Accuracy-reducing Factors in Pap test for Patients with Invasive Cervical Cancer

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Background: While cytologic screening for cervical cancer has been highly effective in decreasing the incidence of invasive cervical cancer, approximately 10,000 cancer cases are still diagnosed in the US each year. It is well known that tumor diathesis, blood and inflammation are present in the background of frankly malignant Pap tests that can potentially hamper specimen adequacy and accurate interpretation. This study was undertaken in an effort to document the diagnostic implications of these limiting factors in Pap Tests from women with cervical cancer.

Methods: 2937 women recruited into the SUCCEED study from 2002-2010 had ThinPrep Pap and HPV tests performed and interpreted in our laboratory. 276 of these women had a histologic diagnosis of invasive cervical cancer. In addition to adequacy, quality indicators were noted. HPV testing was performed on an aliquot of the cytologic sample using Linear Array (Roche) that uses PCR to detect 37 individual HPV genotypes. All findings were prospectively entered into a database for subsequent analysis.

The women were divided into Invasive Cancer (n=276) or No Cancer (Normal, CIN or AIS) based on the worst surgical pathology result. Cytologic and HPV results (positive/negative) were analyzed by cross sectional analysis using Pearson’s chi square and Fishers Exact test.

Result: The unsatisfactory rate of cytology specimen from Invasive Cancer patients (2.9%, 8/276) was significantly higher than that in samples from the No Cancer group (0.9%, 23/2568) (p=0.008). The percentage ThinPrep slides with quality indicators noting the presence of obscuring blood or inflammation, or scanty cellularity was 37.7% (104/276) in specimens from Invasive Cancer patients compared with only 4.5% (116/2568) of the slides from the No Cancer group (p<0.0001).

In 5.4% (15/276) of patients with invasive cancer, the cervical cytology result was unsatisfactory, negative or ASC-US which suggests a delay to colposcopy and biopsy. Although absolute numbers for these cases were small, there was no difference in the HPV results for these cases (93.9%) versus those cancer cases with a diagnosis of LSIL or greater (91.6%) that would have referred the woman to colposcopy.

Conclusions: Higher rates of unsatisfactory and sub-optimal Pap tests from women with invasive cervical cancer challenge our ability to detect cervical cancer in women who have not participated in regular screening. It is important to recognize that such poor quality samples can harbor a malignancy and to design protocols to enhance detection in this setting. HPV tests can be abnormal even in samples unsatisfactory for cytology. Possible aids to diagnosis in this setting include 1) HPV co-testing in women over the age of 30; 2) reprocessing bloody, hypocellular samples to enhance cellularity; 3) rescreening unsatisfactory Pap tests in women with a poor screening history as “high risk”.

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