The Early Screening Methods for Cervical Cancer

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Abstract. Cervical cancer is a major threat to global women's health, and early screening is crucial for reducing its incidence and mortality. This paper systematically reviews four mainstream cervical cancer early screening methods: cytological screening, HPV DNA testing, visual inspection with acetic acid (VIA), and combined testing, and compares their sensitivity, specificity, cost, and operational complexity. It further summarizes recommendations from global authoritative guidelines (WHO, USPSTF, ACS) and regional application cases (Rwanda, the United States, the United Kingdom, China), revealing that screening strategy selection is closely tied to regional economic levels and medical resource allocation. The study also identifies current challenges in global screening promotion, including uneven resource distribution, gaps between guidelines and clinical practices, and low public screening willingness. Finally, it proposes future directions: developing low-cost and user-friendly screening techniques, optimizing HPV-positive triage strategies, and enhancing health education and policy support to advance cervical cancer screening and improve women's health outcomes.

Keywords: Early screening methods; cervical cancer; early detection methods; human papilloma virus (HPV).

1. Introduction

Cervical cancer is one of the most common gynecological malignancies worldwide, with approximately 570000 new cases and 311000 deaths annually. Although incidence rate and mortality in high-income countries have declined significantly in the past few decades, 88% of global deaths still occur in low-income and middle-income countries, which reflects the huge difference in screening and treatment resources [1]. As the second level of cervical cancer prevention, early screening is crucial for detecting precancerous lesions and blocking cancer progression [2]. It is worth noting that HPV vaccination (as primary prevention) cannot cover all high-risk HPV types, and transient infections are common, so screening remains an irreplaceable part of the cancer prevention system.

The global research on cancer screening has gone through three stages: centered on cytological screening, assisted by HPV testing, and primarily focused on HPV testing. At present, authoritative organizations such as the United States Preventive Services Task Force (USPSTF), American Society of Clinical Oncology (ASCO), American Cancer Society (ACS), National Health Service (NHS), and World Health Organization (WHO) have issued corresponding screening guidelines. However, due to differences in regional economic levels and medical resource allocation, there are differences in recommended strategies. In China, thin-layer preparation cytology (TCT) and HPV DNA testing are the main screening methods, but there are also significant regional differences in their application [3]. This paper systematically reviews mainstream screening methods, compares their technical characteristics, integrates global guidelines and typical regional application cases, explores the challenges and optimization directions faced by early cancer screening, and provides reference for promoting the fairness and effectiveness of screening services.

2. Mainstream Early Screening Methods for Cervical Cancer

Current mainstream cervical cancer early screening methods include cytological screening, HPV DNA testing, Visual Inspection with Acetic Acid (VIA) testing, and combined testing. Each method

has unique technical characteristics and applicable scenarios, and their sensitivity, specificity, cost, and operational difficulty vary significantly.

2.1. Cytological Screening

Cytological screening detects precancerous lesions or cancerous changes by observing cervical exfoliated cells under a microscope, and its development goes through two stages: routine Pap smear and liquid based cytology (LBC). The traditional Pap smear has the characteristics of low cost and wide availability, and has played a key role in reducing the incidence rate and mortality of cancer in high-income countries. However, its accuracy is severely limited by sample quality - issues such as cell aggregation and overlap are common, resulting in a sensitivity of only 50-70% and a high false negative rate. In addition, the results are highly dependent on the professional level of cell pathologists, leading to significant differences in the quality of testing in areas with uneven medical resources.

LBC is an improved cytology technique that processes cervical samples through liquid preservation and concentration, achieving uniform cell distribution and clear background, thereby improving sample adequacy and abnormal cell detection rate. Compared with conventional Pap smears, the sensitivity of LBC has increased to 70-80%, and the remaining samples can be used for HPV testing simultaneously, improving detection efficiency. Its main limitations are that it is more expensive than traditional Pap smear testing and still relies subjectively on pathological interpretation. Both of these cytological methods have high specificity (about 90-95%), but their common drawback is insufficient sensitivity, which may lead to missed diagnosis of early lesions [2].

2.2. HPV DNA Testing

HPV infection (especially high-risk HPV, HR-HPV) is the core cause of cancer. HPV DNA testing directly detects HR-HPV in cervical samples through molecular biology techniques and targets the root cause of cancer, demonstrating significant technological advantages. Its most prominent feature is its extremely high sensitivity, which can effectively identify women at high risk of cervical cancer [2]. The negative predictive value is close to 100%, which means that women with negative results have a very low risk of developing severe cervical tumors in the next 5-10 years. Therefore, the screening interval can be extended to 5 years or longer to reduce screening frequency and long-term medical burden.

The main disadvantage of HPV testing is relatively low specificity (about 85-90%). Due to the fact that most HPV infections are transient and can be cleared by the human immune system within 1-2 years, only a few persistent infections can progress to precancerous lesions or cancer. This leads to a high false positive rate in initial HPV screening, which may cause unnecessary psychological anxiety in women and increase the burden of subsequent diagnosis and treatment. Therefore, for HPV positive results, effective triage methods are needed, such as combined cytology, p16/Ki-67 dual staining detection, or methylation marker detection, to distinguish between transient infection and persistent infection/precancerous lesions and avoid overtreatment [3,4].

2.3. VIA Testing

VIA testing is a simple screening method that involves applying 3-5% acetic acid to the surface of the cervix and observing with the naked eye for white lesions 1-2 minutes later. It has the advantages of low cost, simple operation, and quick results, without the need for complex equipment or professional pathologists. Especially suitable for low resource areas with insufficient medical equipment and a lack of professional technical personnel. However, its accuracy largely depends on the experience of the operator, with significant differences in sensitivity (50-80%) and specificity (60-90%), and it is often used as a triage method for HPV positive results rather than preliminary screening [5].

2.4. Combined Testing (cytology+HPV testing)

Joint testing refers to simultaneous cytological screening and HPV testing. This strategy combines the high sensitivity of HPV testing with the high specificity of cytology screening, and has the highest overall sensitivity among all screening methods, which can minimize the risk of missed diagnosis. However, its obvious drawbacks are high detection costs and high resource consumption. As the high negative predictive value of a single HPV test is confirmed, the additional benefits of adding cytology testing in initial screening are limited. Therefore, most authoritative guidelines no longer recommend it as the preferred strategy, but only as an alternative option [6].

3. Global Authoritative Guidelines and Regional Application Cases

The recommendation of cancer screening strategies is closely related to regional economic level, medical resource allocation, and population health needs. The globally authoritative guidelines have formed relatively consistent recommendations on the core position of HPV testing, but there are differences in details. Meanwhile, typical regional application cases provide practical experience for the promotion of screening methods.

3.1. Global Authoritative Guidelines and Recommendations

As a global public health authority, the World Health Organization emphasizes the universality of screening strategies and recommends HPV DNA testing as the preferred primary screening method. It is recommended that ordinary women start screening at the age of 30, with a screening interval of 5-10 years; Women at high risk of HPV infection should shorten the interval to 3-5 years. The World Health Organization strongly advocates for a comprehensive screening treatment strategy, which requires timely treatment of positive cases to improve the effectiveness of screening.

USPSTF and ACS have adjusted their recommendations in recent years to confirm the core position of HPV testing. USPSTF recommends that women aged 21-29 undergo cytological screening every 3 years; Women aged 30-65 can choose to undergo cytology screening every 3 years or joint testing every 5 years. If there are no high-risk factors after comprehensive screening, screening can be stopped. ACS also has similar recommendations, both recognizing that HPV testing has more advantages in long-term risk assessment [6].

European countries, represented by the UK, have basically unified their screening strategies centered around HPV testing. The UK National Health Service has implemented a nationwide cervical cancer screening program for women aged 25-64: women aged 25-49 are screened every 3 years, and women aged 50-64 are screened every 5 years. HPV positive samples are automatically classified by LBC, and only samples with cytological abnormalities (critical or above) will be referred for colposcopy examination. HPV positive but cytological negative cases will be re screened after 12 months, forming a standardized triage process [7].

In China, due to uneven economic development, screening strategies show significant regional differences. In economically developed regions, it is recommended to use HPV DNA testing as the preferred method; In economically underdeveloped areas, due to cost constraints, cytological screening (mainly TCT) remains the main method. The National Health Commission of China has promoted cervical cancer screening programs in rural areas, gradually increasing the coverage of HPV testing [8,9].

3.2. Regional Application Cases

Rwanda is a low-income country in Africa and a typical case of successfully promoting HPV testing in resource poor areas. Before 2010, due to economic backwardness, low status of women, shortage of gynecologists and poor medical conditions, the incidence rate and mortality of cancer in Rwanda were very high. After adopting the recommendations of the World Health Organization in 2010, Rwanda promoted HPV testing on a large scale and innovated the self-sampling VIA triage+immediate cryotherapy model based on its national conditions. Community health workers

guided women to complete self-sampling at home to improve screening coverage; VIA can quickly classify HPV positive cases; Visible lesions are immediately subjected to cryotherapy on site. This model effectively solves the problems of insufficient medical personnel and poor accessibility, significantly improving screening coverage and treatment rates [10-12].

As a high-income country, the United States faces the challenge of a disconnect between guidelines and practices in promoting HPV testing. Although USPSTF has been recommending initial HPV testing for women aged 30-65 since 2018, the pace of promotion has been slow. On the one hand, reimbursement policies are lagging behind: the Centers for Medicare and Medicaid Services (CMS) and many private insurance companies still primarily cover traditional cytology testing every 3 years or joint testing every 5 years, while reimbursement for HPV testing every 5 years is still unclear. On the other hand, clinical habits and patient awareness hinder this transformation: obstetricians and gynecologists are accustomed to cytological screening and are concerned about missing rare cases of HPV negative but cytological positive cases; Most women are familiar with the "Pap smear" but lack understanding of HPV testing, which requires clinical doctors to spend extra time explaining and increases the clinical burden. Therefore, the current screening practices in the United States are in a transitional state of "guidance and practical hesitation"[13,14].

In contrast, the UK National Health Service has achieved widespread access to HPV testing through a centralized and standardized management model. Since the end of 2019, HPV testing has been fully implemented for all women aged 25-64. The highly integrated digital information system ensures the traceability of the entire process from sampling, detection to triage and referral. Standardized operating procedures reduce the impact of human factors and maintain high screening coverage while ensuring testing quality.

4. Challenges and Future Prospects

Despite the continuous advancement of cancer screening technology, global popularization still faces many challenges. Unequal distribution of resources, low - and middle-income countries still face problems such as high HPV testing costs and shortage of professionals; Secondly, there is a gap between the guiding principles and practices, with high-income countries facing issues such as lagging reimbursement policies and difficulty in changing clinical habits; Furthermore, there is a lack of public awareness, with women in some areas lacking disease knowledge, shyness, and traditional beliefs leading to a low willingness to undergo screening.

Future research and promotion should focus on developing low-cost and easy-to-use screening techniques. Secondly, optimizing the triage strategy for HPV positive cases to reduce false positive rates and overtreatment; Thirdly, strengthen health education and policy support, raise public awareness of screening, develop reimbursement policies that match evidence-based guidelines, and promote the implementation of preferred strategies.

5. Conclusion

Early screening is a key link in reducing the incidence and mortality of cervical cancer. Among the mainstream screening methods, HPV DNA testing has become the preferred strategy recommended by global authoritative guidelines due to its high sensitivity and high negative predictive value, while cytological screening, VIA testing, and combined testing still have their applicable scenarios in specific regions and populations. The global cervical cancer screening work should adhere to the principle of stratified and classified, promote HPV testing as the core in low- and middle-income countries through technological innovation and model optimization, and solve the problem of guideline-practice disconnection in high-income countries through policy adjustment and health education. It is worth noting that screening is only part of the cervical cancer prevention system, and the combination of primary prevention (HPV vaccination) and secondary prevention (screening) is the fundamental way to eliminate cervical cancer. In the future, with the progress of

technology and the improvement of health systems, it is expected to achieve full coverage of high-quality cervical cancer screening services globally and ultimately reduce the global burden of cervical cancer.

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