vaccination information recorded in our study.

The sensitivity of each HPV type to detect a lesion is equivalent to the proportion of cervical lesions detected in positive cases of that type out of all cases with lesions. Our study found that the top most prevalent HPV types - HPV52 (4.44%), HPV58 (2.10%) and HPV53 (1.96%) in the region tended to have higher sensitivity of detecting high-grade lesions in TCT, colposcopy and biopsy. We found that the sensitivity and specificity of detecting high-grade lesions showed strong linear correlation with the infection rate of that type in all cases of TCT, colposcopy and biopsy. This suggests that the sensitivity of predicting high-grade cervical lesions based on HPV typing is determined primarily by the prevalence of infection for each type.

To mitigate the effect of infection rates, we assessed several parameters including odds ratio (OR), positive predictive value (PPV), and self-defined pathogenicity risk. A strong correlation was observed between OR and PPV in TCT and biopsy, with a Pearson correlation coefficient (r) greater than 0.98. However, this correlation was weaker in colposcopy, with a Pearson correlation of 0.67. The self-defined pathogenicity risk displayed perfect correlation with PPV, achieving a Pearson correlation of 1.0 across all cases. Pathogenicity risk provides a more effective scale for comparison than PPV across TCT, colposcopy, and biopsy. Nonetheless, the pathogenicity risk in colposcopy did not align well with that in TCT or biopsy, showing a Pearson correlation $|r|$ of less than 0.23. In contrast, the pathogenicity risk in TCT demonstrated a good correlation with that in biopsy, with a Pearson correlation greater than 0.75.

Variability was noted in the risk of high-grade lesions using different parameters across TCT, colposcopy, and biopsy. Our study confirmed that HPV16 presents a higher risk of CIN2 + in biopsy, exceeding the 95% confidence interval of the 18 high-risk HPV types. The top five HPV types with the highest and statistically significant PPV and pathogenicity risks of CIN2 + in biopsy were HPV45, HPV16, HPV58, HPV33, and HPV18.

About 22.6% of HPV infections in this study consisted of co-infections of two or more types. Several large cervical cancer screening studies suggest that co-infection, especially high-risk HPV co-infection, may be more closely related to the risk of cytological abnormalities or high-grade squamous intraepithelial lesions (HSIL), but there are also screening studies that show that co-infection has no cumulative or synergistic effect on the risk of cervical lesions [20, 21]. It requires further analysis to compare the differences in cervical lesions caused by single infections and co-infections.

The early detection of high-grade cervical lesions provides several preventative options, including vaccination, surgery, and other therapeutic strategies. Numerous studies have been conducted to identify the primary determinants of recurrence risk. The persistence of HPV is strongly associated with a significantly increased risk of disease recurrence [22]. A multi-center retrospective study supports the adoption of HPV vaccination in patients treated for HPV-related diseases. Even in the absence of the uterine cervix, HPV vaccination could protect against the development of lower genital tract dysplasia [23]. In our retrospective study, individuals with a history of cervical cancer and other genital malignancies were excluded. It would be valuable to conduct prospective studies on the recurrence of cervical malignancies to explore any associations with specific high-risk HPV types and HPV vaccination.

Conclusion

Our study demonstrates diverse risks of high-grade cervical lesions associated with different HPV types, revealing a strong linear correlation between the sensitivity and specificity of detection methods and the infection rates. Specifically, the most prevalent types, HPV52, HPV58, and HPV53, accounted for a significant proportion of high-grade lesions in Changsha. After adjusting for infection rates, HPV58, HPV45, HPV33, HPV18, and HPV16 emerged as having the highest risks. Therefore, we recommend focused monitoring of these prevalent high-risk HPV types, which display the greatest pathogenicity risks in our region.

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Author contributions

YX：Project Management，Case Collection，Data Analysis and Writing of original draft, review & editing; RL: Methodology, Data Analysis and Writing of original draft, review & editing; SW: Data curation, Data Analysis and Software Development；YW: Data curation and Experiments; WM: Writing of original draft and review & editing; MC: Experiments and Supervision; XL: Data Statistics and Patient Follow-up; YC: Data Statistics; YW: Patient Follow-up and Information Entry; ZD: Assay Development and Methodology; LD: Project Design and Writing review & editing; ZM: Project Design and Writing review & editing; JH: Project Design and Writing review & editing; All authors reviewed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval

The studies involving human participants were reviewed and approved by Medical Ethics Committee of Changsha Hospital for Maternal & Child Health Care Affiliated to Hunan Normal University (EC-20240308-12). The patients/participants provided their written informed consent to participate in this study.

Competing interests

The authors declare no competing interests.

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