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Application of HPV-16 in Liquid-Based thin Layer Cytology of Host Genetic Lesions Based on AI Diagnostic Technology Presentation of Liquid

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Abstract: ***Nowadays, with the continuous improvement of people's health awareness and the increasing incidence of cancer year by year, the screening work of various clinical diseases, especially cancer, is also widely promoted. Cervical lesion screening is a common type. Cervical lesion screening is used to judge whether women have cervical lesions and increase attention to cervical lesions[1]. Proper prevention, diagnosis and treatment play an important role in ensuring women's health and life safety, and have been widely promoted in many places in our country. At the same time, in the screening of cervical lesions, how to adopt a more efficient and accurate diagnosis is very important to improve the screening effect of cervical lesions. With the rapid development of science and technology, AI and other advanced technologies have been gradually introduced in clinical disease diagnosis, especially in the liquid-based thin-layer cytology examination[2]. To further analyze the application effect of liquid based thin layer cytology AI diagnostic technology in the pathological diagnosis of cervical lesions. In this paper, we investigate the occurrence of HPV-16 integrated human host genome in cervical cancer and precancerous lesions and its application in cervical cancer screening. 50 cases of cervical cancer, 127 cases of LSIL, 83 cases of HSIL were collected, in addition, 22 cases of normal cervical epithelial tissues extracted by total hysterectomy were collected. The integration status of HPV-16 infection was detected by overlapping PCR.***

Keywords: Liquid-Based thin Layer Cytology; AI Diagnostic Technology; Cervical Lesions; Diagnosis.

1. INTRODUCTION

Nowadays, with the continuous improvement of people's health awareness and the increasing incidence of cancer year by year, the screening work of various clinical diseases, especially cancer, is also widely promoted. Cervical lesion screening is a common type. Cervical lesion screening is used to judge whether women have cervical lesions and increase their attention to cervical lesions, so as to do a good job in prevention, diagnosis and treatment. It has played a vital role in ensuring women's health and life safety[3-5]. At present, extensive promotion has been carried out in many places in China. At the same time, in the screening of cervical lesions, how to adopt a more efficient and accurate diagnosis is crucial to improve the screening effect of cervical lesions. With the rapid development of science and technology, AI and other advanced technologies have been gradually introduced in clinical disease diagnosis, especially in the liquid-based thin-layer cytology examination. Studies have shown that the incidence of cervical cancer is lower in those infected with HPV, but there is high-risk HPV infection, and there is integration between HPV virus and host genes, and the incidence of cervical cancer is significantly increased. A number of studies have shown that HPV virus can integrate with host genes at different DNA open reading frame positions. Studies have confirmed that the common deletion site of the integration of host genes of high-risk HPV is in the hinge region of E2 gene. There are many types of high-risk HPV viruses, such as HPV-16, HPV-18, HPV-30, etc., among which HPV-16 is the most common virus.

2. RELATED WORK

Cervical cancer ranks second only to breast cancer in the incidence of female malignant tumors. The key to reduce the incidence and mortality of cervical cancer is early prevention, early detection and early treatment for the diagnosis of cervical precancerous lesions and cervical cancer patients mostly according to the degree of lesions

and the specific situation of patients[6]. CIN is usually treated with LEEP, physical therapy, hysterectomy and cold-knife conectomy, etc. After early detection of cervical cancer, timely treatment usually has a good prognosis and a high cure rate. The occurrence of cervical cancer is a gradual process, and it takes about 7-8 years or more to progress from CIN to cervical cancer[7-8]. At present, the main methods of clinical screening cervical cancer are macroscopic examination, colposcopy and cytology detection, but the above examination methods have some errors. Experts propose that high-risk HPV gene detection can be used for cervical cancer screening, diagnosis and treatment. Compared with conventional cervical cancer screening methods, high-risk HPV gene monitoring can not only detect precancerous lesions earlier, but also reduce the high-risk groups of HPV and improve the detection probability of precancerous lesions for effective prevention of cervical cancer[9-11]. Studies have shown that HPV persistent infection is the main factor for cervical cancer, and high-risk HPV is closely related to its occurrence." At present, with the continuous research on HPV subtype infection and cervical cancer and precancerous lesions, it is shown that different subtypes of HPV have different disease-causing abilities, and high-risk HPV infection can directly take the lives of patients." Therefore, in 2007, the relevant research society proposed to use HPV typing as one of the early screening methods for cervical cancer. In 2012, the Cervical Cancer Society pointed out that if a patient is infected with HPV-16.HPV-18, even if the cytological test is negative, further colposcopy is required [12]. Previous investigations have shown that cervical cancer is an infectious disease, which is the main risk factor for cervical cancer and CIN. Prevention of HPV infection Monitoring of HPV infection targets is the key point to prevent intraepithelial neoplasia from rising to precancerous lesions and cervical cancer.

According to the latest global Cancer data for 2020 released by the World Health Organization International Agency for Research on Cancer (IARC), The number of new cases and deaths of female cervical cancer in the world were 604,100 and 341,800 respectively, making it the fourth largest malignant tumor threatening the health and life safety of women worldwide. In China, the number of new cases of cervical cancer in 2020 is 109,700, which is the sixth most common malignant tumor in women." In recent years, the incidence of cervical cancer is increasing year by year and the incidence is younger. Without timely treatment and intervention, it will pose a serious threat to the life safety of patients. A large number of data show that more than 90% of cervical cancer patients are accompanied by high-risk human papilloma virus (HPV) infection. The relationship between high-risk HPV infection and the occurrence and development of cervical cancer was studied as early as the 1970s, and it was proposed that the continuous infection of high-risk HPV is the main risk factor and cause of cervical cancer. Therefore, to carry out standardized HPV detection and cervical cytological screening for women of childbearing age can screen out those with high risk of cervical cancer as early as possible, which is of great significance for early diagnosis and treatment of cervical cancer. Early diagnosis and early treatment can significantly improve the cure rate and long-term quality of life of patients with cervical cancer." In view of the relationship between HPV infection and cervical cancer, early HPV vaccination can effectively prevent high-risk HPV infection and thus prevent the occurrence of cervical cancer. This paper will review the current commonly used clinical cervical cancer screening methods and the clinical application and research progress of HPV vaccine, so as to improve the population's awareness of cervical cancer screening and prevention. Prevent and reduce the incidence of cervical cancer, protect women's life and health.

3. METHODOLOGY

(1) Preparation before collection: Patients with cervical TCT and HR-HPV samples were required to have no sexual activity, no vaginal medication and gynecological examination one day before sampling, and were in a non-menstrual period at the time of sampling. (2) Collection method: The shed cells in the cervical transitional zone and cervical canal were collected, and the brush head was taken and placed in a special cell preservation liquid bottle.

3.1 TCT Detection

The specimens were processed using the new Broker-Broker-ThinPREP2000 specimen processing system (CDI) and the liquid-based cell preparator (Beijing New Jiulu Technology Company). The results were interpreted according to the universal cervical liquid-based thin layer cytology diagnostic standard, namely the Bethesda system.

The application value of TCT cytology detection in screening of cervical precancerous lesions showed that the accuracy, sensitivity and specificity of TCT cytology results were higher than that of Pap smear, fully indicating that TCT cytology has a high value in the application of cervical lesions, which can detect cervical lesions as early as possible and reduce the risk of cervical cancer. The analysis of the reasons shows that the traditional Pap smear

is easily affected by factors such as mucus, blood and inflammation, resulting in fuzzy samples and easy to appear test errors. The special cell brush used in the TCT cytology detector can better obtain the cells in the cervical tube, avoid interference by mucus and other vaginal secretions, and collect the sample cells into a special preservation solution, which retains the natural cell shape to a great extent and maintains its mechanical uniform dispersion.

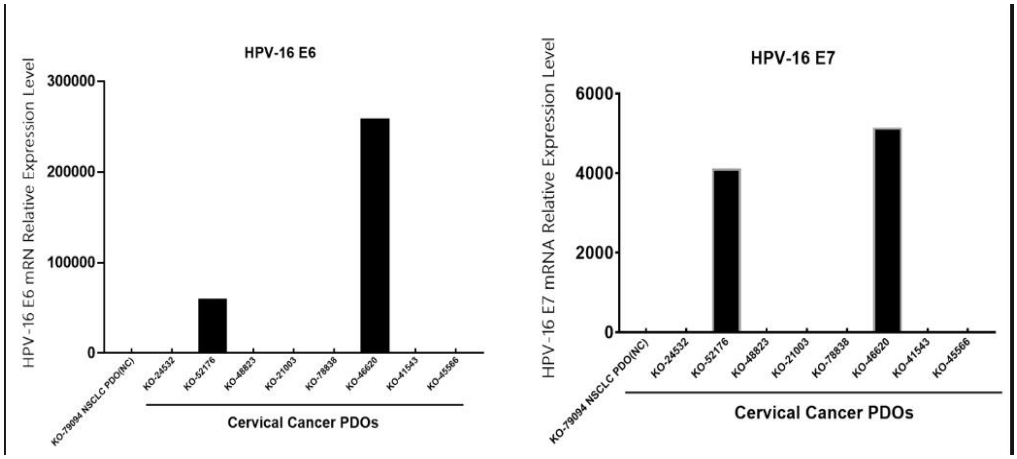

Figure 1: HPV-16 TCT detection model

3.2 HPV-DNA Testing

As early as the 1970s, German pathologist Haraldzur Hausen found that HPV infection was closely related to the incidence of cervical cancer through years of observation and research, and published his book Human Pathogenic Papilloma-viruses in 2006. Professor Hausen was also awarded the 2008 Nobel Prize in Physiology/Medicine for this important discovery. Since then, a large number of studies have confirmed that continuous infection of high-risk HPV is the main pathogenic factor of cervical cancer. At present, more than 200 HPV genotypes have been clinically detected, and HPV is divided into high-risk and low-risk types according to the relationship between HPV infection and the risk of cervical cancer. The study found that 99.7% of cervical cancer specimens had high-risk HPV infection, of which about 70% were associated with HPV types 16 and 18, and 18 other high-risk HPV infections were directly related to the occurrence of cervical cancer. HPV16, 18, 31, 33, 35, 39, 45, 51 in exuded cervical cells were detected with HR-HPV typing nucleic acid assay kit (Shanghai Liemai Bioengineering Co., LTD.) by fluorescent polymerase chain reaction. The specific DNA nucleic acid fragments of 15 types, including 52, 56, 58, 59, 68, 66, 82, were tested qualitatively. The amount of DNA copy of HR-HPV virus was quantitatively calculated according to CT value of HPV-positive specimen.

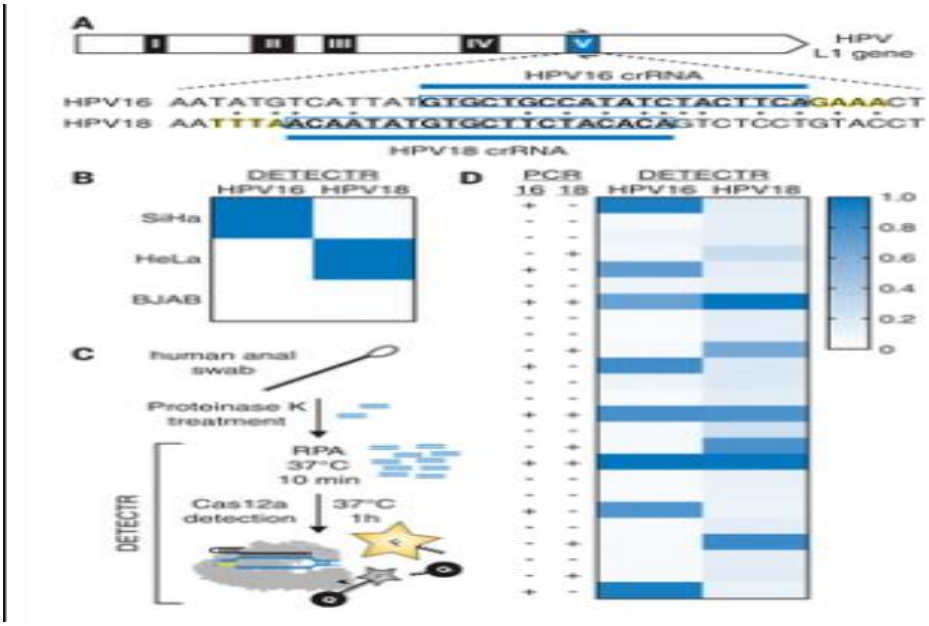

Figure 2: HPV-16, DNA testing model

3.3 Pap Smear Test

The mucus on the surface of the cervix should be wiped clean in advance, and then the sampling brush should be inserted into the cervical canal 1 cm and rotated for 5 weeks in the clockwise and counterclockwise directions, respectively, to collect the cells removed from the external opening of the cervix and the cervical canal, and 95% alcohol should be evenly applied to the collected specimens for fixation. The diagnosis was performed according to the Pap grading criteria: Normal: Grade I; Negative: different degree of inflammation (grade I); Positive: Suspected cancer (sub-grade), highly suspected cancer (grade IV), cancer (grade V) during Pap smear test positive and highly suspected patients were re-biopsied colposcopy. The procedure of colposcopy is as follows: Select the subject's bladder lithotomy position to fully expose the cervix and vagina, wipe the subject's cervical secretions with cotton balls, align the colposcope objective with the subject's cervix and the lesion site, adjust the focal length reasonably according to the specific conditions, and observe the subject's cervix morphology, color and blood vessels in detail with the low stop lens. Moreover, a cotton ball with a concentration of 3% acetic acid was used to wipe the cervix and vagina repeatedly to ensure that the epithelium was fully purified, and then the compound iodine solution was evenly applied on the cervical surface of the subject, and acetic acid test was carried out. Biopsy was performed on the abnormal places and the places that were not colored by iodine test.

4. EXPERIMENT RESULTS

In normal cervical epithelial tissue, LSIL, HSIL and cervical cancer tissue, the positive rate of HR-HPV was 13. 64, 33. 07%, 61. 45% and 94. 00%, any two groups above were statistically analyzed, $P<0.05$, see Table 1

Table 1: Detection of HR-HPV in each group (%)

Degree of cervical cancer	number	HR-HPV positive
Epithelial tissue	22	3(13.6)
LSIL	127	42(33.07)
HSIL	83	51(61.45)
tissue	50	47(94.00)
X^2		6433.801
P		0.000

The common screening method for cervical cancer is mainly HPV DNA. In recent years, as the relationship between high-risk HPV and cervical cancer has been gradually determined, HPV DNA combined cytological examination has gradually attracted more and more researchers' attention, and has been widely used in clinical detection. However, HPV DNA method has some defects. That is, it is not possible to determine the integration of the HPV virus with the host gene. Some studies have shown that in patients with condyloma lesions and LSIL patients, the rate of HPV integration is low, and it only appears in cancer. The results of this study found that there were 17 cases of HPV-16 infection in LSIL. The integration rate is 32%, and the integration rate in HSIL is also 9.0%. In addition, the HPV-16 integration rate reached 58% in cervical cancer tissues, indicating that high-risk HPV integration throughout the entire process of cervical tissue lesions. This further indicates that rapid HPV DNA detection and combined detection of HPV integration status can effectively improve the detection specificity.

5. CONCLUSION

For the screening of cervical lesions, there are many clinical methods, and liquid-based thin layer cytology is a common type. This method collects test samples by applying a cell brush to the cervical tube, rotating the cervical tube for 1 week, then brushing the cervical surface, and finally collecting the cell brush samples in the preservation liquid for examination, which has many advantages, such as simple operation and convenience. Low cost. The results of this study showed that the satisfaction rate of liquid based thin layer cytology smear was significantly higher than that of Pap smear, and the difference was statistically significant ($P<0.05$). The positive rate of liquid thin layer cytology was significantly higher than that of Pap smear, the difference was statistically significant ($P<0.05$). The positive coincidence rate of liquid thin layer cytology was significantly higher than that of Pap smear, and the differences were statistically significant ($P<0.05$). It was proved that the diagnostic efficiency of liquid thin layer cytology was better than that of Pap smear. The reason was analyzed and the cell preservation technique was perfect. During the examination, systematic treatment and high-precision filtration minimize the influence of blood, mucus and other causes, and ensure that the cell structure has a high clarity. The examiner can carefully observe a variety of small or minority cells such as squamous epithelial lesions, and can also easily find

trichomonas, chlamydia, candida, herpes simplex virus, etc. Therefore, a higher positive detection rate can be obtained, which is also consistent with the conclusion reported by Li Gang [13-15].

In recent years, prophylactic HPV vaccine has achieved good results in preventing HPV infection, but it has no obvious effect on patients with existing HPV infection. Therefore, in-depth research on therapeutic HPV vaccine plays an important role in the clinical treatment of patients with HPV infection and related lesions. With the in-depth research on the molecular mechanism of carcinogenesis of high-risk HPV, it is known that the high expression of HPV E6/E7 gene is a key factor in the continuous infection of high-risk HPV in the cervix leading to SIL and cervical cancer progression[16-17]. Che et al. presented a pivotal advancement in the realm of biomedical text classification, specifically focusing on Cancer Doc Classification. By delving into the complex task of analyzing lengthy research papers related to cancer, this research stands out from previous endeavors that predominantly concentrate on succinct abstracts[18].The treatment of HPV E6/E7 targeted genes will provide broad ideas and new directions for the treatment of high-risk HPV-positive cervical cancer and its precancerous lesions[19-22]. Therapeutic HPV vaccine "by using different ways to express HPV E6 or E7 antigen, activate the body's immune response, clear the cells that have been infected with high-risk HPV, so as to achieve the purpose of cervical cancer and precancerous lesions."

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This work describes a highly original and novel methodology for early Alzheimer's disease detection studies. It will be of wide interest to the large community of scientists using such techniques to study the disease[17].

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