What is the prevalence of cervical cytologic abnormalities and high-risk HPV in the screened population?

The prevalence of abnormalities was 7.1% and the prevalence of high-risk human papillomavirus (HPV), HPV 16, and HPV 18 was 12.6%, 2.8%, and 1.0%, respectively, in the ATHENA prospective evaluation of more than 45,000 women. Notably, the prevalence of both cytologic abnormalities and high-risk HPV positivity decreased with increasing age; high-risk HPV was detected in 31% of women 21 to 24 years old, 7.5% of women 40 to 44 years old, and 5% of women older than 70 years, for example.

After adjustment, the prevalence of cervical intraepithelial neoplasia (CIN) 2 or greater among women 25 to 34 years old was 2.3%; it declined to 1.5% among older women.


EXPERT COMMENTARY
Rachel Kupets, MD, Assistant Professor, Division of Gynecologic Oncology, University of Toronto, Toronto, Ontario.

Details of the ATHENA study
The study was designed to evaluate the cobas HPV test (Roche), a new polymerase chain reaction–based DNA test that yields a pooled result for 12 high-risk HPV types as well as individual results for HPV 16 and HPV 18.

The Pap test wrought a sea change in the medical profession’s approach to cervical cancer screening, dramatically lowering the rate of invasive cervical cancer among women who underwent the test on a regular basis. That said, the sensitivity of a single Pap test in the detection of cervical dysplasia or cancer is less than 60%.1

It is well established that oncogenic HPV strains, otherwise known as high-risk HPV infection, are responsible for the development of severe preinvasive dysplasia and cervical cancer. Munoz and colleagues identified subtypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 73 as having the greatest oncogenic potential.2 They also noted that HPV 26, 53, and 66 are probably carcinogenic.2

HPV DNA diagnostic tests are available to identify 14 high-risk HPV types. Current guidelines from the American Society for Colposcopy and Cervical Pathology (ASCCP) recommend both cytology and HPV testing to determine the optimal interval between screening tests and for triage to colposcopy.3 HPV DNA diagnostic tests have evolved one step further and can now detect HPV 16 and HPV 18 individually; these two types of HPV account for 70% of all cervical cancer cases.4 Research is needed to determine what combination of tests will further improve outcomes in the screened population.
lesions or malignancy (NILM)
• as a potential first-line test in the screening of women 25 years and older, regardless of the cytology result.
The primary endpoint in all three scenarios was to detect CIN 2 or greater.

The baseline results of this study are outlined above. Data from a 3-year follow-up of the women in the ATHENA study will be published at a future date.

Other screening studies are under way
Now that we have identified HPV as the cause of cervical cancer, researchers can investigate the best way to detect high-grade CIN. Published studies have determined that HPV testing is more sensitive and less specific than the Pap test in the detection of CIN 3 and cancer.5

The HPV FOCAL trial is under way to establish the efficiency of testing for high-risk HPV DNA as primary screening and as triage in three arms. In all three arms, CIN 3 is the outcome.1

ATHENA adds a second tier to similar studies by genotyping for HPV 16 and 18.

Unanswered questions
There is no doubt that the Pap test will be replaced as a stand-alone screening test for cervical cancer. Existing ASCCP guidelines already recommend HPV testing in patients who have normal cytology; it remains to be determined how testing specifically for HPV 16 and 18 will be incorporated into the algorithm. The ATHENA trial, and others like it, will be the basis of future cervical cancer screening guidelines.

Among the issues that need to be resolved are:
• the age at which testing for HPV 16 and 18 is appropriate
• the follow-up protocol for women who test positive for HPV 16 and 18, as well as for those who test negative
• the cost of adding testing for HPV 16 and 18 to screening

WHAT THIS EVIDENCE MEANS FOR PRACTICE
The findings of the ATHENA study do not alter current cervical cancer screening guidelines—yet. Until the most effective strategy of incorporating HPV 16 and 18 genotyping into screening is determined, you should follow current ASCCP guidelines. Algorithms for different abnormal cytologic findings are available at http://www.asccp.org/Portals/9/docs/pdfs/Consensus%20Guidelines/algorithms_cyto_07.pdf

References