

## RESEARCH ARTICLE

# Application of Human Papillomavirus in Screening for Cervical Cancer and Precancerous Lesions

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### Abstract

Cervical cancer is a commonly-encountered malignant tumor in women. Cervical screening is particularly important due to early symptoms being deficient in specificity. The main purpose of the study is to assess the application value of cervical thinprep cytologic test (TCT) and human papillomavirus (HPV) detection in screening for cervical cancer and precancerous lesions. In the study, cervical TCT and HPV detection were simultaneously performed on 12,500 patients selected in a gynecological clinic. Three hundred patients with positive results demonstrated by cervical TCT and/or HPV detection underwent cervical tissue biopsy under colposcopy, and pathological results were considered as the gold standard. The results revealed that 200 out of 12,500 patients were abnormal by TCT, in which 30 cases pertained to equivocal atypical squamous cells (ASCUS), 80 cases to low squamous intraepithelial lesion (LSIL), 70 cases to high squamous intraepithelial lesion (HSIL) and 20 cases to squamous cell carcinoma (SCC). With increasing pathological grade of cervical biopsy, however, TCT positive rates did not rise. Two hundred and eighty out of 12,500 patients were detected as positive for HPV infection, in which 50 cases were chronic cervicitis and squamous metaplasia, 70 cases cervical intraepithelial neoplasia (CIN) I, 60 cases CIN II, 70 cases CIN III and 30 cases invasive cervical carcinoma. Two hundred and thirty patients with high-risk HPV infection were detected. With increase in pathological grade, the positive rate of high-risk HPV also rose. The detection rates of HPV detection to CIN III and invasive cervical carcinoma as well as the total detection rate of lesions were significantly higher than that of TCT. Hence, HPV detection is a better method for screening of cervical cancer at present.

**Keywords:** Cervical thinprep cytology test - human papillomavirus - colposcopy - screening - cervical cancer

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### Introduction

Cervical cancer, the third commonly-encountered worldwide tumor in women, threatens the women health in the world (Croswell et al., 2012). In 1974, Zur first proposed that human papillomavirus (HPV) infection was closely associated with cervical neoplasms. A lot of studies on epidemiology and molecular biology also revealed that HPV infection is an indispensable factor to cause cervical cancer and precancerous lesions (Jabłonowska et al., 2012; Konno, 2013). In recent years, cervical cancer screening and its early diagnostic techniques have gradually become mature, hence, effective screening methods can timely find and treat precancerous lesions effectively to prevent the occurrence of cervical cancer. Application of thinprep cytology test (TCT) and HPV detection can conspicuously improve the detection rate of cervical lesions, which arouses wide concern from scholars (Galarowicz et al., 2012; Pruski et al., 2012). The aim of this study is to explore the clinical application value of TCT and HPV detection in cervical cancer and precancerous lesions.

### Materials and Methods

#### General data

12500 patients conducted screening of cervical lesions in gynecological clinic of our hospital from April, 2009 to March, 2011 were selected as research objects. They were 21-56 years old, and the mean age was (33.5±4.6) years old. Their chief complaints included abnormal leucorrhea, contact bleeding and pruritus of vulva, and gynecological examinations mainly showed cervical erosion, so cervical TCT and HPV detection were performed on all patients. Among 12500 patients, 300 ones demonstrated the positive by TCT and/or HPV detection were given cervical biopsy under colposcope, then pathological examination was conducted, and the pathological results were considered as the diagnostic standard.

#### Cervical TCT

The patients had no application of drugs in the vagina, washing, sexual life, vaginal and cervical performance 3 days before examination. A speculum was used to expose

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the cervix, and cotton swab to wipe out secretions in the uterine orifice. The specified brush was placed into the cervical canal and rotated, and then it was taken out and put into the specified container, finally, the liquid was sent to exam after the brush was washed 10 times. ThinPrep 2000 automatic pelleter was adopted to make smears, automatic cell meter to disperse and filtrate samples, and microscope to observe and diagnose.

*HPV detection*

The patients had no application of drugs in the vagina, washing, sexual life, vaginal and cervical performance 3 days before examination. If patients were complicated by vaginal infection, the treatment should be given first. A speculum was used to expose the cervix, and HPV sampler to take samples. After being put into the container with preserving fluid, the samples were sent to detect in laboratory. The major steps included DNA extraction, polymerase chain reaction (PCR) amplification and flow-through hybridization genotype. Finally, analysis software was used to asses the detection results.

*Cervical biopsy*

The patients had no sexual life, vaginal and cervical performance 24 h before examination, and vaginal infection was excluded. Cervical biopsy was performed through the colposcope in non-menstrual period. According to the allotypic degree and epithelial involvement range, cervical intraepithelial neoplasia (CIN) was classified into: CIN I, mild atypical hyperplasia and cellular atypism; CIN II, moderate atypical hyperplasia and distinct cellular atypism; CIN III, severe atypical hyperplasia and significant cellular atypism.

*Statistical analysis*

SPSS13.0 statistical analysis software was applied to descriptively analyze the data distribution, enumeration data to calculate the constituent ratio/rate and measurement data to perform a significant test with  $\chi^2$ .

**Results**

*Cervical biopsy results under the colposcope*

Among 12500 patients, 300 ones demonstrated the positive by TCT and/or HPV detection were given cervical biopsy under colposcope, then pathological examination was conducted, and pathological results were considered as the diagnostic standard. In the study, the pathological results of 300 patients were as follows: chronic cervicitis and squamous metaplasia 50 cases, CIN I 90cases, CIN II 60 cases, CIN III 70 cases and invasive cervical carcinoma 30 cases.

*TCT results*

Two hundred out of 12500 patients were abnormal by TCT, in which 30 cases pertained to equivocal atypical squamous cells (ASCUS), 80 cases to low grade squamous intraepithelial lesion (LSIL), 70 cases to high grade squamous intraepithelial lesion (HSIL) and 20 cases to squamous cell carcinoma (SCC). With the pathological grade of cervical biopsy increasing, TCT positive rate in

**Table 1. Cervical Biopsy Results of Patients with Abnormal TCT [n(%)]**

Classification	ASCUS	LSIL	HSIL	SCC	Total
Chronic cervicitis	20(50.0)	10(25.0)	10(25.0)	0(0.0)	40
CIN I	40(66.7)	10(16.7)	10(16.7)	0(0.0)	60
CIN II	40(66.7)	10(16.7)	10(16.7)	0(0.0)	60
CIN III	20(66.7)	10(33.3)	0(0.0)	0(0.0)	30
Invasive cervical carcinoma	0(0.0)	0(0.0)	0(0.0)	10(100.0)	10
Total	120(60.0)	40(20.0)	30(15.0)	10(5.0)	200

**Table 2. Comparison of HPV Positive Classification and Cervical Biopsy [n (%)]**

Classification	High-risk HPV	Low-risk HPV	Total
Chronic cervicitis	40(80.0)	10(20.0)	50
CIN I	50(71.4)	20(28.6)	70
CIN II	50(83.3)	10(16.7)	60
CIN III	60(85.7)	10(14.3)	70
Invasive cervical carcinoma	30(100.0)	0(0)	30
Total	230(82.1)	50(17.9)	280

**Table 3. Comparison of Two Detection Methods in Detection Rates of Cervical Lesions [n(%)]**

Classification	Pathological examination	HPV examination	TCT
CIN I	90	70(77.8)	60(66.7)
CIN II	60	60(100.0)	60(100.0)
CIN III	70	70(100.0*)	30(42.9)
Invasive cervical carcinoma	30	30(100.0*)	10(33.3)
Total	250	230(92.0*)	160(64.0)

Compared with TCT, \* $p < 0.05$

200 patients with abnormal TCT was not on the rise (Table 1).

*HPV detection results*

Two hundred and eighty out of 12500 patients were detected positive HPV infection, accounting for 2.24% of the total. The patients with positive HPV included chronic cervicitis and squamous metaplasia 50 cases, CIN I 70 cases, CIN II 60 cases, CIN III 70 cases and invasive cervical carcinoma 30 cases. High-risk HPV infection was found in 230 out of 280 patients with HPV infection. With the pathological grade increasing, high-risk HPV positive rate was on the rise (Table 2).

*Comparison of TCT and HPV detection results*

With pathological diagnostic results of cervical biopsy under colposcope as the gold standard, the detection conditions of cervical lesions by TCT and HPV detection were compared. The detection rates of HPV detection to CIN III and invasive cervical carcinoma as well as the total detection rate of lesions were conspicuously higher than that by TCT, and statistical significance was presented ( $p < 0.05$ ) (Table 3).

**Discussion**

Cervical cancer is a commonly-encountered malignant tumor in women. In our country, its morbidity still ranks

the first in gynecological malignant tumors (Li et al., 2011). The surveys demonstrated that the increase of women with cervical cancer less than 35 years old is particularly significant (Jach et al., 2012; Rai et al., 2013). The possible causes that result in cervical cancer to tend to occur in the young (Berois N et al., 2013; McCann et al., 2013) include remarkable increase of HPV infection rate, especially the high-risk HPV 16 and 18 infection closely related to cervical cancer, unhealthy sexual behavior and unmaturing age on the first sexual intercourse (Zhao et al., 2012). Cervical cancer is an extremely-seen complication after virus infection. According to current reports, its etiology is mainly associated with HPV infection. The risk factors related to HPV infection involve in history of smoking, multiparity, application of contraceptive, unmaturing age at the time of sexual intercourse, multiple sex partners, history of sexually transmitted disease and long-term low immunity (Zeng et al., 2012). The occurrence and development of cervical cancer gradually evolved from cervical precancerous lesions usually need a long time. The time from precancerous lesions to invasive cervical carcinoma is usually about 10-20 years (Li et al., 2013). CIN is a lesion occurring before cancer. Its appearance can be normal, but cytological or histological examination demonstrates the changes of abnormal proliferation. The probabilities of CIN at different grades into cancer are respectively 15%, 30% and 45%, and increase in a step-wise way (Bolgova et al., 2012; Corcoran et al., 2012; Piura and Piura, 2012).

In an extremely early stage, the patients with cervical cancer may not have symptoms, or has watery vaginal secretions and bleeding or intermittent drip bleeding after sexual intercourse, whereas those with advanced cervical cancer may have foul vaginal discharges, abnormal vaginal bleeding or pelvic pain. The early symptoms of cervical cancer are frequently ignored by patients due to lack of specificity, hence, conducting a cervical screening to find abnormal cells is particularly important (Canadian Task Force on Preventive Health Care et al., 2013; Dollin 2013; Ohta et al., 2013).

TCT, short for thinprep cytology test, is the most advanced cytological examination technique for cervical cancer in the world nowadays, and its detection rate to cervical cancer cells is near to 100% (Xue et al., 2011). Application of TCT which is a significant progress in the process of collecting cytological samples and preparing slides is certified by American FDA and recommended to replace the traditional cervical smear by College of American Pathologists. The detection rate of TCT cervical anti-cancer cytological examination to cervical cancer cells comes up to 100%, meanwhile, a part of precancerous lesions and microbial infection like moulds, trichomonas, viruses and chlamydias are also found (Ding et al., 2008). Thereby, TCT is the most advanced technique in screening of cervical cancer in women. Cervical TCT greatly enhances the cytological smear quality, consequently improving detection rates of intraepithelial lesions LSIL and HSIL and achieving more opportunities to discover early signs of lesions. In the study, 200 out of 12500 patients were detected abnormal by TCT, including

ASCUS 30 cases, LSIL 80 cases, HSIL 70 cases and SCC 20 cases. With the pathological grade of cervical biopsy increasing, TCT positive rate in 200 patients with abnormal TCT was not increased.

HPV infection has universally acknowledged as the major cause of cervical cancer and its precancerous lesion (Gerli et al., 2012; Giralaldi and De, 2012). HPV is a small double stranded DNA virus. At present, over 200 subtypes have been discovered and identified. According to HPV cancer-inducing risk, HPV infection in the genital tract and anus is classified into low-risk and high-risk types. HPV infection rate in people is related to the incidence of cervical cancer. In the countries with high incidence of cervical cancer, chronic HPV infection rate is 10%-20%, whereas in those with low incidence, its infection rate is only about 5%-10% (Singhal et al., 2013). HPV detection is an effective way to screen cervical cancer at present. Its higher sensitivity to CIN screening may become a major tool to screen cervical cancer in women over 30 years old. HPV virus can not be cultivated in vitro, and the immunoreactions easy to detect can also not be induced in vivo (Salehi et al., 2012), so its diagnosis and classification are not be detected with serological test. In recent years, a lot of literatures revealed that persistent HPV infection is a high-risk factor of cervical cancer, especially high-risk HPV infection which is one of the causes that result in the high-grade lesion of cervical cancer and CIN. Due to screening, HPV detection can effectively reduce the progression of cervical cancer, but it is necessary to know simple positive HPV is not represented occurrence of cervical cancer, and HPV infection is a requirement for it (Balbi et al., 2012). In the study, 280 out of 12500 patients were detected positive HPV infection, accounting for 2.24% of the total. The patients with positive HPV included chronic cervicitis and squamous metaplasia 50 cases, CIN I 70 cases, CIN II 60 cases, CIN III 70 cases and invasive cervical carcinoma 30 cases. High-risk HPV infection was found in 230 out of 280 patients with HPV infection. With the pathological grade increasing, high-risk HPV positive rate was on the rise. In addition, with pathological diagnostic results of cervical biopsy under colposcope as the gold standard, the detection conditions of cervical lesions by TCT and HPV detection were compared. The results demonstrated that the detection rates of HPV detection to CIN III and invasive cervical carcinoma as well as the total detection rate of lesions were conspicuously higher than that by TCT.

To sum up, cervical cancer and precancerous lesions are intimately associated with HPV infection. At present, the prevention of cervical cancer in our country basically depends on screening. The current frequently-used methods include TCT, HPV detection and biopsy under colposcope. HPV detection combined with cervical TCT greatly increases sensitivity, and there are almost no missed diagnosis cases, hence, it can be considered as a diagnostic method in CIN screening to be conducive to confirming the therapeutic regimen and follow-up plan. However, it is still an extremely important problem regarding the diagnosis, treatment and standardization of cervical cancer and precancerous lesions.

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