Updates in Cervical Cytology

The 90-Year-Long Journey from Battle Creek to Today

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KEYWORDS

• Pap test • HPV testing • ASCCP guidelines • The Bethesda System • HPV vaccine

Key points

- Major improvements have been made to the "Pap test" since Papanicolaou first introduced exfoliative cytology for the diagnosis of cervical cancer and its precursors.
- Discovery of causal association between cervical cancer and human papilloma virus (HPV) infection opened the door for molecular tests for detection of HPV DNA.
- Several immunomarkers have been studied to increase the sensitivity and specificity of cervical cytology for detection of high-grade squamous intraepithelial lesion.
- A standardized terminology and reporting system, The Bethesda System, was first implemented in 1988 and has undergone 4 revisions.
- Advancements in cervical cancer screening, detection, and reporting led to implementation of the 2012 consensus guidelines for the management of women with abnormal cervical cancer screening test.

ABSTRACT

Ninety years ago, at the Battle Creek conference, Papanicolaou introduced cervical exfoliative cytology. Since then, the "Pap test" has come a long way. The discovery of a causal relationship between cervical carcinoma and HPV infection opened the door for molecular testing and immunomarkers for HPV. The Clinical Laboratory Improvement Amendments, 1988, established quality assurance and quality control programs to monitor performance of cytology laboratories. The Bethesda System for reporting cervical cytology laid the foundations for cervical cytology education, implementation of management guidelines, and further research on cervical carcinogenesis. HPV vaccine penetration in both genders remains 62% or less.

UPDATE ON CERVICAL CANCER SCREENING AND REPORTING

CERVICAL CANCER SCREENING IN THE UNITED STATES

Statistics

The National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) Program

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compiles a statistics fact sheet composed of survival statistics, prevalence, stage at diagnosis, and changes over time regarding cervical cancer.[1] According to their data, in 2014 there were an estimated 256,078 women living with cervical cancer in the United States, and approximately 0.6% of women will be diagnosed with cervical cancer at some point in their lifetime. The risk factors for development of cervical cancer correlate with the risk factors for acquiring human papillomavirus (HPV), which include number of sexual partners and immunocompromised states.

There were an estimated 12,820 new cases of cervical cancer in 2017 (0.8% of all new cancer cases), and 4210 deaths as a result (0.7% of all cancer deaths). Compared with other cancer cases and subsequent deaths, cervical cancer comprises a small subset. The number of deaths from cervical cancer over all races was 2.3 women per 100,000 per year from 2010 to 2014. Looking specifically at races, the number was highest for African American women at 3.8 per 100,000 women dying of cervical cancer and lowest for Asian/Pacific Islanders at 1.7 women per 100,000. Many more women, however, are diagnosed with cervical cancer than die as a result of it. Based on 2010 to 2014 cases, the number of new cases of cervical cancer was 7.4 per 100,000 women per year, with 49 being the median age of diagnosis. Regarding extent at diagnosis, almost half (45.7%) of cervical cancers are detected early. Diagnosis at a low stage has a 5-year survival of 91.5%, evincing the numerical distinction between the number of women with new diagnoses of cervical cancer and those who die from the disease.

Based on 2007 to 2013 data, the overall 5-year survival for cervical cancer is 67.1%.[2] According to the SEER Program statistical analysis, rates for new cervical cancer cases have not changed significantly over the past 10 years, but death rates have been falling on average 0.8% each year over 2005 to 2014.[1] Attempts to combat the rate of cervical cancer include screening compliance and concurrent development and adherence to appropriate screening guidelines. Additional factors include HPV testing and cervical cytology detection and diagnosis, along with HPV vaccine utilization and efficacy.

Compliance with Screening

Within the past 3 years, an estimated 14 million women aged 21 to 65 had not been screened for cervical cancer. Watson and colleagues,[3] using 2015 National Health Interview Survey data to examine recent cervical cancer screening practices, found that 81.1% of eligible women reported having a Pap test within 3 years. Women without a usual source of income, women without health care, and recent immigrants to the United States had lower odds of being up to date with screening.[4,5] These studies highlight the factors that make adherence to screening guidelines difficult, such as lack of access to health care and low income.

It is additionally problematic that the United States has no national cervical cancer screening program. Screening is then opportunistic, as evidenced by studies showing low income and lack of access to health care prevent women from being up to date with screening. There is also an issue with providers not necessarily following updated screening guidelines, as well as algorithms that might be deemed confusing to follow. Additionally, without a national screening program conveying an overlying message, women may receive varying viewpoints from providers regarding cervical cancer screening and prevention.[2] Such issues delineate the trends causing declines in cervical cancer screening compliance, which is falling below the *Healthy People 2020* goal of 93%.[6]

CERVICAL CANCER SCREENING GUIDELINES: RECENT UPDATES

BASIC PRINCIPLES

The objectives of screening for cervical cancer are to prevent morbidity and mortality from the disease and prevent overtreatment of precursor lesions that will most likely regress. When cervical cancer screening guidelines were established, the emphasis was placed on detecting persistent high-risk HPV (hr-HPV) infection, cervical intraepithelial neoplasia 3 (CIN3), CIN2 in older women, and persistent CIN2 or CIN3. Fundamentals of cervical cancer screening are based on accepting minimal risk, because no screening test is 100% sensitive, and because zero risk cannot be achieved. The optimal balance between benefit and harm is achieved by screening at the least frequent interval. Women with a comparable risk for cancer (CIN3) should be managed similarly, regardless of how the risk is assessed. In 2001, The American Society of Colposcopy and Cervical Pathology (ASCCP) initiated the implementation of a comprehensive, evidence-based consensus guidelines for the clinical management of women diagnosed with abnormal cervical cytology. Since then, several revisions of these guidelines were implemented, as knowledge on the biology of cervical cancer in various age groups has expanded.