The role of HPV integration testing in preventing underdiagnosis in women with a transformation zone type 3

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Results: Among the 50,784 patients, we screened a total of 674 female patients aged over 45 years with a TZ3, of which 151 patients had paired colposcopic biopsy and LLETZ samples. In the detection of CIN3+, HPV integration testing had higher specificity than cytological testing (82.1% [95% CI 78.6-85.1%] versus 55.7% [95% CI, 51.4-59.8%], $P < 0.05$). The risk of CIN3+ for the triage strategy of HPV16/18 genotyping with HPV integration test (59/100, 59.0%) was higher than that of HPV16/18 genotyping with ASCUS+ (45/124, 36.2%). In 151 patients with paired data on biopsy and LLETZ specimens, 65 women were diagnosed with normal and CIN1, of which 13 women had under-diagnosis (13/65, 20.0%). 11 under-diagnosed patients (11/13, 84.6%) could be screened by HPV integration testing, while cytological testing could only screen out 3 underdiagnosed patients (3/13, 23.0%). Combining HPV integration testing with high-grade cytology screening strategies, 13 under-diagnosed patients were screened (13/13, 100%).

Conclusion: HPV integration testing could improve the specificity of screening, was conducive to screening CIN3+ patients, and played an important role in preventing under-diagnosis.

Table 2 Performance of cytology and human papillomavirus (HPV) integration among HPV-positive and HPV16/18-positive women for detection of CIN3+.

	HPV-positive women(n=669)		
Characteristic	**HPV integration**	**Cytology**	***p* Value**
Positivity, no./total patients	174/669	326/669	
Positivity, % (95% CI)	26.0(22.7-29.5)	48.7(44.8-52.5)	<0.001
Detection of CIN3+			
Sensitivity, % (95% CI)	69.8(60.0-78.1)	71.6(61.9-79.8)	0.88
Specificity, % (95% CI)	82.2(78.7-85.2)	55.5(51.3-59.7)	<0.001
PPV, % (95% CI)	42.5(35.1-50.2)	23.3(18.9-28.3)	<0.001
NPV, % (95% CI)	93.5(90.9-95.4)	91.2(87.6-93.9)	0.228

Note: Thresholds: Cytology≥ASCUS; HPV integration >5 reads.