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Application of different methods for cervical cancer detection

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Abstract. Cervical cancer remains a widespread and challenging malignancy that affects women worldwide and poses significant clinical and public health issues. Since it is difficult to find early cervical lesions in the patient's own state, it is very important to apply appropriate and effective detection and screening for cervical cancer and precancerous lesions. This research investigates the development of cervical cancer and the various subtypes of HPV, which are the primary cause of cervical lesions. Combined with the investigation of the three most common clinical screening methods, including liquid-based thin-layer cell assay (TCT), human papillomavirus detection (HPV) and colposcopy detection operating methods and screening standards, data were used to comprehensively analyze the accuracy, sensitivity and specificity of single or combined screening of the three detection methods. This research examines various methods and technologies for cervical cancer screening, with the goal of determining their clinical effectiveness in detecting cervical lesions. Based on screening data, the results are positive and the methods are deemed suitable for early diagnosis of the condition. It is recommended that these screening tools be utilized in a clinical setting.

Keywords: cervical cancer; cervical lesions; detection.

1. Introduction

As time passes, people's daily schedules are becoming increasingly packed. Consequently, more and more individuals are experiencing sub-optimal health which, in turn, raises the incidence of cancer. Amongst the many types of cancer, cervical cancer is one that is widespread. The World Health Organization has reported that the incidence of cervical cancer in China is 14.6 per 100,000 people. Importantly, its onset age has been dropping over recent years, posing a significant threat to women's health. Cancer of the cervix is a long-term and complex pathological process. Its development is mainly caused by the human papilloma virus (HPV). Data shows that it takes about 10 to 15 years for cervical intraepithelial lesion (SIL) to develop into invasive cervical cancer. And this can be detected through medical screening for early intervention, which can significantly improve the five-year survival rate of women with the disease by 90% [1]. It can be seen that early detection is an effective method for preventing cervical cancer.

Since Laverty's discovery of HPV in cervical cancer tissues in 1977, it has lent further support to Zur Hausen's hypothesis of the association between HPV and cervical cancer. Extensive research by scholars globally has identified various gene subtypes of HPV. This ongoing investigation is crucial in the development of efficient diagnostic methods and treatment strategies. About 40 subtypes are involved in genital tract infections, and each subtype has varying pathogenicity to the cervical epithelium. HPV subtypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59 are considered high-risk and have been linked to the development of cervical cancer. These findings are supported by academic research and are important for the general public to understand [2].

At present, the primary clinical screening methods for cervical cancer include cervical thin-layer liquid-based cytology (TCT), HPV testing, and colposcopy. The three detection methods are used together to enhance their clinical value in gynecology. Cervical cytology is performed in the TCT test. After excluding female patients from menstruation, cell brushes are used to collect exfoliated cells and place them in cell storage fluid. Thin slices are then made using relevant technologies, and Papanicolaou-stained thin slices are used for microscopy. Cervical cancer is categorized into different types based on the TBS recommended by the International Cancer Society. These include squamous

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cell carcinoma, high and low-grade squamous intraepithelial lesions, inflammation, and normal cells. HPV testing involves using an HPV sampling brush to collect a sample from the external orifice of the cervix. The collected cell fluid is then stored for examination. The most common method of colposcopy involves the use of electronic colposcopy to identify suspected lesions. After wiping secretions with a dry cotton ball, acetic acid is applied for smearing the cervix to enhance the visibility of any abnormal cervical areas, allowing for better observe changes in shape, color, and boundary. If it is not obvious, the sample can also be sent for pathological examination to further determine the nature of the lesion [3]. Through the study of these three clinical detection methods, this research aims to further explore their application value and significance in female gynecological health.

2. Pathogenesis of cervical cancer

Cervical cancer is predominantly attributed to HPV virus infection. For women's lives, especially young women, are extremely susceptible to infection. However, the symptoms of cervical cancer are difficult for patients to detect in the early stages of formation, and can only be identified through medical screening. In the current medical environment, early screening for cervical cancer is challenging, and the general accuracy is not guaranteed [1]. When the patient's cervical cancer develops in the later stage, patients may face psychological, physical, and even life-threatening challenges due to its irreversible nature. Early detection and treatment are also effective means to inhibit cervical cancer. In order to effectively diagnose patients in the early stages of the disease, it is also necessary to select an efficient screening and diagnostic program for intervention. The most commonly used clinical detection programs at this stage mainly include TCT, HPV and electronic colposcopy. The accuracy of combined screening has also been highly recognized by patients and clinicians.

There are many factors that contribute to the development of cervical cancer lesions in female patients. However, it is widely recognized that cervical cancer is known to be a cervical tumor mainly induced by HPV. After HPV was discovered by a German scientist, the structure and pathogenic mechanism of the HPV virus have also been widely studied and discussed by the medical community. HPV is an icosahedral symmetrical nucleocapsid virus with a diameter of 43-53 nm [4]. The shell of HPV virus is composed of 72 shell particles. Through nucleic acid testing, it was found that the virus has no envelope, and the nucleic acid is stranded circular DNA. At present, there are more than 100 subtypes of HPV infection. HPV can be divided into high pathogenic genotypes, such as HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59, and low pathogenic genotypes, such as HPV6, 11, 40, 42, 54, 61, 70, 72, and 81. Other genetic pathogenic types are currently undetermined. In patients, infections can be divided into epithelial HPV types, such as 1, 5, 8, 14, 20, 21, 25, and 47, and mucosal HPV types, such as 6, 11, 16, 18, 31, 33, 35, 39, 41, 45, 51, 52, 56, 58, 59, 68, and 70. These classifications are based on the pathogenicity of the virus and the type of infection it causes in patients. Further research is needed to fully understand the genetic and pathogenic diversity of HPV.

The pathogenesis of cervical cancer arises from a complex interplay of multiple factors and biological processes. HPV itself has strong organizational ability and host specificity. After the HPV virus gene is partitioned, the L1 and L2 genes of the late gene block encode the viral capsid protein and collectively form the viral coat. The proteins E1, E2, E4, E5, E6, and E7, found in the early gene region, play a crucial role in the replication and transcription of viral genes. This can lead to the abnormal transformation of host cells, ultimately causing detrimental effects. This leads to the abnormal situation of hyperplasia of the body's own mucosa, causing the host itself to develop tissue verrucous lesions and papillomas due to DNA viruses [5].

3. Screening for cervical cancer

3.1. TCT Detection

The main process of liquid-based thin-layer cell detection is to rotate the specialized cervical brush clockwise around the cervix for five times in the cervical canal. After removal, the collection and cell preservation solution are placed in a vial for gentle agitation to ensure that the cells are fully immersed in the liquid. Then, a new Berg's smear is prepared. After systematic treatment, fixation with 95% alcohol and papanicolaou staining are performed [6]. Finally, a comprehensive diagnosis report of TBS is obtained. Negative results were observed for intraepithelial lesion cells or malignant cells (NILM), whereas positive results were obtained for squamous cell carcinoma (SCC), low-grade squamous intraepithelial lesion (LSIL), atypical squamous cell lesion (ASCH), high-grade squamous intraepithelial lesion (HSIL), and atypical glandular epithelial cell lesion (AGC) [7].

3.2. HPV Testing

Human papillomavirus testing is performed using an HPV sampling brush outside the cervical orifice. The brush is rotated clockwise and counterclockwise for 10 seconds per time, for a total of five times. The cells obtained are also stored in the cell fluid for inspection. The inspection office will utilize the cross-capture testing method to analyze samples for HPV virus types, consisting of five low-risk subtypes and fifteen high-risk subtypes such as HPV 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 70, 73, and 82. These high-risk types will be considered positive for the test [1].

3.3. Colposcopy

Colposcopy will first use an electronic colposcope to locate the suspected lesion in the patient. After delicately cleaning any vaginal discharge with a dry piece of cotton, the surface of the cervix will be treated with a solution of 3% acetic acid. After one minute, observe whether there is any abnormal area. If no lesion is found based on the previous test results, the doctor will collect a sample from the surface of the cervix and perform a pathological examination. Finally, the collected cells are classified into different categories based on the degree of abnormality.

3.4. Relevant data and analysis of the three detection methods

Citing data from 90 patients with suspected cervical lesions at the First People's Hospital of Shangqiu City, the results showed that 31 of them had confirmed cervical lesions through pathological and histological examination. Four patients with cervical cancer were studied, with two cases testing positive for TCT, three cases for HPV, and four cases being detected through colposcopy. Among a total of 16 patients diagnosed with HISL, 11 cases tested positive for TCT, 10 cases were positive for HPV, and colposcopy detected 15 cases. Furthermore, 11 patients were diagnosed with lSIL, of which seven tested positive for TCT, 10 for HPV, and nine cases were detected through colposcopy. These findings highlight the importance of regular screening and testing for cervical abnormalities, particularly in those at higher risk for developing cervical cancer. Among the 90 patients with suspected cervical cancer, 48 cases tested positive through single TCT screening, 44 cases tested positive through HPV screening, and 40 cases were detected through colposcopy [3]. However, after conducting combined screening, only 32 cases were confirmed as positive. The accuracy of the screening reached 96% when compared to the most direct and clear pathological tissues. This shows that the clinical diagnostic value of combined examinations is higher than that of a single examination. However, the sensitivity, specificity and accuracy of a single examination are all above 55%.

3.5. Traditional Pap smear

After searching for historical data, it was found that in 1941 cytopathologist George Papanicolaou first used cervical smear cells to screen the occurrence of cervical cancer. This detection method is also referred to as cervical Pap smear (CPT). This detection method is a wooden or bamboo scraper at the junction of the cervical squamous columnar epithelium to scrape off epithelial cells and a little

mucus on the glass slides. This method has been widely used clinically for half a century because of its simplicity and affordability [8]. This method has also reduced the cervical cancer incidence rate by about 80% and reduced the mortality rate by 70% [7]. Pap smear screening has indeed made great medical contributions. However, in subsequent studies, scholars have found that due to the failure to the diseased site; a large number of diseased cells have not been transferred from the diseased site, as shown in Figure 1. A large number of smeared cells and impurities in the lesions often contain red. The data show that the false negatives range from 5% to 40%, and the sensitivity is only about 50% [9, 10]. The Bethesda system proposed by the NCI Research Institute in 1988 gradually replaced Pap cytology smears. This system is based on Pap smear, some shortcomings of the Pap smear have been modified.

3.6. Automated cytology testing system

In recent years, automated cytology testing systems have been introduced in order to improve the examination of traditional cytology smears in the clinical assessment of cervical cancer. The automated cytology testing system is also called the liquid-based cytology testing system (LCT). In 1999, the US FDA granted approval for clinical use of this technology. The LCT test method involves placing the cell collector directly into a collection bottle containing cell preservation solution and spinning it through centrifugation. After natural precipitation, the collection bottle will separate the mucus, blood, and inflammatory cells in the sample. The remaining epithelial cells are then collected and arranged into a thin layer with a diameter of 13 mm, which is then placed on the slide. In the subsequent slide production process, a centrifugal precipitation technology, which is completely different from liquid-based cytology (TCT), is used [11, 12]. This technology can process 48 specimens at a time and complete cell staining during the automatic film production process, thereby achieving higher quality and efficiency. Moreover, this technology can reduce the reading range to within a diameter of 13 mm, and the reading time can be greatly reduced to 2.5 minutes. This method allows for easier observation of each visual field and can also improve sensitivity. According to the literature, the cytology sensitivity of the LCT test method has been reported to be 81.6%, which is more than 15% higher than that of the traditional Papanicolaou smear [2]. The LCT test can not only avoid missed diagnoses caused by positive abnormal cells being covered by blood, inflammatory cells, and mucus in the traditional smear and going undetected, but it can also reduce the strain on the examiner's eyes when reading the film, greatly facilitating large-scale cytology screening.

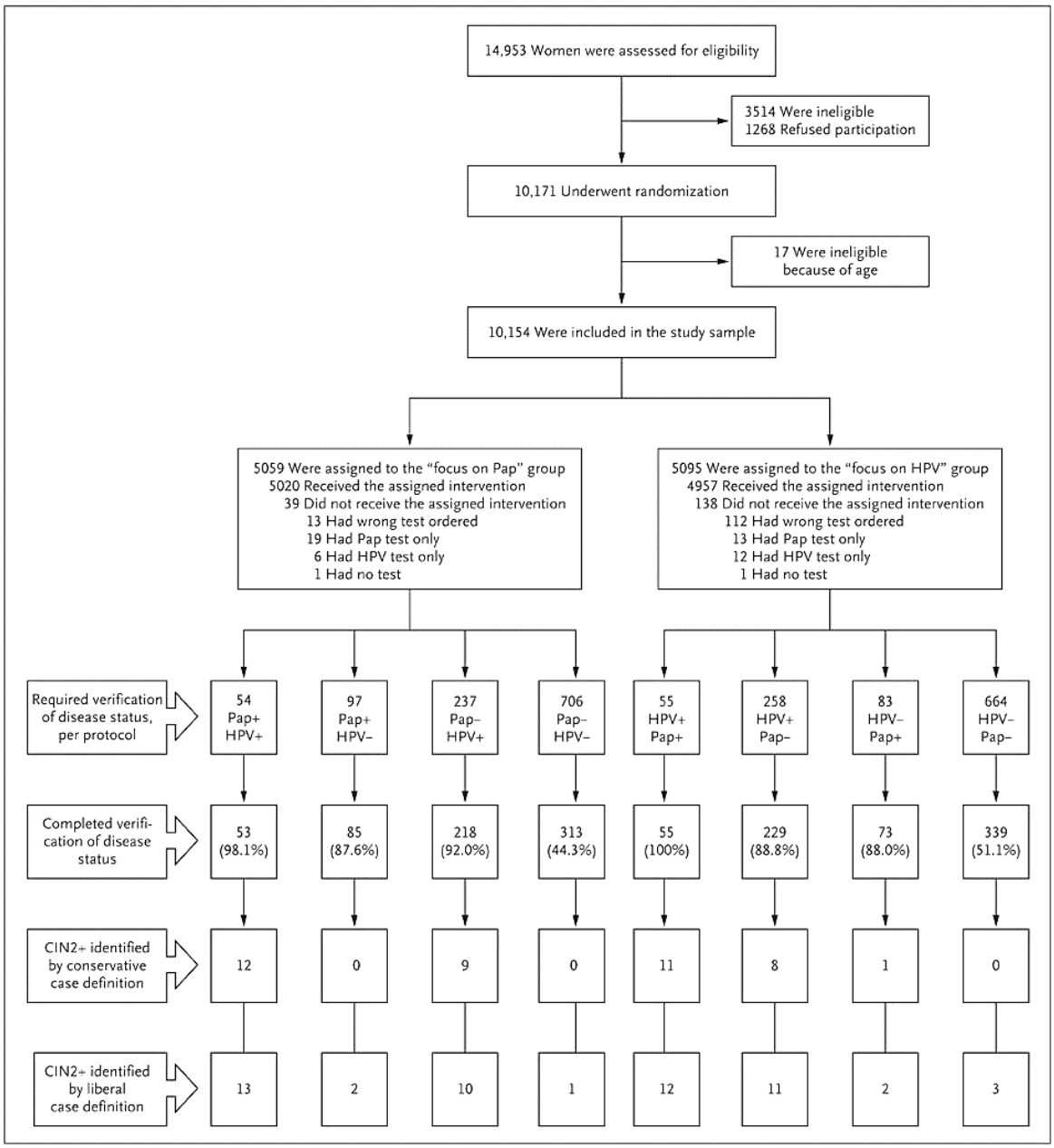

Figure 1. Enrollment and outcomes analysis [10].

3.7. Fluorescence in situ hybridization

Due to the limitations of current cervical cancer screening methods, researchers are searching for alternative approaches, including molecular cytogenetic testing. Fluorescence in situ hybridization (FISH) has gained significant attention in recent years as a representative method using this technology. Its potential for detecting cancerous cells through the labelling of specific DNA sequences makes FISH a promising tool in the fight against cervical cancer. FISH test first collects cell samples, extends the liquid-based cytology special brush into the cervical mouth, and evenly rotates for three to five weeks with the junction of the squamous column epithelium as the center. It will collect cervical exfoliated cells, and then put the brush into the liquid-based cytology preservation solution for storage. It will also take five to ten milliliters of cell samples, and perform FISH slide sample preparation, pretreatment, denaturation, probe and sample hybridization. Finally, the slides are eluted and fluorescence signals are detected under a fluorescent microscope. The rapid development of cervical cancer is predicted by fluorescence signals. Its simple operation, repeatability and good stability make it have good sensitivity and specificity [13]. FISH technology is generally used to detect human cervical cancer cells in TERC genes. Dysregulation of TERC gene

expression is a crucial factor in the pathogenesis of cervical cancer. The assessment of TERC gene expression can be used as a diagnostic tool for early identification of cervical cancer.

4. Conclusion

Cervical cancer, as a malignant tumor, is a malignant disease that can be treated in clinical practice. The presence of cervical precancerous lesions in women has a strong correlation with HPV infection. Early intervention of cervical lesions in clinical practice is of great significance to protect women's lives and health. With the continuous development and improvement of clinical detection and screening technology, the accuracy rate of a series of individual tests for TCT, HPV and colposcopy are about 65%, while the accuracy rate of combined screening is as high as 96%. It can be seen that combined screening is helpful to better identify abnormal cells of cervical epithelium and effectively improve the detection rate of cervical lesions. However, due to interference from other factors such as the subjective judgment of doctors, the results may be false negative. It can cooperate with multi-party screening such as LCT technology and FISH technology to better observe the response of the cells themselves, and even pay attention to cervical precancerous lesions and cervical cancer lesions caused by special gene variants, providing a better reference for clinical diagnosis and treatment.

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