Usefulness of p16/Ki67 dual stain in triaging women with ASCUS/LSIS cytology - compared with HR-HPV testing

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Background:

• Atypical squamous cells of undetermined significance (ASCUS) and low grade squamous intraepithelial lesions (LSIL) are the most common cytologic abnormalities, which are with low risk of having underlying high grade lesion, so need further evaluation.

• Our purpose was to examine p16/Ki67 dual stain (DS) in identifying underlying high grade dysplastic cells in cytology specimens with ASCUS or LSIL.

Method:

• 177 ThinPrep cytology specimens including 95 ASCUS and 82 LSIL with histologic follow-up of CIN1 or CIN2+ were included.

• The cytology materials were preserved in -80℃ and dual stain (DS) with p16/Ki67 was performed on smear slides made from stored cytology materials.

• High risk HPV test using HC2 was also performed.

Results:

• Among 95 cases with ASCUS, 38 showed CIN2+ and 57 showed CIN1 on histology. 33 in 38 (86.8%) ASCUS with CIN2+ were DS positive, 7 in 57 (12.3%) ASCUS with CIN1 (7/57, 12.3%) were DS positive.

• Among 82 cases with LSIL, 32 showed CIN2+ and 50 showed CIN1 on histology. 26 in 32 (81.3%) LSIL with CIN2+ were DS positive, 9 in 50 (18%) LSIL with CIN1 were DS positive.

• The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of dual stain identifying CIN2+ in ASCUS/LSIL were 94.2%, 85.0%, 80.5% and 95.8% respectively.

• HR-HPV was positive in 67 cases with CIN2+ (67/70, 95.7%) and 83 cases with CIN1 (83/107, 77.6%).

DS showed a little lower sensitivity, but significantly higher specificity, PPV and NPV than HR-HPV testing in identifying underlying CIN2+ in ASCUS or LSIL.

<table>
<thead>
<tr>
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<th>ASCUS</th>
<th></th>
<th>CIN1</th>
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<th>CIN2+</th>
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<tbody>
<tr>
<td>(n=95)</td>
<td>DS+</td>
<td>71</td>
<td>12.3%</td>
<td>36/94.7%</td>
<td>30/93.8%</td>
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</tr>
<tr>
<td>(n=82)</td>
<td>DS+</td>
<td>9</td>
<td>10.0%</td>
<td>21/93.8%</td>
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</tr>
<tr>
<td>ASCUS&amp;LSIL</td>
<td>DS+</td>
<td>16/51.5%</td>
<td>30/93.8%</td>
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Table 1. Differences of sensitivity, specificity, PPV, NPV between p16/Ki67 dual stain and HR-HPV testing in identifying underlying CIN2+.

Figure 1. A: LSIL, few atypical cells scattered in the LSIL background, Papanicolaou-stained smear B: p16/Ki67 dual stain shows positive (same case as A), biopsy follow up was HSIL(CIN3) C: ASCUS, a few atypical cells dispersed with small size, Papanicolaou-stained smear D: p16/Ki67 dual stain show positive, (same case as C), biopsy follow up was HSIL(CIN3)

Conclusion:

• Our data demonstrated that P16/Ki-67 dual stain was able to identify underlying high grade dysplastic cells, suggested its potential utility in triaging ASCUS/LSIL cytology specimens.