p16/Ki67 dual stain triage versus cytology in primary human papillomavirus-based cervical cancer screening with limited genotyping

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Abstract

Background: The introduction of primary HPV cervical cancer screening requires the implementation of an appropriate triage strategy that will be effective in detecting high-grade cervical disease without losing diagnostic specificity. **Methods:** From the 30.066 screening tests results, a total of 1086 with available high-risk human papillomavirus (HRHPV) with limited genotyping, cytology and p16/Ki67 dual-stain were selected. Two triage strategies for primary HPV screening were analyzed retrospectively based on the study group. Performance characteristics for p16/Ki67 and cytology triage in detection of cervical intraepithelial neoplasia grade 2 or worse (CIN2+) and grade 3 or worse (CIN3+) were calculated, detected in colposcopic biopsy. **Results:** In HPV16/18-positive cases, primary HPV with p16/Ki67 triage was significantly more specific than cytology (53.1%/16.8% for CIN2+; p<0.0001; 45.9%/17.0% for CIN3+; p<0.0001), with yielded sensitivity (95.7%/84.8% for CIN2+; p=0.0955; 100.0%/87.5% for CIN3+; p=0.0832). In other HRHPV-positive cases (N16/N18), p16/Ki67 triage was also significantly higher specific (51.3%/15.3% for CIN2+; p<0.0001; 44.5%/16.5% for CIN3+; p<0.0001), with sensitivity (92.3%/74.4% for CIN2+; p=0.0522; 90.9%/81.8% for CIN3+; p=0.5637). Diagnostic predictive values were significantly higher for p16/Ki67 triage with the highest PPV in HPV16/18-positive cases for CIN2+ (45.4%; 95% CI: 35.2-55.8; p<0.0001) and very high NPV in all HPV-positive cases regardless of detected genotype (96.3%-100.0%). The risk (1-NPV) for CIN3+ in HRHPV16/18-positive/p16/Ki67-negative women was 0.0%. **Conclusions:** Superior diagnostic performance compared to cytology for detecting cervical cancer precursors indicates that p16/Ki67 dual-immunostain may be a highly effective tool of triage in primary HPV screening with limited HPV 16/18 genotyping in the secondary cervical cancer prevention.

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