MAYO CLINIC

Screening Women at High Risk for Cervical Cancer: Special Groups of Women Who Require More Frequent Screening

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Abstract

The updated cervical cancer screening guidelines recommend that women at average risk who have negative screening results undergo cervical cytological testing every 3 to 5 years. These recommendations do not pertain to women at high risk for cervical cancer. This article reviews recommendations for cervical cancer screening in women at high risk.

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Since the advent of cervical cytological testing for cervical cancer screening, the incidence and mortality rates associated with cervical cancer have significantly decreased.[1] In the United States in 1975, the incidence of cervical cancer was 14.8 and the mortality rate was 5.55 per 100,000 women; these statistics have improved to an incidence of 6.7 and a mortality rate of 2.3 per 100,000 in 2011.[2] This improvement was seen in women receiving regular cervical cancer screening.

In 2012, the American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology provided consensus guidelines for

cervical cancer screening.[3] These guidelines recommend that women aged 21 to 29 years be screened with cervical cytological testing every 3 years and with reflex human papillomavirus (HPV) testing for women older than 25 years.[4] Reflex HPV testing is an easily performed add-on test of the residual cytology liquid, if the cytological results indicate abnormalities. It is preferred that women aged 30 to 65 years undergo *cotesting*—cervical cytological testing and testing for high-risk HPV—every 5 years. If cotesting is not available, cervical cytological testing every 3 years is an acceptable alternative.[2,3,5] Cervical cancer screening can be discontinued in women at age 65 years if they had adequate negative results of screening on 3 consecutive tests or 2 negative cotesting results in the past 10 years.[3,6]

These guidelines, however, are for women at average risk for cervical cancer and do not pertain to women who are at increased risk. Certain medical conditions place women at a higher risk for cervical cancer, such as solid organ or stem cell transplants, human immunodeficiency virus (HIV) infection, in utero exposure to diethylstilbestrol (DES), personal history of cervical dysplasia or cervical cancer, and immunosuppression from other causes. Several existing guidelines provide recommendations for screening in some of these high-risk women. With regard to immunosuppression, only HIV-positive women have been evaluated extensively enough to provide data-driven recommendations; recommendations for other women with immunosuppression are extrapolated from those for HIV-positive patients. The aim of this concise review is to discuss the screening recommendations for these women at higher risk for cervical cancer.

HPV INFECTION IN HIGH-RISK WOMEN

Human papillomavirus is transmitted by skin and genital contact and is found in 99.7% of all invasive cervical cancers, and it is considered to be essential for cervical cancer development.[7] Persistent infection with the highly oncogenic types of HPV is strongly associated with the development of cervical cancer.[8,9] High-risk HPV subtypes 16, 18, 31, 33, and 35 are most commonly associated with genital carcinomas (cervical, vaginal, vulvar, and anal), with subtypes 16 and 18 causing more than 70% of the cervical cancers.[10] Fortunately, this infection is transient in most immunocompetent women, clearing in 70% by 12 months and in 91% by 24 months (median duration, 8 months).[11] As in women at average risk, the individual risk of HPV infection in women at high risk depends on sexual behavior and the number of sexual partners.[8] Of note, HPV infection has been identified in many women in lifelong monogamous relationships and is now considered the most common sexually transmitted infection.

CERVICAL CANCER SCREENING IN WOMEN WITH SOLID ORGAN OR STEM CELL TRANSPLANTS

Recipients of solid organ and stem cell transplants now have longer life expectancy. As a result, secondary cancers are becoming more common in this patient population.[12] Carcinomas found to occur most commonly in the stem cell transplant group are those associated with HPV (cancers of the vulva, vagina, cervix, and anal area).[9]

Although women who require immunosuppressant medications after transplant are not at a higher risk for acquiring new HPV infections,[8] they have decreased capacity for viral clearance if they are newly infected with HPV and have an increased risk of reactivation of latent infection.[8-14] Several factors affect immunity and viral clearance, including the duration of immunosuppressant therapy, number and dosing of immunosuppressant medications, history of ionizing radiation and/or chemotherapy, and age.[8,9,12] Once infected with HPV, immunosuppressed women have higher viral loads than immunocompetent women.[12]

Renal transplant recipients have a higher prevalence of both cervical and anal dysplasia.[11] After kidney transplant, women are at a 50-fold increased risk for vulvar cancer and a 15-fold increased risk for cervical cancer.[13] DNA damage caused by most immunosuppressants, altered DNA repair, and reduced immunologic tolerance account for the increased incidence of cancers in posttransplant patients.[1] The calcineurin inhibitor class of medications (cyclosporine and tacrolimus) most likely increases cancer incidence through promotion of angiogenesis and production of cytokines.[1] Therefore, cervical cytological testing and HPV testing are recommended