The role of human papillomavirus testing after treatment for high-grade cervical dysplasia

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The introduction of human papillomavirus (HPV) testing into cervical cancer screening programs has significantly improved the detection of premalignant lesions and continues to improve the detection and prevention of invasive cervical cancer. The results of 4 large trials successfully demonstrated higher detection rates of cervical intraepithelial neoplasia (CIN) 3 with HPV-based screening compared to cervical cytology [1-5], and a recent meta-analysis of long term follow up in those trials demonstrated 60% to 70% greater protection against invasive cancer compared to cytology screening [6]. While the role of HPV screening is well established with well-conducted randomized controlled trials, there are fewer consensuses regarding the utility of HPV testing after treatment for premalignant cervical lesions. Typically, CIN 2/3 lesions are treated with excisional or ablative procedures, and post-treatment these women are then entered into more intensive surveillance protocols. Post-treatment surveillance targets an important population, as women treated for CIN 2/3 have nearly a 300% greater risk of developing invasive cancer over the subsequent 20 years [7]. Two articles in this issue provide significant data to support the role of HPV testing after treatment for high-grade dysplasia. In “A human papillomavirus (HPV)-16 or HPV-18 genotype is a reliable predictor of residual disease in a subsequent hysterectomy following a loop electrosurgical excision procedure for cervical intraepithelial neoplasia 3” in volume 27, e2.

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See the article “Posttreatment human papillomavirus testing for residual or recurrent high-grade cervical intraepithelial neoplasia: a pooled analysis” in volume 27, e3.
residual or more advanced disease after LEEP for CIN 3 and demonstrates the clinical utility of HPV testing in this setting.

“Posttreatment human papillomavirus testing for residual or recurrent high-grade cervical intraepithelial neoplasia: a pooled analysis” by Onuki et al. [9] utilizes different methodology to lend the same support to posttreatment screening. A systematic review of 33 articles published between 1996 and 2013 found 5,319 cases; each case had been treated for CIN 2/3+, was tested for HPV within 12 months, and documented the presence or absence of CIN 2/3+ in follow-up. The rate of CIN 2/3+, either recurrent or residual, was 8.4%. The sensitivity of HPV testing was significantly better than ASCUS+ cytology threshold (0.92 vs. 0.76). More importantly, the negative predictive value of HPV testing alone was 0.99 with a 95% CI of 0.99 to 1.00. In addition, the presence of disease at the excisional margin did not significantly affect the sensitivity or specificity of carcinoigenic HPV testing. The authors evaluated both cytology and HPV testing alone and in combination, for risk stratification of residual/recurrent CIN 2/3+ after treatment for CIN 2/3+. They found the highest risk in HPV+/cytology+ women, followed by HPV+/cytology−, and finally HPV−/cytology+.

Current guidelines in Japan and the UK recommend cytology alone during posttreatment follow-up for high-grade dysplasia [10,11]. United States guidelines recommend HPV testing for surveillance since 2012, albeit without level 1 evidence. However, the known pathogenesis and carcinogenic properties of HPV strongly support the use of HPV testing in this setting. The data presented in this issue by Kang et al. [8] and Onuki et al. [9] provide strong clinical evidence to support the use of HPV testing to evaluate risk for recurrent or residual high-grade dysplasia in patients previously treated for high-grade dysplasia. Their work continues to build on the library of data that demonstrate the utility and value of HPV testing in detecting cervical dysplasia and preventing cervical cancer.

REFERENCES


