Transcript Details

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ReachMD

www.reachmd.com

info@reachmd.com

(866) 423-7849

Individual Detection of 14 High-risk HPV Genotypes by the PapType Test for the Prediction of High-grade Cervical Lesions

Review by Mark H. Einstein, MD, MS

Interpretation:

A recent article published by Cuzick and colleagues in the *Journal of Clinical Virology* has helped clarify the value of extended HPV genotyping in triage of high-risk HPV (hrHPV) positive women. In addition to routinely assessed HPV 16 and 18, HPV genotypes 11, 31, 33, 35, 45, 51, 52, 56, 58, 59, 66, and 68 were also evaluated as predictors for development of high-grade cervical lesions.

The authors evaluated *PapType*, a commercially available test designed to perform individual genotyping for hrHPV types in a single assay. They compared the rate of hrHPV detection and the accuracy of CIN2+ prediction between *PapType* and other commercially available tests. A critical question was *what is the benefit of extended genotyping in the triage setting*? More specifically, *might the incorporation of extended genotyping into screening algorithms lead to potentially better outcomes with regard to assessing a woman's risk for developing a high-grade cervical lesion*?

Previously-collected samples from 1099 women referred for abnormal cervical cytology taken at the time of colposcopy were assessed. DNA was extracted and tested with *PapType* and other widely available commercial HPV tests. The main outcome measures were sensitivity, specificity, and positive predictive value (PPV).

A hierarchy of hrHPV genotypes was constructed based on relative PPV for developing a high-risk cervical lesion. The performance of *PapType* was similar to other DNA-based assays, with a specificity of 22.4% and a sensitivity of 94.6%. There was also good agreement with other sensitive assays for overall hrHPV genotype detection, PPV for CIN2+, and detection of HPV 16 and 18.

Based on PPV, hrHPV genotypes clustered into 3 hierarchical groups. Group A was very highly predictive and contained HPV 33 and HPV 16; Group B was highly predictive and contained HPV 31, 18, 52, 35, 58, and 51; and Group C had intermediate prediction and contained HPV 68, 45, 39, 66, 56, and 59. Use of this classification doubled the specificity to 44.5% but only slightly reduced sensitivity for CIN2+ and CIN3+ to 91.5% and 94.0%, respectively.

Cuzick and colleagues concluded that the diagnostic performance and genotyping accuracy of *PapType* were found to be comparable to other assays using well-documented routine clinical samples. HPV 18 and HPV 45 ranked lower than previously cited for cancer risk; and HPV 33 was associated with a PPV for CIN2+ as high as HPV 16 and substantially more predictive than HPV 18 or other genotypes.

The authors believe further prospective validation of the role of HPV 33 as a differentiating cervical cancer screening test should be explored, as well as the usefulness of employing a hierarchical HPV grouping to improve the triage of women who are hrHPV positive.

In a related publication from Joura and colleagues in *Cancer Epidemiology, Biomarkers and Prevention*, the study demonstrated that 7 carcinogenic high-risk HPV types included in the 9-valent HPV vaccine were attributed to 43-55% of CIN 1, 70-78% of CIN 2, 85-91% of CIN 3, and 95-100% of adenocarcinoma in situ. Further, they reinforced the value of HPV immunization in reducing risk for developing high-grade cervical lesions. Of note, more than half of women who developed CIN2+ or worse had a normal pap at study entry, *strongly supporting the body of evidence establishing* high-risk *HPV testing as an important part of cervical cancer screening*.