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Exploration of High-Risk HPV Genotyping Test as an Initial Screening Method for Cervical Cancer

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Abstract: *Objective:* The purpose of this study was to evaluate the clinical value of high-risk HPV typing as a primary screening method for cervical cancer. *Methods:* From July 2023 to June 2024, 871 women, aged 23 to 77 years old, with an average age of (42.5 ± 3.45) years old, were selected for initial screening of cervical cancer in the health examination center and gynecological clinic of the hospital. All patients underwent HPV-DNA typing and cervical fluid-based thin-layer cytology (TCT). Colposcopic cervical biopsy was performed in women with high-risk HPV single or multiple infection or with TCT ≥ ASC-US. The diagnostic efficacy of HPV-DNA typing, TCT and HPV + TCT combined detection was calculated using the pathological results of biopsy as the gold standard. *Results:* Compared with TCT alone, HPV-DNA typing was significantly more sensitive in the diagnosis of cervical lesions ($P < 0.05$), and the rate of missed diagnosis was significantly reduced ($P < 0.05$). At the same time, the efficacy of the HPV-DNA typing test is similar to that of HPV + TCT combined screening. In terms of misdiagnosis rate and specificity, there was no statistical difference among the three screening strategies ($P > 0.05$). *Conclusion:* HPV-DNA typing alone has the same effect as TCT + HPV combined screening for cervical cancer.

Keywords: Cervical cancer; Screening; HPV-DNA; TCT; Pathological examination

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1. Introduction

Cervical cancer, as one of the most common malignancies among women, poses a serious threat to the physical and mental health of a wide range of females. According to 2022 statistics, there were up to 150,700 new cases of cervical cancer in China, accounting for 22.7% of the total global incidence, and close to 56,000 deaths, representing 16% of the global mortality rate [1]. Given the severity of cervical cancer incidence, effective screening and treatment are particularly important. With in-depth research on the risk factors of cervical cancer, persistent infection with high-risk human papillomavirus has been identified as the definite cause of cervical cancer. On July 6, 2021, the World Health Organization (WHO) released the latest guidelines for the screening

and treatment of precancerous cervical lesions, which recommend HPV-DNA testing as the preferred method for cervical cancer screening. This study conducted an in-depth analysis of HPV, TCT, and colposcopy biopsy results from 871 women.

2. Materials and methods

2.1. General information

In this study, 871 women who voluntarily underwent initial cervical cancer screening at our hospital's health examination center and gynecology clinic from July 2023 to June 2024 were selected as the research subjects. Their ages ranged from 23 to 77 years old, with an average age of (42.5 ± 3.45) years old. All participants had a history of sexual activity and were currently not pregnant. To ensure the accuracy of the study, women with a history of cervical surgery or hysterectomy, as well as a history of pelvic radiotherapy and chemotherapy, were excluded. HPV-DNA typing and cervical liquid-based thin-layer cytology (TCT) were performed simultaneously or sequentially. Colposcopy biopsy and pathological examination were performed on those with positive HPV or TCT test results. Using pathological diagnosis as the gold standard, the diagnostic efficacy of HPV, TCT, and combined HPV + TCT detection was calculated separately. The optimal effects of the three screening methods were evaluated.

2.2. Methods

2.2.1. HPV genotyping and TCT cytology testing

Samples were collected during non-menstrual periods, ensuring no vaginal douching or medication history within 72 hours before sampling and no sexual activity within 24 hours. During sampling, the vulva was first lubricated with normal saline, the cervix was exposed through a vaginal speculum, and then the cervical mucus was wiped off with a cotton swab. The sampling order was to collect the TCT sample first, followed by the HPV sample. A specialized cervical sampling brush was placed at the external of the cervix and rotated clockwise for 3 to 5 weeks to fully collect cervical exfoliated cells, which were immediately placed in a specialized specimen tube for testing. HPV-DNA genotyping was performed using the PCR-based fluorescence probe method, which can simultaneously detect 18 high-risk HPV types (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82). If any one or more high-risk HPV subtypes tested positive, it was judged as HPV positive. The diagnostic criteria for TCT followed the new TBS grading evaluation standard recommended by the National Cancer Institute (NCI) in 2001 [1]. A TCT test result ≥ ASC-US (Atypical Squamous Cells of Undetermined Significance) was used as the positive criterion.

2.2.2. Colposcopy and cervical tissue biopsy for pathological examination

Multiple biopsies were performed on suspicious lesions of the cervix under colposcopy. For those without visible lesions, biopsies were taken at 3, 6, 9, and 12 o'clock positions. For type III transformation zones, cervical canal curettage was also performed. The biopsy sites were labeled, and the specimens were fixed with formaldehyde before sending for pathological examination. Pathological examination results ≥ CIN2+ (Cervical Intraepithelial Neoplasia grade 2 and above) were considered positive for cervical lesions.

2.3. Criteria

In this study, histopathological examination was used as the "gold standard" for diagnosis.

2.4. Statistical analysis

SPSS 26.0 statistics was used to process and analyze the data. Measurement data were expressed as mean ± standard deviation (SD), and count data were expressed as a percentage (%). The chi-square test was used to compare rates between groups. A statistically significant difference was considered when $P < 0.05$. Diagnostic efficiency was calculated based on the following formulas: sensitivity = true positive / (true positive + false negative), specificity = true negative / (true negative + false positive), misdiagnosis rate = false positive / (false positive + true negative), missed diagnosis rate = false negative / (false negative + true positive), negative predictive value = true negative / (true negative + false negative), and positive predictive value = true positive / (true positive + false positive).

3. Results

3.1. Pathological results using TCT as the primary screening indicator for cervical cancer screening

Using TCT as a screening strategy, 271 positive cases were screened among the 871 women participating in this study. Of these, 28 were judged as high-grade or higher lesions (i.e., true positives), while 243 were diagnosed as normal cervix or low-grade lesions (i.e., false positives). Of the 600 negative screening cases, 22 were false negatives (i.e., missed diagnosis cases), and 578 were true negatives. See **Table 1**.

Table 1. Pathological results using TCT as the primary screening indicator for cervical cancer screening

TCT test results	Pathological biopsy (Gold standard)	
	High-grade cervical and cervical cancer	Normal cervix and low-grade
Positive	28 (true positive)	243 (false positive)
Negative	22 (false negative)	578 (true negative)

3.2. Pathological results using HPV as the primary screening indicator for cervical cancer screening

Among the 871 women included in this study, using HPV as a screening strategy, 376 positive cases were identified. Pathological diagnosis revealed 64 cases of high-grade or higher lesions (i.e., true positives) and 312 cases diagnosed as normal cervix or low-grade lesions (i.e., false positives). Among the 495 negative screening cases, 7 were false negatives (i.e., missed diagnosis cases), and 488 were true negatives. See **Table 2**.

Table 2. Pathological results using HR + HPV as the primary screening indicator for cervical cancer screening

HR + HPV test results	Pathological biopsy (Gold standard)	
	High-grade cervical and cervical cancer	Normal cervix and low-grade
Positive	64 (true positive)	312 (false positive)
Negative	7 (false negative)	488 (true negative)

3.3. Analysis of pathological results using combined TCT + HPV screening as the primary screening strategy for cervical cancer screening

In this cervical cancer screening study involving 871 women, a total of 359 positive cases were identified using

combined TCT + HPV screening as the screening strategy. Pathological diagnosis revealed 67 cases of high-grade or higher lesions (i.e., true positives) and 292 cases diagnosed as normal cervix or low-grade lesions (i.e., false positives). Among the 512 negative screening cases, 6 were false negatives (i.e., missed diagnosis cases), and 506 were true negatives. See **Table 3**.

Table 3. Pathological results of HPV + TCT combined screening as the primary screening indicator for cervical cancer screening

HPV + TCT test results	Pathological biopsy (Gold standard)	
	High-grade cervical and cervical cancer	Normal cervix and low-grade
Positive	67 (true positive)	292 (false positive)
Negative	6 (false negative)	506 (true negative)

3.4. Screening efficacy of three screening strategies

To comprehensively and accurately compare the efficacy of TCT, HPV, and TCT + HPV screening strategies in the primary screening of cervical cancer, we calculated the diagnostic efficacy indicators for TCT, HPV, and TCT + HPV screening strategies based on established formulas (**Table 4**). When evaluating the screening efficacy of the three strategies, the results showed similar performance in terms of misdiagnosis rate and specificity, with no statistically significant difference ($P > 0.05$).

Table 4. Screening efficacy of three screening strategies

Primary screening indicator	*n*	Sensitivity (%)	Missed diagnosis rate (%)	Specificity (%)	Misdiagnosis rate (%)	Negative predictive value	Positive predictive value
TCT	871	56	44	70.4	29.60	96.33	10.33
HPV	871	90.14	9.85	61.0	39.00	98.58	17.02
TCT+HPV	871	91.78	8.22	63.41	36.59	98.83	18.66
χ^2-*value*		49.932	49.932	1.955	1.955		
P-value		< 0.05	< 0.05	> 0.05	> 0.05		

4. Discussion

Cervical cancer, as a preventable and treatable disease, has undergone intensive research on its pathogenesis, which has confirmed that persistent infection with high-risk human papillomavirus (HPV) is the main inducer of cervical lesions [2,3]. The invasion of this virus into cervical epithelial cells is a long process from quantitative to qualitative change, taking 8 to 10 years, providing us with a sufficient time window for early screening and intervention [4,5].

Liquid-based cytology (TCT) testing has been a traditional means of cervical cancer screening and has played an important role in the past 50 years. However, the limitations of its morphological detection, such as the high demand for pathological doctors' professional skills, have led to high rates of missed diagnosis and false positives, especially in primary medical institutions [6].

With the rapid development of molecular biology, cervical lesion screening has shifted from traditional cytological morphology examination to HPV-based molecular screening. Compared with cytological examination,

HPV detection technology exhibits higher screening efficiency [7,8]. Domestic and foreign studies have shown that HR-HPV detection has higher sensitivity for detecting cervical intraepithelial neoplasia grade 2 and more severe lesions (CIN2+) [9,10]. This study also confirms this point, with the sensitivity of HPV screening being similar to that of TCT + HPV combined screening and higher than that of TCT screening. In terms of specificity, although the specificity of HPV screening (61.0%) is slightly lower than that of TCT (70.4%) and combined screening (63.41%), the differences between the three are not statistically significant ($P > 0.05$). However, it is worth noting that the misdiagnosis rate (39.0%) and missed diagnosis rate (9.85%) of HPV screening are both maintained at relatively low levels, especially the missed diagnosis rate, which is significantly lower than that of TCT screening (44%). This is important for reducing missed detections and missed diagnoses of cervical cancer. Additionally, the negative predictive values of HPV screening and combined screening (98.58% and 98.83%, respectively) are higher than that of TCT screening (96.33%), indicating that these two screening strategies have higher accuracy in identifying truly disease-free individuals. Meanwhile, the positive predictive values of HPV screening and combined screening (17.02% and 18.66%, respectively) are also significantly higher than that of TCT screening (10.33%), which helps reduce unnecessary further examination and treatment.

5. Conclusion

In summary, the use of HPV-DNA detection as a primary screening tool for cervical cancer has high diagnostic value, with high sensitivity, low missed diagnosis rate, and high negative and positive predictive values. This screening strategy is not only feasible but also effective in reducing missed detections and missed diagnoses, as well as lowering the incidence and mortality of cervical cancer. Promoting HPV screening in primary hospitals can not only improve the early diagnosis rate of cervical cancer but also effectively protect women's health and safety. Therefore, HPV screening should be regarded as an important tool for cervical cancer screening.

Although this study has achieved certain results in exploring the effectiveness of TCT, HPV, and TCT + HPV screening strategies in primary cervical cancer screening, there are still some limitations. The sample size of this study is limited, with only 871 women included in the screening, which may affect the universality and representativeness of the results to some extent. A larger sample size would help to more accurately evaluate the effectiveness of different screening strategies and reduce the impact of random errors on the results.

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Disclosure statement

The authors declare no conflict of interest.

References

[1] Duan Y, Yin R, 2024, Progress in Immunotherapy for Cervical Cancer. Journal of Practical Obstetrics and Gynecology, 40(10): 769–773.

[2] Perkins RB, Wentzensen N, Guido RS, et al., 2023, Cervical Cancer Screening: A Review. JAMA, 330(6): 547–558.

[3] Bedell SL, Goldstein LS, Goldstein AR, et al., 2020, Cervical Cancer Screening: Past, Present, and Future. Sex Med Rev, 8(1): 28–37.

[4] Zhai J, Gu L, Fan Y, et al., 2024, Correlation Analysis Between High-Risk Human Papillomavirus Load and Cervical Precancerous Lesions. Journal of Hebei North University (Natural Science Edition), 40(10): 11–13 + 19.

[5] Kou Y, Zhang Y, Yao D, 2024, Relationship Between High-Risk Human Papillomavirus Infection and Clinical Characteristics, Immunohistochemical Indicators, and Prognosis of Cervical Cancer Patients. Oncology Progress, 22(1): 56–59.

[6] Zhong C, 2023, Clinical Diagnostic Value of Cervical Liquid-Based Cytology Combined With Cervical Tissue Biopsy in Patients With Cervical Cancer. Primary Medical Forum, 27(32): 73–75 + 108.

[7] Hazazi A, Khan FR, Albloui F, et al., 2024, Signaling Pathways in HPV-Induced Cervical Cancer: Exploring the Therapeutic Promise of RNA Modulation. Pathol Res Pract, 263: 155612.

[8] Zhou Y, Shao J, Huang Q, 2024, Effects of Lactobacillus Combined With Kushen Gel on Vaginal Microecology and Micro-Inflammatory Indicators in Female Patients With High-Risk HPV Infection of the Cervix. Liaoning Medical Journal, 38(6): 22–26.

[9] Dovnik A, Poljak M, 2023, The Role of Methylation of Host and/or Human Papillomavirus (HPV) DNA in Management of Cervical Intraepithelial Neoplasia Grade 2 (CIN2) Lesions. Int J Mol Sci, 24(7): 6479.

[10] Derbie A, Mekonnen D, Woldeamanuel Y, et al., 2020, HPV E6/E7 mRNA Test for the Detection of High-Grade Cervical Intraepithelial Neoplasia (CIN2+): A Systematic Review. Infect Agent Cancer, 15: 9.