



Cervical Cancer, Update on its Diagnosis, Prevention and Treatment

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Abstract

Cervical cancer is a type of cancer that affects the cervix, typically caused by persistent human papillomavirus (HPV) infection. It is often detected through screening tests like Pap smears and colposcopy. The disease is staged based on its extent, and treatment options include surgery, radiation therapy, chemotherapy, and immunotherapy. HPV vaccination is recommended for both males and females to prevent infection and reduce the risk of cervical cancer. Survival rates vary depending on the stage, with early-stage cancers generally having higher cure rates. Immunotherapy with drugs like pembrolizumab and nivolumab has shown promise in advanced or recurrent cases. Regular screenings and timely intervention play a crucial role in managing cervical cancer.(Fig. 1).

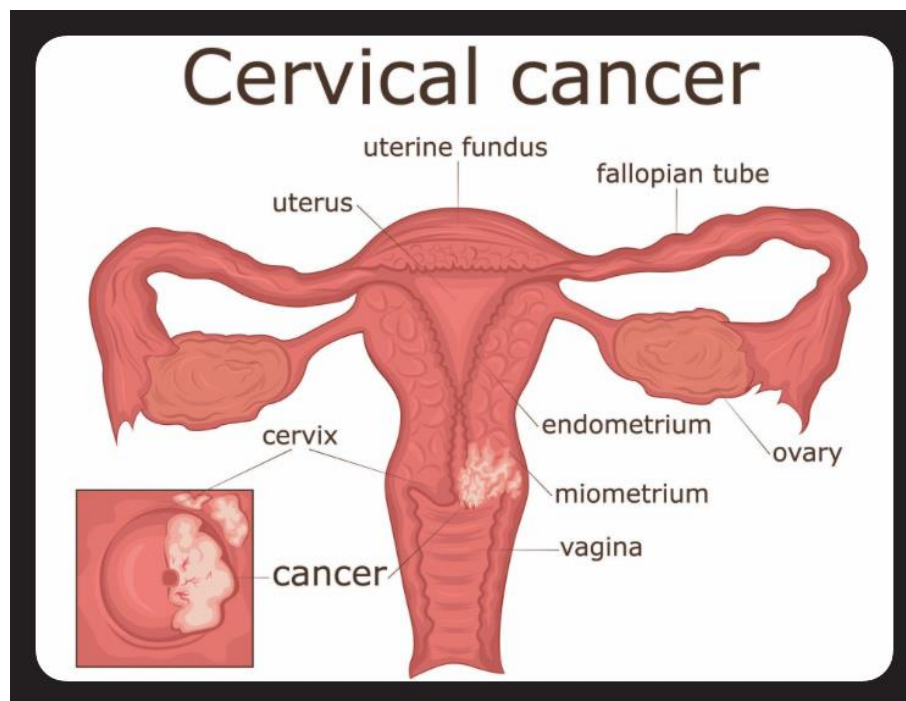


Figure 01

Introduction

Cervical cancer of the uterus is defined as the malignant growth of cells in the cervix, which is the lower part of the uterus that connects it to the vagina. It is characterized by the uncontrolled division and proliferation of abnormal cells in the cervix. These cancerous cells can invade surrounding tissues, spread to nearby lymph nodes, and, in advanced stages, potentially metastasize to other parts of the body.

Cervical cancer is typically classified and defined based on various factors, including the stage of the disease, histological type, and presence of specific molecular or genetic alterations. The stage of cervical cancer is determined by the extent of the disease, including factors like the size of the tumor, involvement of nearby tissues or organs, and presence of distant metastasis.

Histologically, cervical cancer is classified into different types, with the most common being squamous cell carcinoma, accounting for about 70% of cases. Other types include adenocarcinoma, adenosquamous carcinoma, and rare variants.

In summary, cervical cancer of the uterus is defined as the abnormal growth of cells in the cervix, leading to the development of a malignant tumor. The specific classification and characterization of cervical cancer depend on factors such as stage, histological type, and molecular or genetic alterations.

Stages

Cervical cancer is staged based on the extent of the disease and helps determine the appropriate treatment approach. The most commonly used staging system is the International Federation of Gynecology and Obstetrics (FIGO) staging system. Here are the stages of cervical cancer:

- Stage 0: Also known as carcinoma in situ or pre-invasive cervical cancer. At this stage, abnormal cells are present only on the surface layer of the cervix and have not invaded deeper tissues.
- Stage I: The cancer is confined to the cervix.
- Stage IA: The cancer is microscopic and can only be seen under a microscope. It has not spread beyond the cervix.

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- Stage IA1: Invasion is limited to a measurement of less than 3 mm and a width of less than 7 mm.
 - Stage IA2: Invasion is between 3 mm and 5 mm in depth and less than 7 mm in width.

 - Stage IB: The cancer is visible and has invaded the cervix but has not spread to nearby tissues or organs.
 - Stage IB1: The tumor is larger than Stage IA2 but is less than 4 cm in greatest dimension.
 - Stage IB2: The tumor is larger than Stage IB1 or is 4 cm or more in greatest dimension.

 - Stage II: The cancer has spread beyond the cervix but has not reached the pelvic sidewall or the lower third of the vagina.
 - Stage IIA: The cancer has spread to the upper two-thirds of the vagina but not to the pelvic sidewall.
 - Stage IIB: The cancer has spread to the pelvic sidewall or involves the lower third of the vagina.

 - Stage III: The cancer has extended to the lower third of the vagina or has spread to the pelvic sidewall. It may also involve the ureters, causing kidney-related issues.
 - Stage IV: The cancer has spread beyond the pelvic area or has metastasized to distant organs.
 - Stage IVA: The cancer has spread to adjacent organs, such as the bladder or rectum.
 - Stage IVB: The cancer has metastasized to distant organs, such as the lungs, liver, or bones.

These stages provide a framework for determining the extent of cervical cancer. Proper staging helps guide treatment decisions and provides a common language for healthcare professionals to discuss the disease. (Fig. 2).

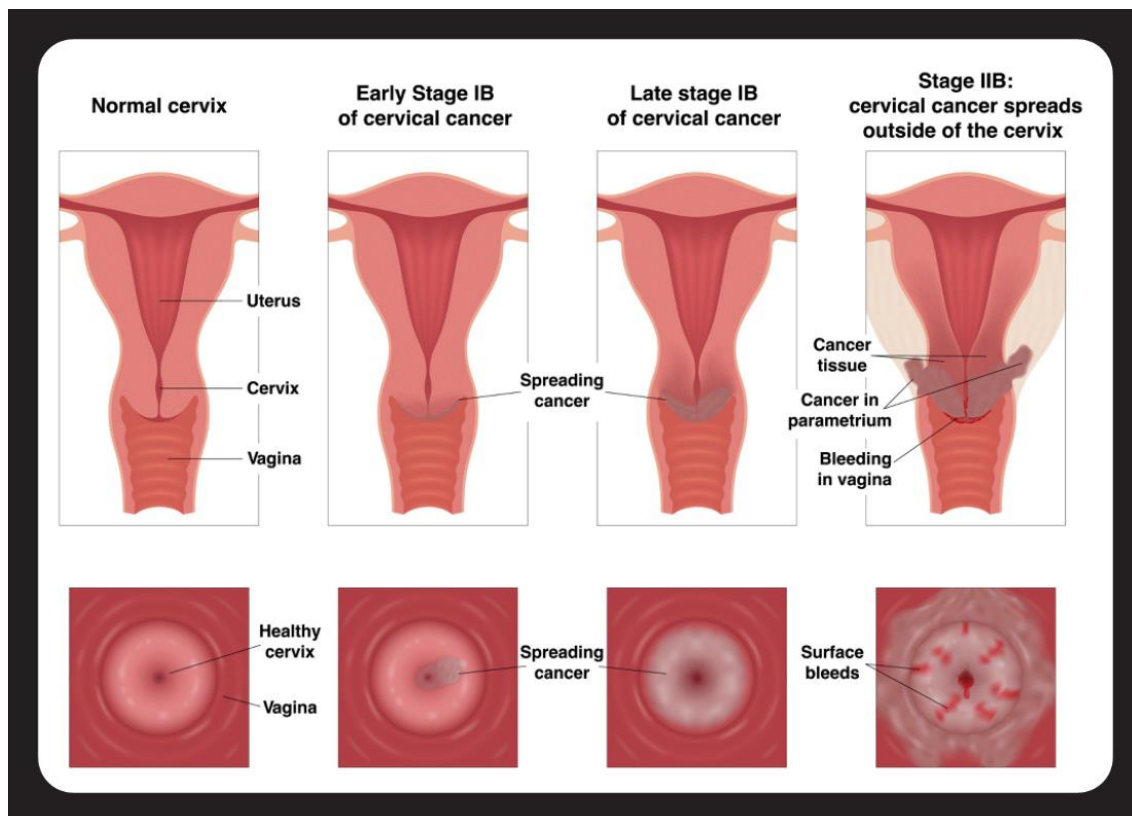


Figure 02

Histological Type

Cervical cancer can be classified into different histological types based on the appearance of the cancer cells under a microscope. The two most common histological types of cervical cancer are:

1. Squamous Cell Carcinoma (SCC): This is the most prevalent type, accounting for about 70-90% of cervical cancer cases. Squamous cell carcinoma originates from the thin, flat cells that line the outer part of the cervix called squamous epithelial cells.

2. Adenocarcinoma: Adenocarcinoma of the cervix develops from the glandular cells lining the cervical canal. It accounts for approximately 10-20% of cervical cancer cases. Adenocarcinoma may be more challenging to detect during screening, as it often occurs higher up in the cervical canal.

There are also other less common histological types of cervical cancer, including adenosquamous carcinoma (a mixture of squamous and glandular cells), small cell carcinoma, and neuroendocrine tumors. These rarer types collectively make up a small percentage of cervical cancer cases.

Determining the histological type of cervical cancer is important because it can have implications for treatment decisions and prognosis. Different histological types may respond differently to certain therapies, and the prognosis can vary depending on the specific type and its characteristics. Therefore, an accurate histological diagnosis is essential for guiding appropriate treatment strategies.

Molecular and Genetic Alterations. Role of HPV Infection

Molecular and genetic alterations play a crucial role in the development and progression of cervical cancer. Here are some common molecular and genetic changes observed in cervical cancer:

- 1. Human Papillomavirus (HPV) Infection:** The primary cause of cervical cancer is persistent infection with high-risk types of HPV, particularly HPV-16 and HPV-18. These viruses can integrate their DNA into the host cell's genome, leading to the dysregulation of cellular processes.
- 2. E6 and E7 Oncoproteins:** High-risk HPV types produce oncoproteins called E6 and E7, which are critical for the progression of cervical cancer. E6 and E7 proteins interfere with the normal cell cycle regulation, inhibit tumor suppressor proteins (such as p53 and pRb), and promote cell proliferation and survival.
- 3. TP53 Gene Mutations:** Mutations in the TP53 gene, which encodes the p53 tumor suppressor protein, are commonly observed in cervical cancer. p53 normally regulates the cell cycle and promotes DNA repair or apoptosis in case of DNA damage. TP53 mutations can impair these functions and contribute to uncontrolled cell growth.
- 4. PIK3CA Pathway Alterations:** Alterations in the PIK3CA gene, which is involved in the PI3K/AKT/mTOR signaling pathway, have been identified in a subset of cervical cancers. These alterations can lead to increased activation of the pathway, promoting cell proliferation and survival.
- 5. PTEN Loss:** PTEN is a tumor suppressor gene that regulates the PI3K/AKT/mTOR pathway. Loss of PTEN function, often due to mutations or deletions, can result in increased pathway activation and contribute to cervical cancer development.
- 6. Other Genetic and Epigenetic Changes:** Various other genetic and epigenetic alterations, including alterations in genes such as RAS, NOTCH, and TERT, have been implicated in cervical cancer. These changes can affect cellular processes involved in cell growth, invasion, and metastasis.

It's important to note that while HPV infection is a primary risk factor for cervical cancer, not all HPV infections progress to cancer. Other factors, such as host immune response, additional genetic alterations, and environmental factors, can also influence the development and progression of the disease. Regular HPV screening, vaccination, and early detection through screening programs are essential for preventing and managing cervical cancer effectively.

Epidemiological data. Role of Sexual Promiscuity and Multiple Couples

Epidemiological data suggests that certain factors, including sexual promiscuity and having multiple sexual partners, are associated with an increased risk of cervical cancer. Here are some key points regarding the role of sexual behavior in cervical cancer:

- 1. HPV Transmission:** Cervical cancer is primarily caused by persistent infection with high-risk types of human papillomavirus (HPV). HPV is a sexually transmitted infection, and the risk of acquiring and transmitting the virus increases with sexual activity.
- 2. Sexual Promiscuity:** Engaging in sexual activity with multiple partners or having a high number of lifetime sexual partners has been identified as a risk factor for cervical cancer. This is because a greater number of sexual partners increases the likelihood of coming into contact with HPV-infected individuals.
- 3. Early Sexual Activity:** Initiating sexual activity at a young age is another factor associated with an increased risk of cervical cancer. Early sexual activity may lead to longer exposure to HPV infection before the immune system can effectively clear the virus.
- 4. Male Sexual Behavior:** While cervical cancer predominantly affects women, the sexual behavior of male partners also plays a role. Men who have had multiple sexual partners or engage in high-risk sexual behaviors may have a higher likelihood of carrying and transmitting high-risk HPV to their female partners.
- 5. Other Risk Factors:** It's important to note that sexual behavior is not the sole determinant of cervical cancer risk. Other factors, such as smoking, a weakened immune system, long-term use of oral contraceptives, and co-infection with other sexually transmitted infections, can also contribute to the development of cervical cancer.

Prevention strategies such as practicing safe sex, including consistent condom use, and HPV vaccination can significantly reduce the risk of acquiring HPV and developing cervical cancer. Regular screening tests, such as Pap tests or HPV testing, are also important for early detection and treatment of precancerous changes or early-stage cervical cancer.

Prevalence Age, Signs and Symptoms

The prevalence of cervical cancer can vary across different populations and regions. However, it is more commonly diagnosed in women of reproductive age. Here are some key points regarding prevalence, age, signs, and symptoms of cervical cancer:

1. Prevalence: Cervical cancer is one of the most common cancers affecting women worldwide. However, the prevalence can vary significantly between countries and regions, mainly due to differences in healthcare access, screening programs, and HPV vaccination rates.

2. Age: Cervical cancer can occur at any age, but it is most frequently diagnosed in women between the ages of 35 and 44. Younger women can also develop cervical cancer, especially if they engage in high-risk sexual behaviors or have been exposed to HPV at an early age.

3. Signs and Symptoms: In the early stages, cervical cancer may not cause noticeable symptoms. However, as the disease progresses, common signs and symptoms may include:

- Abnormal vaginal bleeding, such as bleeding between periods, after intercourse, or after menopause.
- Unusual vaginal discharge that may be watery, bloody, or have a foul odor.
- Pelvic pain or discomfort.
- Pain during sexual intercourse.
- Changes in urinary or bowel habits if the cancer has spread to nearby tissues.

4. Asymptomatic Early Stage: Regular screening tests, such as Pap tests or HPV testing, play a crucial role in detecting cervical abnormalities or precancerous changes before symptoms manifest. This emphasizes the importance of routine screenings for early detection and treatment.

It's important to note that the presence of these signs and symptoms does not necessarily indicate cervical cancer, as they can also be caused by other conditions.

Early detection through screening, HPV vaccination, and adopting a healthy lifestyle are key strategies in reducing the incidence and impact of cervical cancer.

Role of prevention and early detection. Pap smear and colposcopy (Photo 1)

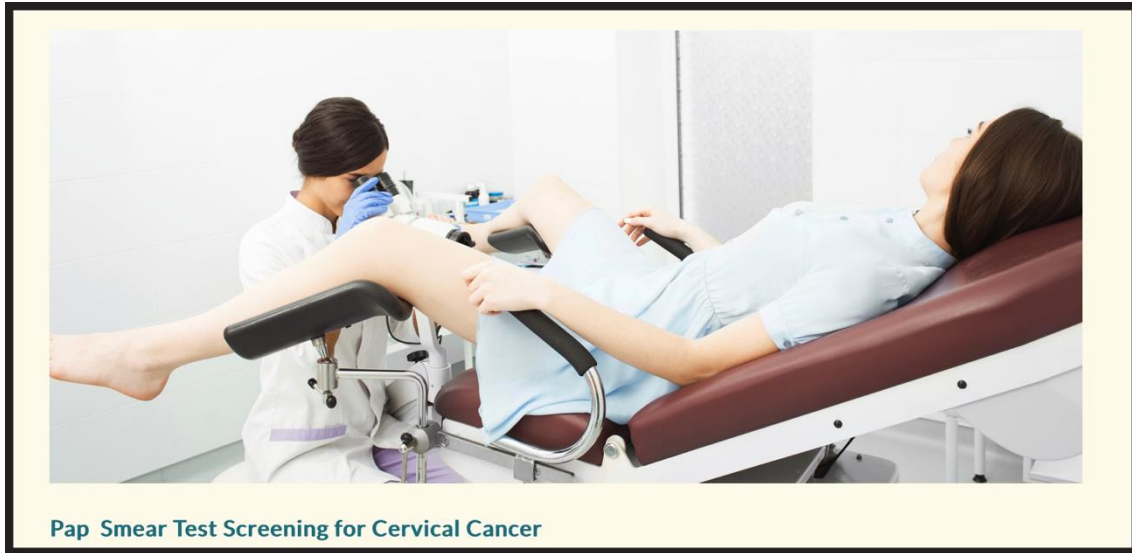


Photo 1

Prevention and early detection play crucial roles in reducing the incidence and impact of cervical cancer. Two important screening methods used for this purpose are the Pap smear and colposcopy. Here's a brief overview of their roles:

1. Pap Smear (Pap Test): The Pap smear is a screening test used to detect abnormal changes in the cells of the cervix. During a Pap smear, cells from the cervix are collected and examined under a microscope to identify any precancerous or cancerous cells. The test aims to identify abnormalities early, allowing for timely intervention and prevention of cervical cancer development.

Regular Pap smears are recommended for women starting around the age of 21 or within three years of becoming sexually active. The frequency of Pap smears can vary depending on factors such as age, risk factors, and previous test results. It's important to follow the guidelines and recommendations of healthcare professionals regarding the frequency of Pap smear screenings.

2. Colposcopy: Colposcopy is a diagnostic procedure performed after an abnormal Pap smear or if there are concerning symptoms or clinical findings. It involves using a specialized instrument called a colposcope to examine the cervix, vagina, and vulva in detail. The colposcope provides magnification, allowing the healthcare provider to identify any abnormal areas more accurately.

During a colposcopy, the healthcare provider may take biopsies (small tissue samples) from suspicious areas for further analysis. These biopsies help determine the presence of precancerous or cancerous changes in the cervix. Colposcopy provides a more detailed assessment of the cervical tissue and aids in determining appropriate management and treatment options.

Both Pap smears and colposcopy are vital components of cervical cancer screening programs. They facilitate early detection of precancerous changes or cervical cancer, enabling timely intervention and treatment.

HPV vaccines. Types, strains, who should be vaccinated. Cost of vaccines

HPV vaccines are an important preventive measure against cervical cancer and other HPV-related diseases. Here's some information about HPV vaccines, including types, strains, recommended recipients, and cost:

1. Types and Strains: There are currently three HPV vaccines available:

- **Gardasil 9:** Protects against nine HPV strains, including HPV types 16 and 18 (which cause most cervical cancers) and several other high-risk types.
- **Gardasil:** Protects against four HPV strains, including HPV types 16 and 18.
- **Cervarix:** Protects against HPV types 16 and 18.

2. Recommended Recipients: HPV vaccines are typically recommended for both males and females. The recommended age for vaccination varies by country but usually falls within the range of 9 to 26 years old. Vaccination is most effective when given before an individual becomes sexually active and is exposed to HPV. However, vaccination may still provide benefits to those who have already been sexually active or have had previous HPV exposure.

3. Men and HPV Vaccination: HPV vaccination is important for males as well. It helps prevent HPV-related diseases such as genital warts, anal cancer, and certain types of head and neck cancers. Men who have sex with men (MSM) may have a higher risk of HPV-related diseases and are strongly encouraged to receive the vaccine.

4. Cost of Vaccines: The cost of HPV vaccines can vary depending on factors such as the country, healthcare system, and availability of vaccination programs. In some countries, HPV vaccines may be available free of charge or covered by public health programs, particularly for eligible age groups. In other cases, the cost may need to be covered out-of-pocket or through private health insurance. It's advisable to consult with healthcare providers or local health authorities to understand the availability and cost of HPV vaccines in specific regions.

It's worth noting that HPV vaccination is a powerful tool for preventing HPV infection and associated diseases. Along with vaccination, regular cervical cancer screening and safe sexual practices remain important for comprehensive cervical cancer prevention.

Diagnostic algorithm, Tomography, resonance, PET

The diagnostic algorithm for cervical cancer typically involves a stepwise approach to evaluate the extent of the disease. Here's a general outline of the diagnostic process and some common studies that may be done:

1. Medical History and Physical Examination: A detailed medical history is obtained, including information about symptoms, risk factors, and previous screenings. A thorough physical examination, including a pelvic examination, is conducted to assess any abnormal findings.

2. Pap Smear: A Pap smear is performed to screen for abnormal cervical cells or precancerous changes. This is often the first step in the diagnostic process and can help identify women who may need further evaluation.

3. Colposcopy: If the Pap smear reveals abnormalities or if there are concerning clinical findings, a colposcopy may be performed. During a colposcopy, the cervix is examined using a colposcope, allowing for a closer evaluation of any suspicious areas. Biopsies may be taken during this procedure to confirm the presence of precancerous or cancerous cells.

4. Imaging Studies: Imaging studies such as computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET) may be recommended to assess the extent of the disease and detect any potential spread to nearby lymph nodes or distant organs. These imaging modalities help in staging the cancer and planning appropriate treatment.

- **CT Scan:** A CT scan provides detailed cross-sectional images of the pelvis and abdomen, helping identify lymph node involvement or distant metastases.
- **MRI:** An MRI may be used to provide more detailed images of the pelvis, allowing for better visualization of the tumor size, invasion of surrounding structures, and lymph node involvement.
- **PET Scan:** A PET scan combined with a CT scan (PET/CT) uses a radioactive tracer to identify areas of increased metabolic activity, helping detect any cancerous spread beyond the cervix.

5. Additional Studies: Depending on the individual case, additional studies such as cystoscopy (to assess the bladder), proctoscopy (to assess the rectum), or specialized imaging studies may be recommended to evaluate specific areas of concern.

Treatments

The treatment approach for cervical cancer varies depending on the stage of the disease. Here's a detailed overview of the treatment options commonly used for each stage:

1. Stage 0 (Carcinoma in situ or cervical intraepithelial neoplasia 3, CIN3):

- **Surgery:** Cone biopsy or loop electrosurgical excision procedure (LEEP) may be performed to remove the abnormal cells from the cervix.
- **Other options:** Cryotherapy (freezing of abnormal cells) or laser therapy may be used in certain cases.

2. Stage IA1 and IA2 (Microscopic invasion of cervical stroma):

- **Surgery:** A simple hysterectomy (removal of the uterus) with or without removal of the cervix may be recommended.
- **Other options:** Cone biopsy or LEEP may be considered in select cases.

3. Stage IB1 (Visible tumor confined to the cervix):

- **Surgery:** Radical hysterectomy (removal of the uterus, cervix, part of the vagina, and pelvic lymph nodes) or trachelectomy (removal of the cervix and upper part of the vagina, while preserving fertility) may be performed.
- **Radiation therapy:** External beam radiation therapy (EBRT) combined with brachytherapy (internal radiation therapy) may be used as an alternative to surgery, especially for patients who wish to preserve fertility.
- **Chemotherapy:** Concurrent chemotherapy with radiation therapy (chemoradiotherapy) may be recommended to enhance the effectiveness of radiation treatment.

4. Stage IB2, IIA, IIB (Tumor extends beyond the cervix or to nearby tissues):

- **Chemoradiotherapy:** This is the standard treatment approach for these stages. It involves a combination of external beam radiation therapy (EBRT), brachytherapy, and concurrent chemotherapy.
- **Surgery:** In select cases, after chemoradiotherapy, a radical hysterectomy may be performed to assess the response to treatment and remove any remaining cancerous tissue.

5. Stage III and IVA (Spread to the pelvic sidewall or to the lower third of the vagina):

- **Chemoradiotherapy:** This is the primary treatment modality. It includes EBRT, brachytherapy, and concurrent chemotherapy.
- **Surgery:** In some cases, after chemoradiotherapy, surgery may be considered to remove any residual disease or for palliative purposes.

6. Stage IVB (Spread to distant organs such as the lungs, liver, or bones):

- **Chemotherapy:** Systemic chemotherapy with various drug combinations is the mainstay of treatment. It aims to control the disease, alleviate symptoms, and improve overall survival.
- **Palliative care:** Supportive care measures are also provided to manage symptoms and improve quality of life.

Biological therapies, monoclonal antibodies, and immunotherapy are areas of ongoing research in cervical cancer treatment. Currently, the use of these therapies is more limited and mostly confined to clinical trials or in cases of recurrent or advanced disease. Examples of targeted therapies being investigated include anti-angiogenic drugs, immune checkpoint inhibitors, and therapeutic vaccines.

The treatment decisions are individualized, taking into account factors such as age, overall health, fertility preservation goals, and patient preferences. A multidisciplinary approach involving gynecologic oncologists, radiation oncologists, medical oncologists, and other healthcare professionals is crucial in determining the most suitable treatment plan for each patient.

Drugs and Protocols

There are several drugs used in the treatment of cervical cancer, either as estándar alone therapies or in combination with other modalities. Here are some of the commonly used drugs and drug protocols approved for the treatment of cervical cancer:

1. Chemotherapy Drugs:

- **Cisplatin:** Cisplatin is the most widely used chemotherapy drug in cervical cancer treatment. It is often administered concurrently with radiation therapy (chemoradiotherapy) to enhance treatment efficacy.
- **Carboplatin:** Carboplatin, an alternative to cisplatin, may be used in cases where cisplatin is contraindicated or not well-tolerated.
- **Paclitaxel:** Paclitaxel is frequently used in combination with cisplatin or carboplatin as part of chemotherapy regimens for advanced or recurrent cervical cancer.
- **Topotecan:** Topotecan is an option for patients with recurrent or metastatic cervical cancer who have previously received cisplatin-based chemotherapy.

2. Targeted Therapies:

- **Bevacizumab:** Bevacizumab is a monoclonal antibody that targets vascular endothelial growth factor (VEGF). It may be used in combination with chemotherapy for advanced or recurrent cervical cancer to inhibit blood vessel formation and tumor growth.

3. Immunotherapy:

- **Pembrolizumab:** Pembrolizumab is a programmed death receptor-1 (PD-1) immune checkpoint inhibitor. It is approved for the treatment of recurrent or metastatic cervical cancer that has progressed on or after chemotherapy.
- **Nivolumab:** Nivolumab, another PD-1 inhibitor, is approved for advanced or recurrent cervical cancer that has progressed on or after chemotherapy.

Drug protocols or regimens used in cervical cancer treatment may vary depending on the stage and extent of the disease. Some commonly used chemotherapy protocols include:

- **Concurrent Chemoradiotherapy:** Cisplatin administered concurrently with radiation therapy is the standard of care for locally advanced cervical cancer (Stage IB2 to IVA).
- **Neoadjuvant Chemotherapy:** Preoperative chemotherapy may be administered to downstage the tumor before surgery or chemoradiotherapy.
- **Adjuvant Chemotherapy:** After surgery or chemoradiotherapy, adjuvant chemotherapy may be given to reduce the risk of disease recurrence.
- Drug protocols and treatment regimens can vary based on individual patient factors, institutional practices, and ongoing clinical trials. (Tab 1)

Targeted therapy	Chemotherapy	Cervical cancer Stage/Type	Phase of trial	Preclinical/Clinical Trial Outcome
Bevacizumab	cisplatin + paclitaxel or topotecan + paclitaxel	Recurrent/persistent/metastatic	Randomized Phase III	Bevacizumab significantly improved overall survival compared with chemotherapy alone (1 months vs 13.3 months). No significant deterioration of health and quality of life reported
Cetuximab	cisplatin	Recurrent/persistent	Phase II	Adequately tolerated but cetuximab did not provide increased benefit beyond cisplatin therapy
	Cisplatin/topotecan	Advanced	Phase II	Induced a high rate of serious adverse and/or fatal events at standard dose and schedule. Cetuximab plus platinum-based

Table 1: Combination treatments of chemotherapy and targeted therapy in clinical trials for cervical cancer. BEHAVIOR BEFORE THE PATIENT WHO RESPONDS AND THEN FALLS TO THE TREATMENT

When a patient initially responds to treatment and then experiences a relapse or progression of the disease, it can be emotionally challenging for both the patient and their healthcare team. Here are some considerations regarding the behavior and approach in such situations:

- 1. Empathy and Emotional Support:** It is crucial to offer empathy, understanding, and emotional support to the patient and their family during this difficult time. Recognize and validate their feelings and concerns, and provide a compassionate environment that fosters open communication.
- 2. Clear Communication:** Maintain open and honest communication with the patient about the treatment response and the subsequent progression. Clearly explain the changes in the disease status, the available treatment options, and the goals of further therapy.
- 3. Reassessment and Evaluation:** A thorough reassessment of the patient's condition, including imaging studies and laboratory tests, should be performed to accurately determine the extent of disease progression. This evaluation helps guide decisions regarding further treatment options and the need for additional diagnostic tests.
- 4. Treatment Options:** Discuss the available treatment options based on the patient's individual situation, including the potential benefits, risks, and expected outcomes. Considerations may include additional chemotherapy regimens, targeted therapies, immunotherapy, participation in clinical trials, or palliative care to manage symptoms and improve quality of life.
- 5. Shared Decision-Making:** Involve the patient and their family in the decision-making process, taking into account their preferences, values, and treatment goals. Ensure they understand the potential benefits and limitations of each treatment option and support them in making informed decisions.
- 6. Supportive Care:** Implement supportive care measures to address the patient's physical, emotional, and psychosocial needs. This may involve pain management, symptom control, counseling services, and access to support groups or palliative care teams.
- 7. Multidisciplinary Collaboration:** Collaborate closely with a multidisciplinary team, including gynecologic oncologists, medical oncologists, radiation oncologists, palliative care specialists, and supportive care professionals. This collaboration helps ensure comprehensive care and coordination of treatment strategies.

Sex After Cervical Cancer

Having cervical cancer can affect your sexuality in various ways. Often people think that cancer can change your sexuality in physical ways, but often neglect the emotional ways as well. Your cancer and treatment can affect your sex life due to these physical and emotional changes.

You may experience low libido during or after treatment. A lack of interest or desire in sex is common during and after treatment due to the physical and emotional effects. This is totally okay and normal. You should talk to your partner about what you are feeling. It is normal to take time for sex to be comfortable again and you may experiment to find new ways to be intimate.

After being diagnosed with cervical cancer or going through treatment, you may be nervous to have sex. If you desire, you may return to a normal sex life a few weeks after finishing radiation therapy or surgery. It is important that you rest during the weeks following your treatment so that your body can heal. After those first few weeks, it is safe to have sex again.

It is important to know that sex will not make your cancer worse or increase the likelihood of it coming back. Additionally, cervical cancer is not infectious. You cannot give your partner cervical cancer. HPV, however, is infectious and can be linked to cervical cancer and other types of cancer. If HPV is a concern for you, talk to your doctor, and practice safe sex.

If you are receiving chemotherapy as a part of your treatment, you should use a condom if you decide to have penetrative sex as a precaution. It is unknown if any drugs used for cancer treatment come through cervical or vaginal mucus therefore they recommend using a condom to be safe.

The thought of starting your sex life again after diagnosis or treatment may make you nervous. You may feel anxious or depressed or worried and this may result in you not wanting to have sex. The important thing is giving yourself the time and space to come to terms with how you are feeling.

Sex can bring back emotional intimacy with your partner. If you can, it is important to have sex again. Couples who have sex often have healthier relationships. It helps to talk to your partner about how you feel and work out what is best for both of you. If you are interested, you can also find a sex therapist to help.

For most people, it just takes some time to return to a normal sex life after the diagnosis and treatment of cervical cancer.

Immunotherapy with Drugs Such as Pembrolizumab and Nivolumab

Immunotherapy with drugs such as pembrolizumab and nivolumab has emerged as an important treatment option for certain patients with advanced or recurrent cervical cancer. Here's an overview of the role of immunotherapy, including indications, responses, toxicity, and cost-benefit considerations:

- 1. Indications:** Pembrolizumab and nivolumab are immune checkpoint inhibitors that target the PD-1 pathway. They are indicated for the treatment of recurrent or metastatic cervical cancer that has progressed on or after chemotherapy. These drugs are typically used when the disease has not responded to standard chemotherapy or has recurred after initial treatment.
- 2. Responses:** Immunotherapy has shown promising response rates in a subset of patients with cervical cancer. While the response rates vary, some patients experience significant tumor shrinkage and prolonged disease control. However, it's important to note that not all patients respond to immunotherapy, and response rates can be influenced by various factors, including tumor characteristics and immune system status.
- 3. Toxicity:** Immunotherapy can have unique side effects known as immune-related adverse events (irAEs) due to the activation of the immune system. Common irAEs include fatigue, skin rashes, diarrhea, and inflammation of organs such as the lungs, liver, or thyroid. These side effects are typically managed with supportive care or immune-suppressing medications. Prompt recognition and management of irAEs are essential for patient safety.
- 4. Cost-Benefit Considerations:** The cost of immunotherapy with drugs like pembrolizumab and nivolumab can be high, as they are innovative and targeted therapies. The cost-benefit of immunotherapy should be evaluated on an individual basis, considering factors such as the patient's overall health, treatment goals, potential for response, and availability of alternative treatment options. It's important to discuss the cost and potential financial implications with the healthcare provider and explore available financial assistance programs or insurance coverage options.
- 5. Clinical Trials:** Participating in clinical trials evaluating immunotherapy and other novel treatments is an option for eligible patients. Clinical trials provide access to cutting-edge therapies and help advance the field of cervical cancer treatment.

Cure Rate, Survival and Disease-Free Survival

The cure rate, survival rates, and disease-free survival rates in cervical cancer vary depending on the stage of the disease at the time of diagnosis, the treatment received, and individual patient factors. Here are some general statistics:

1. Cure Rate: The cure rate refers to the percentage of patients who achieve long-term remission or are considered cured of cervical cancer. The cure rate is highest for early-stage cervical cancer and decreases as the disease advances. For stage IA and IB1 cervical cancer, the cure rate is relatively high, with many patients achieving long-term remission or cure with appropriate treatment.

2. Survival Rates: Survival rates indicate the percentage of patients who are still alive at a certain period after diagnosis. The five-year survival rate is commonly used to assess prognosis in cancer. Survival rates for cervical cancer vary based on the stage at diagnosis:

- Stage IA: The five-year survival rate is generally high, ranging from around 80% to 95%.
- Stage IB: The five-year survival rate is slightly lower than stage IA, ranging from approximately 65% to 85%.
- Stage II: The five-year survival rate for stage IIA is around 60% to 70%, and for stage IIB, it ranges from approximately 50% to 65%.
- Stage III: The five-year survival rate for stage IIIA is approximately 35% to 50%, and for stage IIIB, it ranges from around 25% to 35%.
- Stage IV: The five-year survival rate for stage IVA is typically below 20%, and for stage IVB (metastatic disease), it is around 5% to 15%.

3. Disease-Free Survival: Disease-free survival refers to the period during which a patient remains free of cancer recurrence or progression after completing treatment. The length of disease-free survival varies depending on the stage and aggressiveness of the disease, as well as the effectiveness of treatment. Patients with early-stage cervical cancer who receive appropriate treatment may have a higher chance of achieving longer disease-free survival.

It's important to note that these statistics are general estimates, and individual outcomes can vary widely. Numerous factors can influence prognosis, including tumor characteristics, age, overall health, response to treatment, and access to healthcare.

Conclusions

Cervical cancer is a significant health concern, and understanding its various aspects is crucial for effective management. Here are some key conclusions based on the topics we discussed:

1. Cervical cancer is defined as the abnormal growth of cells in the cervix, typically caused by persistent human papillomavirus (HPV) infection.
2. The staging of cervical cancer helps determine the extent of the disease and guides treatment decisions.
3. The histological types of cervical cancer include squamous cell carcinoma and adenocarcinoma, with squamous cell carcinoma being the most common.
4. HPV infection plays a significant role in the development of cervical cancer, with certain high-risk HPV strains being strongly associated with the disease.
5. Sexual promiscuity and having multiple sexual partners are risk factors for acquiring HPV infection, which can increase the risk of developing cervical cancer.
6. Early detection and prevention are essential in reducing the burden of cervical cancer. Pap smear screening and colposcopy are effective tools for early detection and can lead to timely interventions.
7. HPV vaccines are available and recommended for both males and females to prevent HPV infection and reduce the risk of developing cervical cancer. The cost of vaccines may vary, and access to them should be explored.
8. Diagnostic algorithms for cervical cancer typically involve a combination of physical examinations, Pap smears, colposcopy, and imaging studies such as tomography, magnetic resonance imaging (MRI), or positron emission tomography (PET).
9. Treatment for cervical cancer depends on the stage and may involve surgery (such as hysterectomy or trachelectomy), radiotherapy, chemotherapy (including concurrent chemoradiotherapy), and targeted therapies or immunotherapy in advanced or recurrent cases.

10. The cure rate, survival rates, and disease-free survival rates for cervical cancer vary depending on the stage of the disease, treatment received, and individual patient factors. Early-stage cervical cancer generally has higher cure and survival rates compared to advanced stages.

11. Immunotherapy with drugs like pembrolizumab and nivolumab has shown promise in the treatment of advanced or recurrent cervical cancer, with some patients experiencing positive responses. However, response rates can vary, and careful consideration of the cost-benefit ratio and potential side effects is necessary.

Overall, a comprehensive approach that includes prevention, early detection, and appropriate treatment strategies can significantly improve outcomes and quality of life for individuals affected by cervical cancer. Regular screenings, HPV vaccination, and timely medical intervention are crucial in combating this disease.

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