Cervical cancer

Summary Article: Cervical Cancers
from Encyclopedia of Cancer

Definition
The regions of the uterus are the corpus and the cervix. Cancer originating from the cervix is defined as cancer of the cervix. When cancers are simultaneously detected in the cervix and corpus, squamous cell carcinoma (SCC) is designated as a cancer of the cervix and adenocarcinoma is designated as a cancer of the corpus. When cancer occupies both the cervix and vagina without the junctional area (the fornix), the cancer extending to the exocervix is recognized as a cancer of the cervix. Thus, cervical cancer is defined apart from cancer of the uterine corpus (cancer of the uterine endometrium) and cancer of the vagina.

Characteristics
The main gynecological cancers originate from the cervix, endometrium, and ovary. Among them, cervical cancer is the most common malignancy in women. The main risk factors are:

- Young age at first intercourse, especially shortly after the menarche
- High number of sexual partners
- High number of sexual partners of the partner
- High number of children
- Excessive douching

Smoking appears to increase the incidence of SCC, but not of adenocarcinoma or adenosquamous carcinoma. Immunosuppression by smoke-derived nicotine and its metabolite cotinine in the cervical mucus may enhance the effects of sexually transmitted disease (STD) including human papillomavirus (HPV) infection. Most epidemiological risk factors for cervical cancer are associated with STDs. HPV induces an STD, human venereal condyloma, which is associated with cervical, vaginal, and vulvar dysplasia, and invasive carcinomas. HPV particles and DNA, especially HPV-16, HPV-18, and HPV-33, are detected in cervical and vulvar dysplasia and in invasive carcinomas. Additionally, it has been demonstrated that HPV transforms human cell lines. HPV infection of the cervix is a main etiology of cervical cancer.

Symptoms
Main symptoms of cervical cancer are

- Vaginal bleeding, which may be recognized as postmenopausal bleeding, irregular menses, or postcoital bleeding
- Abnormal vaginal (watery, purulent, or mucoid) discharge

In advanced cases, corresponding local symptoms occur. A Pap smear even in unsymptomatic cases is
useful for the early detection of cervical dysplasia and cancers. Among women over the age of 18 who have had sexual intercourse, high-risk women should be screened at least yearly.

**Pathology**

Histopathological types in cervical cancers are mainly SCC and adenocarcinoma, which account for about 90% of all cervical cancers (adenosquamous carcinoma, glassy cell carcinoma, adenoid cystic carcinoma, adenoid basal carcinoma, carcinoid, small cell carcinoma, and undifferentiated carcinoma also occur). SCCs are keratinizing or nonkeratinizing in most cases and may be verrucous, condylomatous, papillary, or lymphoepithelioma-like carcinomas in a few cases. Adenocarcinomas are classified into mucinous, endometrioid, clear cell, serous, and mesonephric adenocarcinomas; mucinous adenocarcinomas are subclassified with endocervical type into adenoma malignum and villoglandular papillary adenocarcinoma, and intestinal type adenocarcinoma.

**Staging**

Clinical staging represents the degree of advancement of the tumor, and is defined by the FIGO classification established in 1994 and by the TNM classification of malignant tumors set by the UICC in 1997 as follows (classified by FIGO [TNM]):

- **Stage 0 (Tis):** carcinoma in situ (preinvasive carcinoma)
- **Stage I (T1):** cervical carcinoma confined to the uterus
- **Stage II (T2):** tumor invades beyond the uterus but not to the pelvic wall or to the lower third of the vagina
- **Stage III (T3):** tumor extends to the pelvic wall and/or involves the lower third of the vagina and/or causes hydronephrosis or nonfunctioning kidney
- **Stage IVA (T4):** tumor invades the mucosa of the bladder or rectum and/or extends beyond the true pelvis
- **Stage IVA (M1):** distant metastasis

Stage IA (T1a) has been further classified by microinvasive depth and width into stage IA1 (T1a1) (depth of stromal invasion ≤3 mm, horizontal spread ≤7 mm) and stage IA2 (T1a2) (depth of stromal invasion >3 mm, ≤5 mm; horizontal spread ≤7 mm). Stage IB (T1b) has been further classified by tumor size into stage IB1 (T1b1) (greatest dimension ≤4 cm) and stage IB2 (T1b2) (greatest dimension >4 cm). In cases staged IA2 (T1a2) or less advanced, colposcopically directed biopsy in the transformation zone of the cervix, endocervical curettage, or cervical conization are required.

**Prognosis**

Unfavorable prognostic factors include younger age, advanced clinical stage, certain histopathological types, vessel permeation, large tumor volume, parametrium involvement, and lymph node metastasis. Nodal metastasis is an especially critical prognostic factor after curative resection. Vascular endothelial growth factor (VEGF)-C and osteopontin contribute to the aggressive lymphangitic metastasis in uterine cervical cancers. Platelet-derived endothelial cell growth factor (PD-ECGF) contributes to the advancement of metastatic lesions as an angiogenic factor. PD-ECGF, VEGF-C, and osteopontin levels in metastatic lesions are prognostic indicators. Furthermore, serum PD-ECGF level reflects the status of advancement of cervical cancers and is recognized as a novel tumor marker for both SCC and

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adenocarcinoma of the cervix, while the tumor marker SCC is well known only as an indicator for SCC of the cervix. VEGF-C and osteopontin contribute to the aggressive lymphangitic metastasis in uterine cervical cancers.

**Therapy**

The treatment for cervical cancer consists mainly of surgery and radiation. Chemotherapy is performed in combination with surgery and/or radiation for advanced cases, and immunotherapy is an adjuvant treatment for surgery, radiation, and chemotherapy. The standard treatment for carcinoma in situ is cervical conization or total hysterectomy. The standard treatment for microinvasive carcinoma stage IA (T1a) is modified radical hysterectomy regardless of regional lymphadenectomy. The standard surgical treatment for invasive carcinoma is radical hysterectomy with regional lymphadenectomy. Although oophorectomy can be avoided in some cases during the reproductive period, ovarian metastasis must be considered especially in adenocarcinoma of the cervix. When oophorectomy is avoided, the ovary is better shifted out of radiation area. For patients who undergo oophorectomy, hormone replacement therapy can be useful. In more advanced cases, extended radical hysterectomy or pelvic exenteration is appropriate. After surgery external irradiation is followed in some cases. The standard radiotherapy without surgery for invasive carcinoma is intracavitary and/or external irradiation. Recently, neoadjuvant therapy (chemotherapy) has been tried in order to make surgery more successful, and concurrent radio-chemotherapy has been tested for the purpose of enhancing the effect of radiation.

**References**


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