

Modern Strategies for Enhancing Screening Efficiency and Treatment Processes for Cervical Cancer: A Narrative Review

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Abstract

Cytological screening plays a crucial role in reducing the incidence of cervical cancer in affluent countries. Determining the optimal approach for treating cervical cancer is critical before implementation. Chemotherapy can be administered as an adjuvant or as a standalone treatment. For patients with International Federation of Obstetrics and Gynecology stage IB1-IIA1 cervical cancer, type IIB, or C1 extended hysterectomy is typically recommended. Although surgery is an option, it increases the likelihood of morbidity and negatively affects patients' quality of life (QoL). The primary objective of this review was to evaluate the current methods and programs for screening and treating cervical cancer at various stages, including early, locally advanced, and advanced stages. Human papillomavirus screening is a reliable method for detecting cervical cancer in women at an early stage and offers better results than cytological testing. The screening frequency, due to the varying intervals implemented by different countries, ranges from annually to once every 5–10 years. Self-sampling can improve cervical cancer screening by providing convenience, and offering various testing options may encourage individuals who have not yet been screened. Early cancer detection programs, innovative screening initiatives, and improved accessibility and quality of treatment are crucial to improving oncological care. In addition, training oncologists, promoting a healthy lifestyle through interagency collaboration, and establishing a registry for chancery cases can help enhance the QoL.

Key words: Cervical cancer, concurrent chemoradiotherapy, cytological screening, papanicolaou smear, quality of life

INTRODUCTION

Cervical cancer is the third most prevalent gynecological cancer among women, with high incidence and mortality rates.^[1] The 5-year survival rate ranges from 15% to 80% depending on the International Federation of Obstetrics and Gynecology (FIGO) stage of the disease.^[2] Patients with pre-invasive, microinvasive, and FIGO stage 1A cervical cancers have a 5-year survival rate of

98%. For FIGO stage 1B, the rate was 78–92%, for stage II, it was 54–68%, and for stage III, it was 19.6–58.4%.^[2]

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Received: 22-04-2024

Revised: 11-06-2024

Accepted: 23-06-2024

The Papanicolaou smear, a widely used screening method in Western Europe and the United States, has been successful in reducing cervical cancer incidence by 70–80% and mortality rates by 80% in countries such as Sweden and Finland.^[3-5] Cytological screening plays a crucial role in reducing the incidence of cervical cancer in affluent countries. However, in countries with established screening systems based on Papanicolaou smears, steady or increasing trends in cervical cancer incidence have been observed, suggesting that this approach may reach its limits.^[6,7]

Determining the optimal approach for treating cervical cancer is critical before implementation. A personalized treatment plan can be developed by establishing the best method. Generally, women with early-stage cancer undergo surgery, whereas those with advanced disease receive combination or integrative therapy.^[8] Combination therapies can reduce the risk of recurrence; however, relapses often occur within the first 24 months of treatment, particularly in advanced cases.^[9,10]

Chemotherapy can be administered as an adjuvant or as a standalone treatment. For individuals with fertility concerns, radical trachelectomy, pelvic lymph node dissection, and modified extended hysterectomy may be performed alongside pelvic lymph node dissection in patients with FIGO stage IA2 malignancies.^[9,11]

Choi *et al.* reported that cisplatin and 5-fluorouracil consolidation chemotherapy after concurrent chemoradiotherapy (CRT) were effective and well-tolerated for locally advanced cervical cancer.^[12] Similarly, Zhang *et al.* used paclitaxel (135 mg/m²) and nedaplatin (60 mg/m²) for concurrent CRT, followed by consolidation chemotherapy every 3 weeks for four cycles, with 91% of patients with FIGO stage IIB-IIIB cervical cancer completing more than three cycles.^[13]

For patients with FIGO stage IB1-IIA1 cervical cancer, type IIB or C1 extended hysterectomy is typically recommended. The extent of lymph node dissection depends on tumor size. Type III/C extended hysterectomy is recommended for tumors >2 cm. The decision to pursue adjuvant treatment was based on a risk of progression assessment, which was performed after receiving a scheduled histological report.^[14] Patients with FIGO stages IB3 and IIA2 should undergo CRT; surgery is not recommended for these patients because of their high probability (80%) of requiring post-operative radiotherapy (RT) or concurrent CRT.^[15] Although surgery is an option, it increases the likelihood of morbidity and negatively affects patients' quality of life (QoL). Moreover, relying solely on surgical interventions can place significant strain on surgical and radiation facilities, which may be scarce in low-resource settings.

The primary objective of this review was to evaluate the current methods and programs for screening and treating

cervical cancer at various stages, including early, locally advanced, and advanced stages. In addition, it aimed to propose practical strategies for enhancing screening and treatment processes and provide suggestions to the Ministry of Health in the Kyrgyz Republic to prevent cancer and educate the public about malignant tumors in women.

CURRENT TECHNIQUES FOR CERVICAL CANCER SCREENING

The accuracy of Pap tests in detecting intraepithelial neoplasia and early-stage cervical cancer varies between 50% and 87%, with approximately 24–32% of women testing negative for invasive cervical cancer.^[16] These findings emphasize the need for alternative screening techniques. Research has identified a link between cervical cancer and human papillomavirus (HPV),^[17] which is more prevalent in women >50 years of age, decreasing from 11.1% to 2.9%.^[18] The prevalence of HPV varies significantly, ranging from 10% in China to 46% in Italy. Persistent HPV infection increases the risk of cervical cancer ten-fold, making it crucial to identify high-risk HPV strains and develop new screening methods.^[19]

HPV screening is a reliable method for detecting cervical cancer in women at an early stage and offers better results than cytological testing. The diagnostic value of this test can be improved by triaging women who test positive for HPV.^[20] A negative result in both the Papanicolaou smear and HPV test significantly reduced the risk of developing cervical cancer. Therefore, HPV screening should be included during regular physical examinations. The Netherlands and Turkey have implemented HPV-based cervical cancer screening since July 2019; however, other countries are still in the process of performing it. Experts advise the creation of a centralized information system that would help regions choose the most suitable screening option based on their financial resources while still requiring HPV testing for successful screening.^[9]

SCREENING FREQUENCY

The screening frequency, due to the varying intervals implemented by different countries, ranges from annually to once every 5–10 years. The US Preventive Services Task Force updated its screening guidelines in 2018, recommending a Papanicolaou smear every 3 years and a second 3-year cytology screening or an HPV HCR Genotype test alone every 5 years for women aged 21–29 years.^[19] Research indicates that a negative HPV test ensures no cervical cancer risk for more than 5 years, justifying screening for women aged 30–65 years.^[21] This approach minimizes the detection of HPV, is often self-eliminated, and enables early identification and treatment of anomalies. An effective screening process includes monitoring examination outcomes and ensuring the efficient treatment of any cervical abnormalities.

SCREENING COVERAGE OF TARGET POPULATION GROUPS

Several devices for self-sampling have been proposed, and studies have shown that these devices are effective in making screening more convenient and accessible to women. In Norway, almost 33% of the women who did not attend clinical appointments for Papanicolaou smears were screened using self-sampling devices.^[22] A meta-analysis of 33 studies revealed that individuals who used self-sampling had a higher screening rate than those in the control group (risk ratio: 2.13; 95% confidence interval: 1.89–2.40).^[23] In a review by Lozar *et al.*, the number of women who preferred self-sampling was considerably higher than that of women who visited a doctor for evaluation.^[24]

Self-sampling, in which women collect their samples for cervical cancer screening, may be particularly advantageous for socioeconomically disadvantaged women. Studies in low-income rural areas of Northern Greece showed that only 17% of the women studied underwent regular Papanicolaou smears.^[25] However, they were all keen to participate in self-sampling.

CHOICE OF TREATMENT

Cervical cancer can have a considerable impact on the QoL of young patients, particularly because of the loss of fertility caused by standard treatments. New therapies are being explored to preserve fertility, and radical trachelectomy with pelvic lymph node dissection is the only recommended organ-preserving treatment for invasive cervical cancer.

At present, CRT should be administered to individuals diagnosed with FIGO stages IIA–IV disease using a comprehensive treatment plan that combines RT with cisplatin 40 mg/m² once a week throughout the RT duration. However, neoadjuvant chemotherapy should not be administered to these patients. For patients with low-to-intermediate-risk FIGO stage IIB cervical cancer, surgical intervention may be considered part of a modified extended renal hysterectomy (type III/C2). In addition, ovarian translocation may be performed to preserve ovarian function in younger individuals.^[9,26]

Local hyperthermia has emerged as a promising adjunct to CRT for patients with locally advanced cancer. An increase in temperature within the tumor tissue influences oxygenation and metabolic activation, triggering the delivery of immune cells or natural killer cells to the tumor site. Furthermore, it enhances the energy potential of tumor cells and ultimately inhibits mitosis, leading to tumor cell death. Local hyperthermia alters the resistance of tumor tissues to other external stimuli, particularly ionizing radiation and chemotherapeutic drugs. Moreover, it increases antitumor

blood flow, making it essential to optimize chemotherapy delivery under such conditions to achieve a more significant therapeutic impact.^[27,28] Studies suggest that localized hyperthermia can enhance the effectiveness of chemotherapy by 1.5–2.5 times, potentially allowing for a reduction in chemotherapy dosage without compromising oncological efficacy.

Advanced FIGO stages of cervical cancer (III–IV) often require lymphadenectomy, CRT, and surgical interventions, such as pelvic exenteration, for FIGO stage IV patients who have not experienced cancer spreading to the pelvic wall. Identifying new diagnostic and prognostic factors is crucial to improving the prognosis of cervical cancer. Disease progression and response to RT/CRT have been challenging to predict due to the low accuracy and repeatability of molecular markers. This is often because patient cohorts are mixed and undergo various treatments such as RT, chemotherapy, and CRT.

Research often involves analyzing markers in the tumors of patients with cervical cancer by immunohistochemical examination. A study conducted by Wong *et al.*^[28] revealed that DLL4, a regulator of Notch signaling, was significantly higher in radioresistant stage III patients with cervical cancer who received CRT than in radiosensitive patients. Immunological markers have been shown to predict responsiveness to RT/CRT and serve as predictors of cervical cancer. The low expression of CD8 (T cells) and CD163 (M2 macrophages) was associated with a higher likelihood of achieving a complete pathological response in patients who underwent pre-operative CRT. Higher CD8 expression has been associated with higher mortality rates in patients with cervical cancer.^[29]

RECOMMENDATIONS

The early detection of cervical cancer is critical, and primary care physicians and patients must actively participate in screening programs and vaccination. Education and comprehensive information regarding regular preventive checkups with a gynecologist and specialized diagnostic methods are essential. Quality standards and national guidelines for screening programs must be established and implemented, and primary prevention measures, such as vaccination of teenage females and expanded screening for target groups, must be implemented. Oncologists play a crucial role in observation rooms at the primary care level, where they detect underlying precancerous conditions and conduct early cancer screening through cytological research.

To improve the organization of oncological care for women, it is necessary to focus on several key areas. These include developing and strengthening regulatory and legal frameworks for oncological services, implementing primary prevention measures for malignant neoplasms, introducing

advanced diagnostic and treatment strategies, and conducting public education campaigns. In addition, the remote training of specialists and the enhancement of the resources of medical institutions can help improve the care of patients with malignant neoplasms.

Effective collaboration among healthcare providers is vital to delivering advanced cancer treatments that improve patient outcomes and QoL. To achieve this, primary care physicians should participate in training programs, and surgeons and therapists should attend seminars focused on the early detection of cancer. Health-care organizations can overcome organizational obstacles and achieve success by adopting sound strategic management techniques. Accurate statistical indicators are crucial for developing cancer-care plans and implementing management techniques across all cancer-care levels. To enhance the quality of cancer care, a well-organized system for collecting statistical data and making informed judgments about malignant tumors is essential. Identifying regions with high tumor incidence rates is crucial for assessing malignancy, along with considering factors such as the average occurrence rate, growth in occurrence, timely diagnosis, proactive detection, and 1-year mortality rate.

We propose recommendations to the Ministry of Health in the Kyrgyz Republic to prevent cancer and raise public awareness of cancerous tumors in women. These recommendations include a comprehensive plan, enhanced training for primary health-care professionals, stronger collaboration among

oncologists, and the establishment of oncology departments at primary care centers. In addition, we suggest providing courses for general practitioners and implementing a unified patient registry system. Primary health-care providers are taking extra measures, such as conducting early detection diagnostic screenings for pre-tumor and tumor diseases; emphasizing the importance of screening tests among women; enhancing laboratory diagnosis of cervical cancer through collaboration with private laboratories; and offering cervical cancer screening tests, including acetic acid, Papanicolaou smear, and HPV tests.

Early diagnosis of cancer morbidity and timely treatment under subsequent supervision should be prioritized. Engaging diverse stakeholders, including non-governmental social groups, media, health institutions, and the general public, is necessary for collaborative efforts aimed at combating cancer [Figure 1].

Early cancer detection is crucial and necessitates the incorporation of diagnostic screening at the primary health-care level. Observation rooms in health-care facilities offering primary care are integral to this approach [Figure 2].

Enhancing the care of women with cervical cancer requires a comprehensive approach that encompasses several dimensions, including elevating awareness of screening procedures; educating general practitioners about malignant tumors; refining the competencies of primary care providers

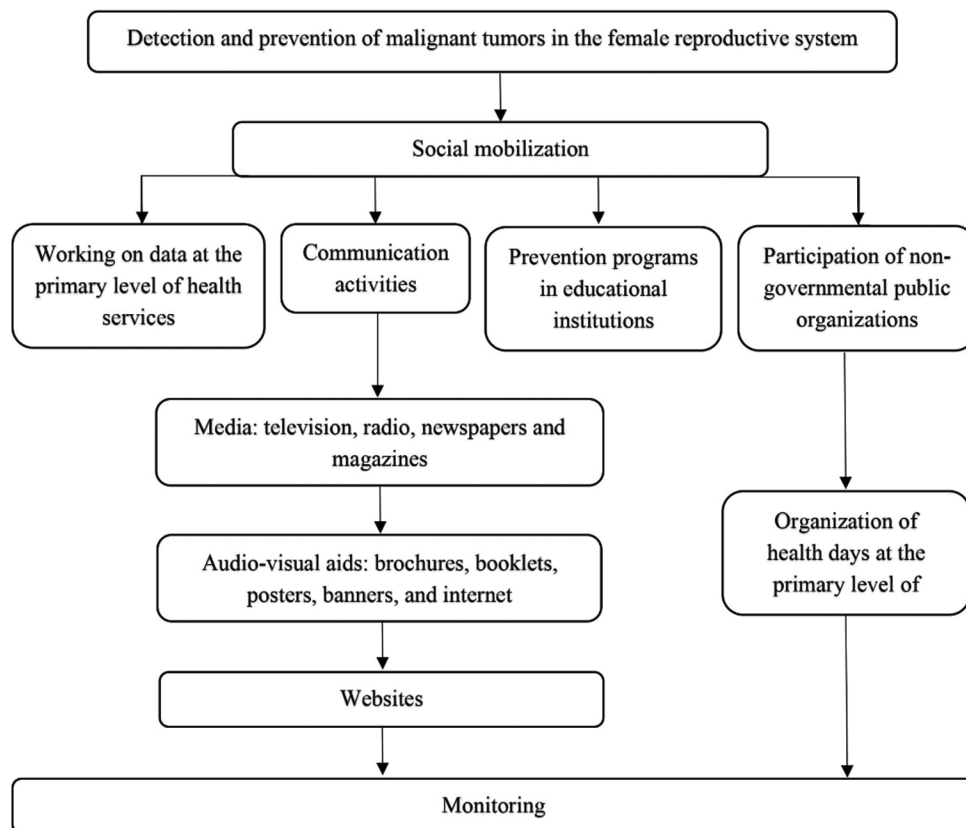


Figure 1: Flowchart for the prevention and detection of malignant tumors of the female reproductive system

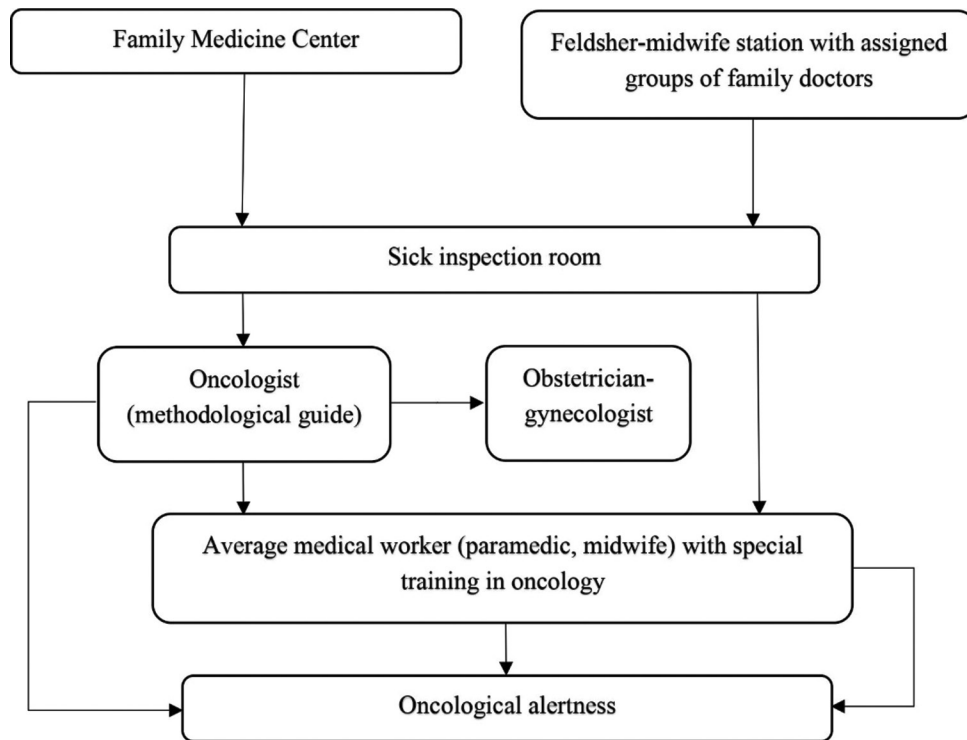


Figure 2: Flowchart for the primary health-care delivery system

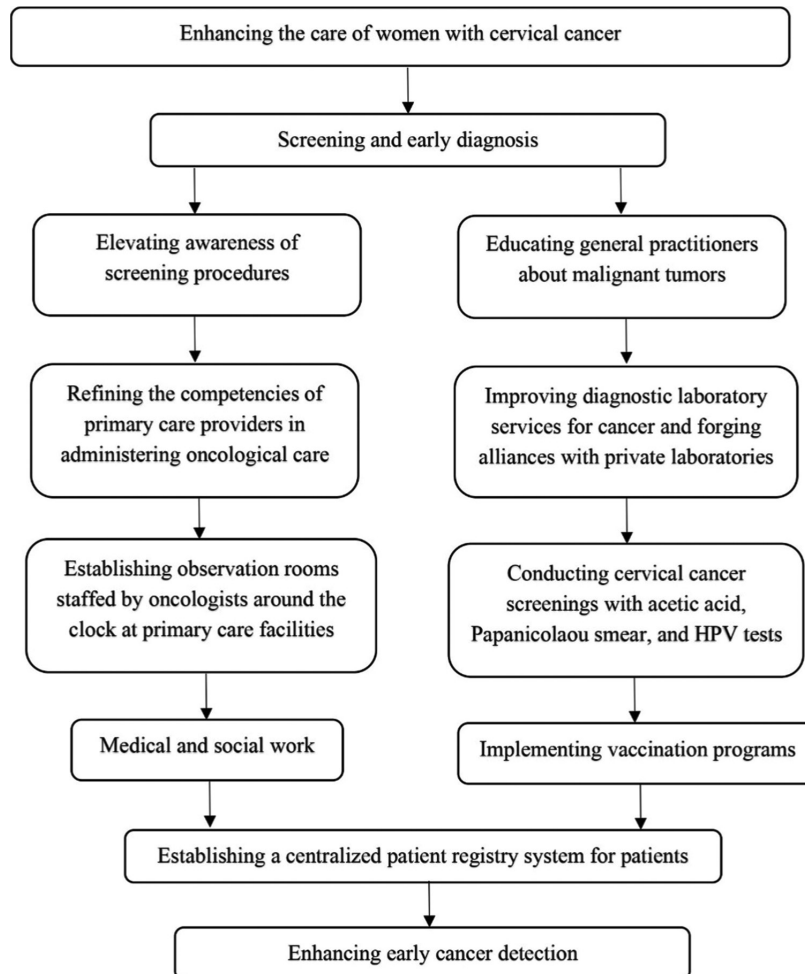


Figure 3: Flowchart for improving oncological care for women with cervical cancer

in administering oncological care; establishing observation rooms staffed by oncologists around the clock at primary care facilities; improving diagnostic laboratory services for cancer; forging alliances with private laboratories; conducting cervical cancer screenings with acetic acid, Papanicolaou smear, and HPV tests; implementing vaccination programs; establishing a centralized patient registry system for patients with cancer; and enhancing early cancer detection [Figure 3].

CONCLUSION

Self-sampling can improve cervical cancer screening by providing convenience, and offering various testing options may encourage individuals who have not yet been screened. However, further research is needed to understand the relationship between radiosensitivity and cancer response to radiation. The identification of new indicators of cancer progression can enhance treatment strategies, prevent metastasis and recurrence, and increase survival rates. Such studies will contribute to personalized treatment plans for patients with cervical cancer.

Early cancer detection programs, innovative screening initiatives, and improved accessibility and quality of treatment are crucial to improving oncological care. In addition, training oncologists, promoting a healthy lifestyle through interagency collaboration, and establishing a registry for chancery cases can help enhance QoL. To address the shortage of cancer beds, a three-tiered approach including specialist medical treatment, facilities for advice and diagnosis, and primary oncological care is necessary. Improved oncological care can lead to lower treatment costs, longer life expectancies, and better statistical databases. This can be achieved using cutting-edge information technology and a monitoring and assessment system that supports cancer prevention.

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Source of Support: Nil. **Conflicts of Interest:** None declared.