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ORIGINAL ARTICLE

The sensitivity of Pap cytology and HPV testing to detect incident cervical cancer: prior testing results in 178 patients with invasive cervical cancer at a large general hospital in China

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Introduction Prior screening results in women diagnosed with cervical carcinoma are only reported in the literature in small numbers. We wish to examine a larger number of prior testing results in women with cervical carcinoma from China to better understand the strengths and weaknesses of Pap (Papanicolaou) cytology and human papillomavirus (HPV) testing.

Materials and methods In our study, 178 patients with histologically diagnosed cervical carcinoma and Pap cytology and/or HPV testing in the year prior to diagnosis were retrospectively studied. Pap cytology was performed using liquid-based preparations and HPV testing was done with mostly Hybrid Capture 2 but also included other methods.

Results In our study, 82.0% of women were symptomatic at presentation with vaginal bleeding or abnormal vaginal discharge. HPV testing was negative in 9.8% of women in the short period before diagnosis of cervical cancer and Pap cytology had a higher rate of false negative results at 16.7%.

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Adenocarcinoma showed a higher negative testing rate than squamous cell carcinoma did with both cytology and HPV testing. Only 1 of 78 patients (1.3%) having both tests showed a double negative result. Negative high-risk HPV testing was noted in 2 of 9 squamous cell carcinoma patients with routine gynecological examination.

Conclusions Both Pap cytology and HPV testing have higher rates of prior negative results in women with cervical carcinoma. When testing is performed using both methods, the greatest number of cervical carcinomas can be detected. These results should also be considered when making screening recommendations with the understanding that HPV testing alone will miss at least a proportion of women with incident cervical carcinoma.

Introduction

Cervical cancer screening with Pap (Papanicolaou) cytology has been effective at decreasing the incidence of cervical cancer in countries with established screening programs. The use of cotesting has been suggested by some to be the preferred screening option and is included in the current recommendations. However, some have also suggested that human papillomavirus (HPV) testing alone might serve as the preferred primary screening modality and such a scenario appears closer to reality given the recent US Food and Drug Administration (FDA) approval of the Roche cobas HPV test (Basel, Switzerland) as a primary screening modality.[1] Despite the recent FDA approval of the Roche cobas HPV test as a primary screening for cervical cancer, there are those who feel such a screening modality would be a disservice to screened women.[2]

A randomized trial reports HPV DNA testing alone to have a greater sensitivity for detection of cervical intraepithelial neoplasia (CIN) 2/3 than does Pap cytology alone (94.6% versus 55.4%) but less specificity (94.1% versus 96.8%).[3] This study considered women 30 to 69 years of age, and it is likely that the specificity of HPV DNA testing alone would be even lower in younger women who are known to have a higher prevalence of transient HPV infection[4]; although a recent study showed a peak incidence of HPV infection in the 55 to 59 year age group in rural China.[5] A recent meta-analysis shows improved detection of CIN 2+ by cotesting compared with Pap testing alone at baseline screening with decreased detection in subsequent screening rounds and recommends the use of cotesting over cytology alone.[6]

Given the low incidence of cervical cancer in developed areas as a result of screening programs, there is limited available data on the results of prior Pap cytology and high-risk human papillomavirus (hrHPV) testing in women with cervical cancer. While randomized trials are essential in determining the best screening modality, many of these trials have low rates of cervical cancer. We feel that knowledge and analysis of prior testing results in patients with cervical cancer offers additional important insights into strengths and weakness of these tests, specifically in the detection of incident cancers. In this study we consider prior Pap cytology and hrHPV testing results from women diagnosed with invasive cervical cancer in China in the hopes of better understanding the roles and limitations of these tests.

Materials and methods

Cases with a histologic diagnosis of invasive cervical carcinoma were retrieved from China-Japan Friendship Hospital (CJFH) during a period of 72 months (January 2009-December 2014). CJFH is one of the largest tertiary A-level modern hospitals in Beijing. Most patients were from Beijing and adjacent areas, although a small proportion of patients were from other provinces. The diagnosis of cervical cancer was established by histopathologic examination, including endocervical curettage, cervical biopsy, and/or diagnostic excisional procedures/hysterectomy. Prior Pap cytology, HPV testing results, and chief complaints for clinic visits were recorded. Only cases with prior HPV testing and/or Pap test results within the 1-year period before histologic diagnosis were included in this study.

Pap cytology tests were performed using 1 of 2 methods—namely ThinPrep (Hologic, Bedford, Mass) and SurePath (BD Diagnostics, Franklin Lakes, NJ). All Pap tests were reported using the Bethesda System 2001 terminology. HPV testing was performed using 1 of 3 methods—Hybrid Capture 2 (HC2) assay (Qiagen, Hinden, Germany), Cervista HR HPV test (Hologic), or HR HPV genotyping Real Time PCR method (ZJ Bio-Tech, Shanghai, China), which tests for 13 hrHPV types (HPV-16, -18, -31, -33, -35, -39, -45, -51, -52, -56, -58, -59, and -68). Specimens were collected by gynecologists such that 2 separate sample vials were used if both Pap cytology and HPV testing were requested. For HPV test, the samples were collected and stored in Digene Standard Transport Medium for HC2 test, ThinPrep medium for Cervista HR HPV test, and the manufacturer's own standard medium for HR HPV genotyping Real Time PCR method. Pathologists signing out Pap cytology were unaware of HPV testing results at the time of cytologic examination.

Statistical analysis was performed with the Pearson chi-squared test using SAS software (version 9.1, SAS Institute, Cary, NC). A P value of <0.05 was considered statically significant. Fisher exact test was used for analysis when smaller study sets were being examined.