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Clinical Effect of HPV-DNA Typing Detection Combined with TCT in Cervical Cancer Screening

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Abstract: *Objective*: To explore the importance of combined diagnosis (TCT+HPV-DNA) in cervical cancer screening for diagnosis and treatment. *Methods*: From March 2024 to December 2024, 35 cases were diagnosed as positive by the gold standard (colposcopy biopsy), and then screened by TCT and HPV-DNA typing respectively, and the different results were analyzed. *Results*: Compared with TCT+HPV-DNA typing, the coincidence rate, specificity and sensitivity of TCT and HPV-DNA typing were significantly lower ($P<0.05$). *Conclusion*: Combined diagnosis (i.e. TCT+HPV-DNA typing test) in cervical cancer screening can ensure the accuracy of the results and prompt patients to obtain targeted treatment plans at an early stage.

Keywords: Cervical cancer; Screening; TCT; Detection of HPV-DNA typing

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1. Introduction

Currently, women worldwide are suffering from the impact of cervical cancer. According to the World Health Organization, a large number of women are diagnosed with cervical cancer every year, and the disease is beginning to affect younger women globally. In China, cervical cancer, as a high-incidence malignant tumor, has a significant impact on women's health and quality of life. However, it is worth noting that cervical cancer is one of the few malignant tumors in recent years with a determined etiology that can be actively prevented and controlled through early screening. Therefore, to ensure effective control of cervical cancer mortality and incidence, it is of great significance to implement effective and scientific screening methods early. In recent years, TCT examination and HPV-DNA typing detection have become common methods for cervical cancer screening. TCT screening mainly focuses on cellular morphology, carefully observing cervical cell conditions with slide preparation techniques, detecting abnormal changes in a timely manner, and subsequently identifying early cervical cancer and precancerous lesions. However, it should be noted that there are some issues with the TCT screening method, including the lack of typical bacterial morphology or insufficient cell collection data, which may increase the risk of subsequent diagnostic errors. HPV-DNA typing detection focuses on the viral level, detecting the gene sequence of human papillomavirus, promptly determining the type of infection, and understanding the patient's risk of subacute infection or HPV infection [1]. However, this method can only

clarify the status of viral infection but cannot reflect the morphological changes of cervical cells affected by the virus, making it difficult to accurately determine the degree of lesions. In view of this, this study selected 62 patients with suspected cervical cancer to carry out research work, followed by different screening methods such as TCT, TCT + HPV-DNA typing detection, etc. The aim is to determine the best diagnostic method to ensure that patients' conditions are controlled at an early stage.

2. Materials and methods

2.1. General information

In this study, 62 patients suspected of having cervical cancer were randomly selected using a random number table for research from March 2024 to December 2024. The mean age was 38.42 ± 5.57 years old (range 29–68 years old), and the mean weight was 58.79 ± 4.47 kg (range 38–76 kg).

Inclusion criteria: (1) Normal organ function; (2) No contraindications to the diagnostic methods used in this study; (3) Signed informed consent; (4) History of sexual activity. Exclusion criteria: (1) Recent pelvic radiation or treatment for cervical disease; (2) Reproductive system infection or communication difficulties.

2.2. Methods

Patients were instructed to abstain from sexual activity and avoid using vaginal medications for 3 days before the examination. HPV-DNA genotyping: Patients were positioned in the lithotomy position to fully expose the cervix. The surface secretions were wiped clean with a sterile swab. A sampler was inserted into the external orifice and rotated clockwise for 5 turns, held for 10 seconds, then broken off, and the sample was preserved for timely examination. After centrifugation, 15 high-risk HPV types were detected using PCR-reverse dot blot hybridization. The samples were first subjected to PCR amplification, and the PCR products were then hybridized with specific probes on a membrane strip to analyze the final results. TCT: The patient's position was the same as for HPV-DNA genotyping. The cervix was exposed, and secretions were wiped away. A sampling brush was inserted to a depth of 1 cm and rotated clockwise for 5 turns. The sampler was placed in Thinprep cell preservation solution. After 10 oscillations, the sample was processed for the separation of inflammatory cells, blood secretions, mucus, and epithelial cells. A thin cell smear was prepared using a liquid-based thin-layer method and stained for microscopic examination. Colposcopy: The patient's position was the same as for HPV-DNA genotyping. The surface secretions of the cervix were wiped clean with a sterile swab. The color and shape of the cervix were observed under a low-power microscope, and blood vessels were examined through a filter. The cervix was treated with glacial acetic acid solution to observe the morphology and color of the blood vessels. Abnormal areas were sampled for examination.

2.3. Observation indicators

2.3.1. Analysis of diagnostic results using different diagnostic methods

Calculate the concordance rate, specificity, and sensitivity of patients undergoing different diagnostic methods. The concordance rate = number of correctly diagnosed cases / total number of cases; sensitivity (true positive rate) = number of true positives / (number of true positives + number of false negatives) × 100%; specificity = number of true negatives / (number of true negatives + number of false positives) × 100%. Here, true negatives mainly refer to cases where the disease is absent and the diagnosis is negative; true positives mainly refer to cases where the disease is actually present and the diagnosis is positive.

2.3.2. Analysis of differences in diagnostic efficacy among different diagnostic methods

Compare and statistically analyze the differences in concordance rate, specificity, and sensitivity among TCT testing, HPV-DNA genotyping, and TCT + HPV-DNA genotyping test results.

2.4. Statistical methods

Statistical analysis was performed using SPSS 24 software. Count data were expressed as percentages (%) and compared using the chi-square test. A P-value < 0.05 was considered statistically significant.

3. Results

3.1. Analysis of diagnostic results using different diagnostic methods

The diagnostic accuracy of TCT was 80.65% (50/62), specificity was 47.83% (11/23), and sensitivity was 38.46% (15/39). The diagnostic accuracy of HPV-DNA genotyping was 83.87% (52/62), specificity was 58.33% (14/24), and sensitivity was 44.74% (17/38). The diagnostic accuracy of combined TCT and HPV-DNA genotyping was 98.39% (61/62), specificity was 97.06% (33/34), and sensitivity was 92.86% (26/28). See **Table 1**.

Table 1. Analysis of diagnostic results of different diagnostic methods (%)

Gold standard	TCT		HPV-DNA Typing Test		TCT + HPV-DNA Typing Test		Total
	Positive	Negative	Positive	Negative	Positive	Negative	
Positive	11	24	14	21	33	2	35
Negative	12	15	10	17	1	26	27
Total	23	39	24	38	34	28	62

3.2. Analysis of diagnostic efficacy differences among different diagnostic methods

Compared with TCT+HPV-DNA typing detection, the coincidence rate, specificity, and sensitivity of TCT and HPV-DNA typing detection were significantly lower (P < 0.05). See **Table 2**.

Table 2. Analysis of diagnostic efficacy differences among different diagnostic methods (%)

Group	Number of Cases	Concordance Rate	Specificity	Sensitivity
TCT	62	80.65%*	47.83%*	38.46%*
HPV-DNA genotyping test	62	83.87%*	58.33%*	44.74%*
TCT + HPV-DNA genotyping test	62	98.39%	97.06%	92.86%

Note: Compared with TCT+HPV-DNA typing detection, *p < 0.05.

4. Discussion

4.1. Clinical manifestations, pathogenesis, and screening significance of cervical cancer

Cervical cancer, as the most common female reproductive system tumor after breast cancer, lacks typical manifestations in its early stages. Only a few patients may experience changes in the texture or increase in vaginal discharge, which is often overlooked. However, as the disease progresses, typical symptoms such as contact vaginal bleeding may appear, for example, spot bleeding after gynecological examination or bleeding signs after

sexual activity. Irregular vaginal bleeding may occur during non-menstrual periods. In the late stages, when surrounding tissues are invaded by cancer tissue, symptoms such as lower extremity swelling and pain, urgency and frequency of urination, and constipation may manifest. In severe cases, uremia and ureteral obstruction may develop, which not only reduces the patient's quality of life but also shortens their life expectancy. Persistent infection with high-risk human papillomavirus (HPV) is closely linked to the pathogenesis of cervical cancer. The E6 and E7 oncogenes of HPV integrate into the host cell genome, leading to complete inhibition of the tumor suppressor genes p53 and Rb, ultimately disrupting cell cycle regulation [3]. Abnormal differentiation and proliferation of cervical epithelial cells gradually evolve into precancerous lesions, and improper or untimely intervention can lead to cervical cancer. Additionally, factors such as multiple sexual partners, reduced immune function, and smoking can accelerate the progression of the disease. Therefore, the combined application of TCT and HPV-DNA typing detection in cervical cancer screening has important clinical value [2]. These two methods can complement each other, allowing for the understanding of the viral infection status and observation of changes in cell morphology, thereby enabling early prevention in the precancerous stage of cervical cancer.

4.2. Limitations of single screening techniques for cervical cancer and the clinical value of combined testing

Scholars have indicated that TCT (ThinPrep Cytologic Test) and HPV-DNA typing have become commonly used diagnostic techniques for cervical cancer. TCT focuses on the morphological analysis of cervical cells, but it may be ineffective in recognizing atypical cells, poor slide quality, or inadequate cell collection, leading to increased misdiagnosis. HPV-DNA typing can accurately identify the type of virus infection, but it cannot determine the morphological changes caused by virus-infected cervical cells, resulting in a high risk of overdiagnosis. If used singly, both methods have limitations, making it difficult for most patients with early-stage cervical cancer or precancerous lesions to detect timely manner and miss the best treatment opportunity. Therefore, the combined application of TCT and HPV-DNA typing in cervical cancer screening has important clinical value. These two methods can form a complementary relationship, allowing for the observation of cell morphological changes besides understanding the state of viral infection, enabling accurate assessment of the risk of cervical lesions and improving the detection rate of precancerous lesions and cervical cancer to a certain extent. This allows patients to receive effective treatment at the optimal time, reducing personal mortality and morbidity rates and ensuring women's health.

4.3. Clinical benefits and value of combined TCT and HPV-DNA genotyping in cervical cancer screening

With the use of cytological screening techniques, the screening rate for cervical cancer has improved to some extent. A series of operations, including slide preparation and TCT sampling, requires systematic processing of specimens according to standard requirements to avoid external factors affecting specimen quality. This helps to view the distribution of bacteria evenly and clearly, increasing bacterial identification and preventing cell contamination or loss, enabling the timely detection of abnormal cervical epithelial cells [4]. However, studies have shown that among adult women who have regular sexual activity, the positive rate of TCT is relatively low, and misdiagnosis is prone to occur, leading to limitations in clinical use [5]. The occurrence and development of cervical cancer and precancerous lesions are closely related to HPV infection, and clinical practice has incorporated HPV-DNA typing as a core screening method. The results of this study indicate that compared with TCT+HPV-DNA

typing, the coincidence rate, specificity, and sensitivity of TCT and HPV-DNA typing are significantly lower [6]. This suggests that TCT+HPV-DNA typing plays a crucial role in early cervical cancer screening, providing valuable information support for clinical disease differential diagnosis. Whether it is the HPV-DNA typing method or the TCT detection method, their sensitivity, specificity, and coincidence rate are not as good as the combined use of the two methods when used singly. The TCT examination method observes cell chromatin, size, and structure under a microscope to determine whether the patient has lesions [7]. However, during the actual operation, factors such as the pathologist's subjective interpretation ability, cell preservation conditions, and the standardization of cell collection can directly affect the final examination results. In other words, differences in physicians' interpretation criteria can increase missed diagnoses and misdiagnoses, especially when faced with atypical hyperplastic cells. If the cell collection volume is insufficient and it is difficult to obtain diseased cells, the final detection coincidence rate and sensitivity will decrease accordingly. HPV-DNA typing can accurately detect viral infections, but it cannot effectively determine the presence of subtypes or viruses, and the degree of cervical cell lesions caused by viral infections is also difficult to visually demonstrate [8].

In clinical practice, some HPV-positive patients remain in the process of transient viral infection without typical cervical lesions. If the diagnosis is made based on HPV test results alone, it may lead to overdiagnosis and significantly reduce specificity. Moreover, some patients experience excessively low viral loads, making HPV test results appear false-negative and ultimately affecting sensitivity. Due to the various issues that arise when these two examination methods are used singly, they cannot meet the high requirements of current precise cervical cancer screening. Based on this, to ensure that the above problems are effectively avoided, the implementation of combined detection methods is extremely important. This can effectively integrate information on cell morphological changes and viral infections, enabling clinicians to obtain more accurate and comprehensive evidence during disease diagnosis. It is helpful to improve the effectiveness of cervical cancer screening and precancerous lesion screening, providing many conveniences. In exploring the clinical value of combining HPV-DNA typing and TCT in cervical cancer screening, Xiong found that using colposcopy pathology results as the gold standard, the positive rate of the gold standard diagnosis was 51.43%, and the negative rate was 48.57% among the 70 selected patients undergoing cervical cancer screening [9]. The combined diagnosis of HPV-DNA typing + TCT achieved a specificity of 94.12%, an accuracy of 95.71%, a positive predictive value of 94.59%, and a negative predictive value of 96.97%. The sensitivity was as high as 97.22%. Compared with the single TCT examination method, which had a negative and positive predictive value of 73.68% and 75.00%, and an accuracy, specificity, and sensitivity of 74.29%, 70.59%, and 77.78%, respectively, and the single HPV-DNA typing method, which had a negative and positive predictive value of 75.00% and 73.53%, and an accuracy, specificity, and sensitivity of 74.29%, 73.53%, and 75.00%, respectively, the results of the HPV-DNA typing + TCT detection method were consistent with those of colposcopy pathology, effectively improving the detection rate of cervical cancer. These findings align with the results of this study, confirming the advantages of combining HPV-DNA typing and TCT in cervical cancer screening.

5. Conclusion

In summary, there is a close relationship between HPV infection and the occurrence of cervical cancer, and the core cause of cervical cancer lesions is persistent infection with high-risk HPV. Therefore, it is crucial to actively carry out HPV-DNA typing diagnosis in cervical cancer patients. However, although single HPV-DNA

typing can detect viral infection, it can only provide risk indications and cannot directly reflect the degree of lesions. Therefore, to compensate for the limitations of single diagnostic methods, clinicians should consider using two methods together, namely HPV-DNA typing + TCT. This approach can not only improve diagnostic specificity and sensitivity but also ensure the accuracy of the final diagnosis, making it worthy of clinical adoption. However, it is important to note that this study has limitations such as time constraints and sample size restrictions. To verify the accuracy of the results, future clinical studies should extend the study duration and expand the sample size to further confirm the reliability of the findings.

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Disclosure statement

The authors declare no conflict of interest.

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