New guidelines redefine the role of HPV testing in cervical cancer prevention

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In January 2016, the American College of Obstetricians and Gynecologists (ACOG) released a practice bulletin and provided guidance supporting the use of an FDA-approved human papillomavirus (HPV) test for first-line cervical cancer screening (primary HPV screening) in women age 25 and older as an alternative to current cytology-based screening methods.¹

ACOG’s guidance culminated more than 50 years of continuing progress led by the introduction of the Pap test and the attendant steady decline in the incidence of cervical cancer. More recently, increased understanding of the role of HPV in cervical cancer development has shed new light on how HPV testing can be integrated into cervical cancer screening, with the goal of identifying patients at risk earlier while reducing overtesting and unnecessary interventions.²

TheAddressing the Need for Advanced HPV Diagnostics (ATHENA) trial, a three-year prospective study of more than 47,000 women, concluded that HPV primary screening in women 25 years and older is as effective as a hybrid screening strategy that uses cytology for the 25-to-29 age group and co-testing for women 30 years and older.³ Based on ATHENA and corroborating studies from around the world, the FDA approved a high-risk HPV test (cobas HPV Test, Roche Diagnostics) for use in primary HPV screening in 2014. The following year, interim guidance was published by a panel of eight experts representing the Society of Gynecologic Oncology (SGO), the American Society for Colposcopy and Cervical Pathology (ASCCP) and five other professional associations. The guidance supports primary HPV screening, using an FDA-approved test, in women 25 years and older as an alternative to current U.S. cytology-based cervical cancer screening.⁴

HPV primary screening and patient care

Prompted by the joint interim guidance and my own clinical experience, our practice began using HPV primary screening for patients 25 years and older in 2015. For patients who test positive for genotypes 16 and 18, which account for 70% of cervical cancer,⁵ we proceed directly to colposcopy. Patients who test positive for other high-risk genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) receive a Pap test. A positive Pap test is followed by colposcopy.

Clinical rationale

As a clinician, my goal is to identify patients at risk early enough to slow or halt disease progression. In the case of younger patients, early detection also means less invasive interventions that can spare the patient from future conception problems. The sharp rise in the incidence of invasive cervical cancer between the ages of 25 and 34, as shown by data from the National Cancer Institute’s SEER Tumor Registry,⁶ prompted me to reassess the previous co-testing algorithm—cytology only for 21- to 29-year-old women and co-testing in women over 30 years of age— and to consider the added value of primary HPV screening, especially in the 25-to-29 age group.

Figure 1: The use of HPV 16/18 genotyping and reflex cytology for women positive for the 12 other hrHPV genotypes achieves a reasonable balance of disease detection with the number of screening tests and colposcopies required to achieve that detection.⁷

Sensitivity is key to identifying more women at risk. The ATHENA trial demonstrated that over three years, primary HPV screening has the highest sensitivity for the detection of CIN3 in the 25-to-29 age group, compared to cytology alone.³ For women concerned about conception in the future, early detection is especially important as it may help avoid more invasive interventions such as the loop electrosurgical excision procedure (LEEP). Topical trichloroacetic acid is another efficacious, simple and noninvasive option.⁸

A third reason for our choice of primary HPV screening was the significantly greater negative predictive value of the hrHPV test evaluated in the ATHENA trial, compared to cytology. This means that a negative hrHPV test result provides greater assurance of low CIN3+ risk than a negative cytology result.⁹

HPV testing in everyday practice

Implementing primary HPV screening is something our practice had considered for several years, as I had personal knowledge of it from my European colleagues. The availability of an FDA-approved hrHPV test indicated for primary screening made it possible, and the support of professional societies reinforced our decision. It should be noted that both ACOG and the joint SGO/ASCCP interim guidance specify the use of a test that is FDA-approved for primary HPV screening, not just co-testing and ASC-US reflex.

Beyond the clinic

Any discussion of cervical cancer screening and prevention should not leave unmentioned the fact that 50% of cervical cancer is found in women who have had either no screening or inadequate screening in the past 10 years. This is a public health issue that...
cannot be neglected and one that stands in the way of eradicating cervical cancer.

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References