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The clinical efficacy of HPV, TCT and colposcopy in cervical cancer screening

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ABSTRACT. *[Objective] To analyze the clinical efficacy of HPV, TCT combined with colposcopy in cervical cancer screening. [Methods] This study took 1,400 patients admitted to our hospital as the study object, and used the liquid-based thin layer cytology test, and human papilloma virus-DNA detection and colposcopy, taking the histopathological results of cervical biopsy as the diagnostic criteria, evaluate the effect of combined detection on the early diagnosis of cervical cancer. [Results] The results of this study showed that among 1400 patients, the liquid-based thin layer cytology test positive rate was 17.63%, and the lesion detection rate was 79.04%. The detection rate of human papilloma virus-DNA testing for squamous cell carcinoma is as high as 100%. The positive rate of detection was 50.86%, and the detection rate of lesions reached 85.62%. The detection rate of liquid-based thin layer cytology test and human papilloma virus-DNA combined with colposcopy for cervical lesions is 100%, which can effectively reduce the missed diagnosis rate, and the detection rate is significantly increased. [Conclusion] The clinical use of HPV-DNA, liquid-based cytology and colposcopy for early screening of cervical cancer is an efficient and feasible program, which can increase the detection rate of cervical precancerous lesions and reduce the missed diagnosis rate. It is great significance for cervical cancer screening.*

KEYWORDS: *Cervical cancer screening; HPV; TCT; Colposcopy*

1. Introduction

Invasive cervical cancer is one of the most common malignant tumors in gynecology, which seriously threatens the health and life of female patients. There are about 520,000 new cases and 275,000 deaths every year, ranking third in female malignant tumors, second only to breast and bowel cancer [1]. In recent years, the incidence of cervical cancer has increased significantly and has a trend of younger age. It is still the main disease that endangers women's health and life. general screening can find the precancerous lesions of cervical cancer ,we can have time give effective treatment to patients. Therefore, regular general screening can reduce the incidence of cervical cancer.

The aim of traditional cervical cancer screening is the early detection of cervical cancer, while the goal of modern screening is the early detection of high-grade

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cervical intraepithelial neoplasia and blocking treatment. The monitoring and research of cervical cancer has gradually developed from the population level, cell level, and subcellular level to the ultrastructure and molecular level. With the application of colposcopy, HPV testing, cervical smears, liquid-based cell smears and other testing methods, cervical cancer is easy to diagnose and treat early. Moreover, the improvement of treatment methods such as surgery, radiotherapy, and chemotherapy have greatly reduced the mortality rate of cervical cancer [2].

Cervical liquid-based cell (TCT) detection has been widely used in the diagnosis of cervical diseases. As a single detection method, it is easy to miss the test or to appear false negative or false positive. Human papillomavirus (HPV) typing has a high detection sensitivity . There are high-risk and low-risk types. The occurrence and development of cervical cancer are closely related to high-risk persistent infection. The biggest feature of the colposcopy is that it is intuitive, can identify the lesion site, and can take samples during biopsy, so it can increase the positive detection rate and reduce the incidence of missed detection. Therefore, this study performed TCT and HPV-DNA typing tests on 1,400 women who were screened for cervical precancerous lesions.For patients whose 1 or 2 tests are positive at the same time, cervical biopsy is performed under colposcopy, and the test results are analyzed to explore the clinical value of HPV, TCT combined with colposcopy in the screening of cervical precancerous lesions.

2 Materials and methods

2.1 General information

This study selected patients who received cervical cancer screening at the gynecological clinic of our hospital between May 2019 and May 2020 as the research object. Inclusion criteria: those who have agreed to be screened in gynecology, the age range is 25-64 years old. A history of sexual life, no history of malignant tumors, no other serious diseases, no history of hysterectomy, non-menstrual period, non-pregnant women (pregnant women 8 weeks after the end of pregnancy), No gynecological examinations, no vaginal douches within 3 days before sampling. Exclusion criteria: Those who have undergone colposcopy biopsy in this hospital or other hospitals; those who have been diagnosed with cervical cancer; and those who have been treated. A total of 1,400 patients were enrolled, and the average age of the patients was (35.74±10.43) years. 968 cases were married and 292 cases had a history of having sex with one another. The average age at first sexual intercourse was (21.54±4.3) years, the average number of pregnancies was (2.82±1.76), and the average number of births was (2.21±0.89).

2.2 Research methods

For all selected 1,400 cases, TCT and HPV-DNA testing were performed. For patients whose TCT and HPV-DNA tests are positive, and those who are clinically

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diagnosed with suspected cervical lesions, colposcopy positioning cervical biopsy and histopathological examination are performed.

TCT: The patient takes the lithotomy position and uses a vaginal dilator to expand the vagina. The medical staff wiped the cervical secretions with a sterile cotton ball, and used the special cervical brush in the liquid-based thin-layer cell kit to collect samples of cervical exfoliated cells by brushing the cervix 5 times. The brush for collecting the specimens was rinsed in a vial containing cell preservation solution, and sliced using the THINPREP-2000 automatic thin-layer cell preparation instrument imported from the United States. The diagnostic criteria refer to TBS grading standards, including: (1)No intraepithelial lesion (NILM);(2)Atypical squamous cell (ASC); (3)Low-grade squamous intraepithelial lesion (LSIL); (4)High-grade squamous intraepithelial lesion (HSIL)); (5) Squamous epithelial carcinoma (SCC). Among them, Article (2)～(5) indicate that the TCT result is positive.

HPV-DNA typing test: The patient takes the lithotomy position and uses a vaginal dilator to expand the vagina. The medical staff wiped the cervical secretions with sterile cotton balls, and used the special cervical sampling brush to evenly rotate the cervical orifice 5 times in the same direction to collect the cervical exfoliated cell samples, and immediately put them into the storage tube containing the preservation solution and cover it. Detection requires 5 steps of HPV-DNA extraction, PCR amplification, hybridization, membrane washing, and color development. Use real-time fluorescence *in vitro* amplification PCR and hybrid capture method to detect HPV-DNA typing. Reagents are HPV genotyping (22 HPV subtypes) detection kits provided by Sun Yat-sen University Daan Gene Co., Ltd., which can be divided into There are two types: low-risk type and high-risk type.Among them, 17 high-risk types including HPV16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 70 and 5 low-risk types including HPV6, 11 , 42, 43, 8[3].The results are judged based on the appearance of the spots. The position of the blue spots can be used to determine the HPV genotype. The occurrence of multiple spots is a multiple infection.

Colposcopy: The patient takes the lithotomy position and uses a vaginal dilator to expand the vagina. In order to fully expose the cervix and vagina, medical staff wipe the cervical secretions with sterile cotton balls, adjust the diopter of the colposcopy eyepiece and the focal length of the colposcopy to the best state, expose the transformation zone, epithelium and blood vessels and observe their changes. During the examination, in order to purify and swell the epithelium, the medical staff rubbed 3% acetic acid cotton balls on the cervix and vagina, and repeated the rubbing every 5 minutes to evenly spread the compound iodine solution on the surface of the cervix. Abnormal colposcopy images include white epithelium, leukoplakia, punctate structures, mosaics, abnormal blood vessels, and early cervical cancer.

Pathological biopsy results are divided into 3 categories: inflammatory changes, CIN, and invasive carcinoma. Among them, CIN is divided into grades Ⅰ, Ⅱ, and

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Ⅲ, including mild dysplasia (CIN Ⅰ), moderate dysplasia (CIN Ⅱ), and severe dysplasia (CIN Ⅲ).

2.3 Statistical analysis

The data of this study was analyzed by statistical software SPSS17.0. The difference between the two groups was compared using the $\chi 2$ test,The difference between multiple groups was compared by F test.$P<0.05$ indicates that the difference is statistically significant.

3. Results

3.1 Screening with liquid-based cytology alone

The production satisfaction rate of all samples was 100%. According to the results of TCT, there were no intraepithelial diseased cells or malignant cells in 1400 patients, that is, 1120 cases (80%) of normal and benign inflammatory reactions, 126 cases (9%) of ASC, 65 cases of LSIL (4.64%), and 45 cases of HSIL (3.21%), 11 cases of SCC (0.78%). The TCT test showed a positive rate of 17.64%.

3.2 HPV-DNA test results

In the study of HPV-DNA testing, it was found that among the 1,400 patients, 712 patients had one or more HPV infections, and the HPV-DNA positive rate reached 50.86%, of which the high-risk accounted for 52.94%.

3.3 Histopathological diagnosis and TCT, HPV test results

Histopathological results showed that there were 184 cases of lesions in CIN Ⅰ and above, including 32 cases of CIN Ⅰ, 76 cases of CIN Ⅱ, 48 cases of CIN Ⅲ, and 11 cases of SCC. The positive rate of CIN I combined with TCT and HPV was 40.63%, the positive rate of CIN II was 73.68%, the positive rate of CIN III was 66.67%, and the positive rate of SCC was 100.00% (5/5). See Table 1.

Table1. Histopathological diagnosis and TCT, HPV test results

Histopathology	Number	TCT(+) HPV(+)	TCT(+) HPV(-)	TCT(-) HPV(+)	TCT(-) HPV(+)
Normal and benign inflammation	486	16	26	391	53
CINI	32	13	11	8	0
CINII	76	56	9	11	0

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CINIII	48	32	8	8	0
SCC	11	11	0	0	0
sum	653	121	61	418	0

3.4 The detection of the three tests combination

The detection rate of TCT, HPV-DNA typing combined with colposcopy detection for invasive cancer was 100. 00%.The detection rates of CIN Ⅰ, CIN Ⅱ, and CINⅢ are higher than TCT and HPV-DNA typing tests.The differences were statistically significant (P<0.05).

Table 2 The detection of the three tests combination

Histopathology	Number	TCT、HPV	TCT、HPV、Colposcopy test	X2 value	P value
CINI	32	13	29	59.12	<0.05
CINII	76	56	71	42.73	<0.05
CINIII	48	32	46	32.16	<0.05
SCC	11	11	11	0.00	>0.05

4 Discussion

The occurrence of cervical cancer is a permanent and gradual complex process. It often takes about 10 years for patients to develop into cervical cancer from the appearance of cervical cancer. Early diagnosis, and timely treatment are not difficult to prevent the occurrence of cancer by strengthening the examination of cervical precancerous lesions [4]. Studies have pointed out that with early surgical treatment, the 5-year cure rate for cervical cancer patients can reach 80% to 90%.Therefore, it is significant for cervical cancer treatment by screening and timely treatment.

The current effective screening methods for cervical cancer mainly include cytology, HPV-DNA typing, colposcopy and so on. Traditional cytological examinations are generally performed with cervical scrapings, but the prepared specimens are not satisfactory. With the development of computer technology and physics technology, TCT has become a new technology for cervical cancer examination. It is easier to identify abnormal epithelial cells, especially for small number of cells and small squamous cells. The results of this study showed that the TCT test positive rate of 1400 patients was 17.63%, and the expected detection rate was 79.04%.

Research at this stage has found that HPV infection is one of the high-risk factors for cervical cancer. The specimens of patients with cervical cancer basically contain HPV. At the same time, the continuous infection of HPV high-risk virus is necessary for the occurrence of advanced cervical lesions [5]. Generally, when human body was infected by HPV , the human body manifests as a recessive

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infection, it is often clinically asymptomatic. However, HPV infection can increase the risk of cervical cancer in the infected person by 250 times, causing more serious consequences.The results of this study show that the detection rate of HPV testing for squamous cell carcinoma is as high as 100%. The results of this study found that the positive rate of HPV test results was 50.86%, and the detection rate of lesions is 85.62%.

This study found that the detection rate of TCT and HPV-DNA combined with colposcopy for cervical lesions reached 100%, which can effectively reduce the missed diagnosis rate, and the detection rate is significantly increased. In addition, the combined detection has higher sensitivity in the detection of CIN Ⅲ or squamous cell carcinoma, indicating that the screening of TCT or HPV combined with the colposcopy has the higher sensitivity of symptoms severity .The combined detection of the three is of great significance to the early screening of cervical cancer. In summary, early screening is essential to prevent and treat cervical cancer. The HPV-DNA, TCT and colposcopy combination for early screening of cervical cancer is an efficient and feasible solution in clinic. Combined detection can increase the detection rate of cervical precancerous lesions and reduce the missed diagnosis rate, so that patients can get correct early diagnosis and timely treatment. It plays an important role in judging the development trend of cervical lesions in the population, espcially indealing with precancerous lesions, blocking the course of the disease, and preventing the occurrence of cervical cancer.

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