

Cervical Cancer, Version 2.2026

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Abstract

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Cervical Cancer provide diagnostic workup, staging, and various treatment recommendations for cervical cancer based on clinical and surgical staging. This selection from the NCCN Guidelines for cervical cancer specifically focuses on diagnosis and workup, principles of staging and surgery, and primary treatment recommendations for early-stage and advanced disease and provides a detailed overview of systemic therapy recommendations for cervical cancer.

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Overview

An estimated 13,360 new cases of carcinoma of the uterine cervix (ie, cervical cancer) will be diagnosed in the United States in 2025, and 4,320 people are estimated to die of the disease^{1,2} Although cervical cancer rates are decreasing in the United States after the introduction of screening, incidence remains high among Hispanic/Latino, Black, and Asian populations.^{3–6} The incidence rates of cervical squamous cell carcinoma are highest in Black and Hispanic individuals assigned female at birth (AFAB), while incidence rates of cervical adenocarcinoma are highest among Hispanic and White AFAB individuals.^{7,8} Overall, cervical cancer is a major world health problem for AFAB individuals. Globally in 2022, there were an estimated 661,021 cervical cancer cases and 348,189 deaths associated with cervical cancer.^{9,10} It is the fourth most common cancer in AFAB individuals worldwide, with 85% of cases occurring in developing countries where cervical cancer is a leading cause of cancer death in AFAB individuals.^{1,10–12} It is the most diagnosed cancer in 23 countries and the leading cause of cancer death in 36 countries.¹³

Squamous cell carcinoma (SCC), adenocarcinoma (AC), adenosquamous carcinoma (ASC) are the 3 common histologies of

cervical cancer. SCC accounts for approximately 80% and AC accounts for approximately 20% of all cervical cancers. In developed countries, the substantial decline in incidence and mortality of SCC of the cervix is presumed to be the result of effective screening and higher human papillomavirus (HPV)-vaccination coverage, although racial, ethnic, and geographic disparities exist.^{3,4,11–14}

However, ACs/ASCs of the cervix have increased over the past 3 decades, probably because cervical cytologic screening methods are less effective for AC/ASC because the lesions are located deeper than the ectocervix.^{15–19} The ASC subtype is rare and accounts for approximately 5%–6% of all cervical carcinomas. Presently, there is no difference in treatment between SCC and AC/ASC cervical cancer subtypes although the clinical features and prognosis of disease vary considerably between these subtypes.

Persistent HPV infection is the most important factor in the development of cervical cancer.^{20,21} The incidence of cervical cancer appears to be related to the prevalence of HPV in the population. In countries with a high incidence of cervical cancer, the prevalence of chronic HPV is approximately 10%–20%, whereas

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To view disclosures of external relationships for the NCCN Guidelines panel, go to <https://www.nccn.org/guidelines/guidelines-panels-and-disclosure/disclosure-panels>

The full NCCN Guidelines for Cervical Cancer are not printed in this issue of JNCCN. The complete and most recent version of these guidelines is available free of charge at NCCN.org.

NCCN CATEGORIES OF EVIDENCE AND CONSENSUS

Category 1: Based upon high-level evidence (≥ 1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus ($\geq 85\%$ support of the Panel) that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus ($\geq 85\%$ support of the Panel) that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus ($\geq 50\%$, but $< 85\%$ support of the Panel) that the intervention is appropriate.

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise indicated.

NCCN recognizes the importance of clinical trials and encourages participation when applicable and available.

Trials should be designed to maximize inclusiveness and broad representative enrollment.

PLEASE NOTE

The NCCN Guidelines® are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult the NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network® (NCCN®) makes no representations or warranties of any kind regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

NCCN CATEGORIES OF PREFERENCE

Preferred intervention: Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.

Other recommended intervention: Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.

Useful in certain circumstances: Other interventions that may be used for selected patient populations (defined with recommendation).

All recommendations are considered appropriate.

the prevalence in low-incidence countries is 5%–10%.¹⁵ Screening methods using HPV testing may increase detection of adenocarcinoma. Immunization against HPV prevents infection with the types of HPV against which the vaccine is designed and, thus, is expected to prevent specific HPV cancer.^{22–29} HPV vaccines may also decrease the incidence of both SCC and AC.^{17,30} Although a majority of studies report that most cervical cancers are caused by HPV, around 5% of the tumors are reported as HPV-independent tumors.^{31,32} Other epidemiologic risk factors associated with cervical cancer are a history of smoking, parity, oral contraceptive use, early age of onset of coitus, larger number of sexual partners, history of sexually transmitted disease, certain autoimmune diseases, and chronic immunosuppression.^{33–35} Smoking cessation should be advised in current smokers, and former smokers should continue to avoid smoking (see the NCCN Guidelines for Smoking Cessation at NCCN.org and <http://smokefree.gov/>).

In 2020, the WHO updated the “Female Genital Tumors” classification of cervical cancer by subdividing cervical cancer lesions into HPV-associated and HPV-independent tumors based on the new pathologic findings.³⁶ Among these, the HPV-associated SCC is the most prevalent subtype, with very rare occurrences of the HPV-independent SCC subtype. The HPV-independent AC has a less favorable prognosis as compared with HPV-associated tumors. The NCCN Cervical Cancer Guidelines panel acknowledges that although the prior versions of the WHO classification discussed these tumors based on morphologic features, the integration of the immunohistochemical and molecular profiles has led to a better classification system that is now adapted in the 2020 WHO Classification of Female Genital Tumors for cervical cancer.³⁶ Regardless of cancer subtype and HPV infection status, primary treatment with curative intent for patients with cervical cancer typically consists of surgery, chemoradiation, or a combination of these treatments; options vary by cancer stage. By definition, the NCCN Guidelines cannot incorporate all possible clinical variations and are not intended to replace good clinical judgment or individualization of treatments. “Many exceptions to the rule” were discussed among the members of the Cervical Cancer panel during the process of developing these guidelines.

Diagnosis and Workup

These NCCN Guidelines discuss SCC, ASC, and AC of the cervix. The primary workup for small cell neuroendocrine carcinoma is discussed in “Small Cell Neuroendocrine Carcinoma of the Cervix (NECC)” section in the complete version of the NCCN Guidelines for Cervical Cancer at NCCN.org. Glassy-cell carcinomas, sarcomas, and other histologic types are not within the scope of these guidelines.

The earliest stages of cervical carcinoma may be asymptomatic or associated with a watery vaginal discharge and postcoital bleeding or intermittent spotting. Often these early symptoms are not recognized by the patient. Because of the accessibility of the uterine cervix, cervical cytology or Papanicolaou (Pap) tests and cervical biopsies can usually result in an accurate diagnosis. Cone biopsy (ie, conization) is recommended if the cervical biopsy is inadequate to define invasiveness or if accurate assessment of microinvasive disease is required. The shape and depth of the cone biopsy may be tailored to the size, type, and location of the neoplastic lesion. For example, if there is concern for invasive adenocarcinoma versus adenocarcinoma in situ in the cervical canal, the cone biopsy would be designed as a narrow, long cone extending to the internal os in order not to miss possible invasion in the endocervical canal. Length of the cold cone of at least 10 mm is preferred and can be increased to 18 to 20 mm in patients who have completed childbearing.³⁷ However, cervical cytologic screening methods are less useful for diagnosing adenocarcinoma, because adenocarcinoma in situ affects areas of the cervix that are harder to sample (ie, endocervical canal).^{18,38}

Workup for these patients with suspicious symptoms includes history and physical examination, CBC, including platelets, and liver and renal function tests (Figure 1). Recommended radiologic imaging includes pelvic MRI, neck/chest/abdomen/pelvis/groin FDG-PET/CT, chest radiograph, CT, or combined PET/CT, and MRI as indicated (eg, to rule out disease high in the endocervix). For detailed imaging recommendations by stage and planned treatment approach, see “Principles of Imaging” in the complete version of these guidelines (available at NCCN.org). Smoking cessation and counseling, as well as HIV testing (especially in younger patients), are recommended. Cystoscopy and proctoscopy are only recommended if bladder or rectal extension is suspected based on symptoms, barrel-shaped lesions,