



# Diagnostic Value of HPV Integration in Cervical Adenocarcinoma and Adenocarcinoma in Situ: A Multicenter Retrospective Study

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## Introduction

Cervical adenocarcinoma (ADC) and adenocarcinoma in situ (AIS) remain challenging targets for screening, partly because cytology has suboptimal sensitivity for glandular lesions. HPV integration is a critical event in cervical carcinogenesis and may improve detection beyond conventional tests. We therefore evaluated the diagnostic performance of HPV integration testing in AIS and ADC.

## Materials and Methods

We conducted a multicenter retrospective cohort study including 207 patients diagnosed between January 2019 and December 2023 (74 AIS and 133 invasive ADC), with Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology as the lead center. All patients underwent HPV genotyping, cervical cytology, HPV integration testing, and histopathological evaluation.

## Results

HPV16 and HPV18 were the predominant genotypes, accounting for 93.10% of HPV-positive cases. On cytology, only 22.71% showed atypical glandular cells (AGC). HPV integration testing achieved a sensitivity of 84.06% for detecting AIS/ADC, significantly higher than cytology ( $\geq$ ASCUS, 64.72%;  $p < 0.01$ ). HPV integration testing combined with biopsy-based histology identified 96.61% of AIS/ADC cases. Integration read counts increased with lesion severity; mean reads were higher in invasive ADC than AIS ( $564.42 \pm 1400.84$  vs  $461.31 \pm 122.35$ ), but the difference was not statistically significant ( $p = 0.615$ ).

**Table 1. Distribution of High-Risk HPV Genotypes Among Patients with AIS and ADC**

| HPV types    | AIS (n=74) |        | ADC (n=133) |        | TOTAL (n=207) |        |
|--------------|------------|--------|-------------|--------|---------------|--------|
|              | n          | N%     | n           | N%     | n             | N%     |
| 16           | 27         | 36.49% | 75          | 56.39% | 102           | 49.28% |
| 18           | 40         | 54.05% | 50          | 37.59% | 90            | 43.48% |
| 31           | 1          | 1.35%  | 1           | 0.75%  | 2             | 0.97%  |
| 33           | 1          | 1.35%  | 2           | 1.50%  | 3             | 1.45%  |
| 45           | 3          | 4.05%  | 4           | 3.01%  | 7             | 3.38%  |
| 52           | 3          | 4.05%  | 5           | 3.76%  | 8             | 3.86%  |
| 56           | 1          | 1.35%  | 1           | 0.75%  | 2             | 0.97%  |
| 58           | 0          | 0.00%  | 1           | 0.75%  | 1             | 0.48%  |
| 59           | 0          | 0.00%  | 3           | 2.26%  | 3             | 1.45%  |
| 68           | 0          | 0.00%  | 1           | 0.75%  | 1             | 0.48%  |
| Not detected | 4          | 5.41%  | 7           | 5.26%  | 11            | 5.31%  |

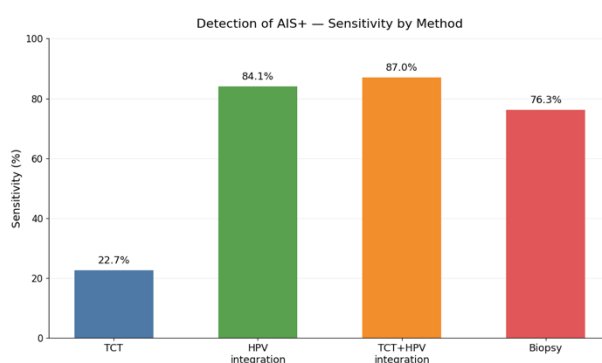
**Table 2. Pap test findings Among Patients with AIS and ADC**

| Cytology               | AIS (n=74) |        | ADC (n=133) |        | Total (n=207) |        |
|------------------------|------------|--------|-------------|--------|---------------|--------|
|                        | n          | N%     | n           | N%     | n             | N%     |
| NILM                   | 33         | 44.59% | 40          | 30.08% | 73            | 35.27% |
| AGC-FN/AGC-NOS/AIS/ADC | 9          | 12.16% | 38          | 28.57% | 47            | 22.71% |
| ASCUS/LSIL             | 21         | 20.79% | 24          | 18.05% | 45            | 21.74% |
| ASC-H/HSIL             | 11         | 14.86% | 31          | 23.31% | 42            | 20.29% |

**Table 3. HPV Integration Test Results in Patients with AIS and Adenocarcinoma**

|              | AIS (n=74) |        | ADC (n=133) |        | Total (n=207) |        |
|--------------|------------|--------|-------------|--------|---------------|--------|
|              | n          | N%     | n           | N%     | n             | N%     |
| Integration+ | 61         | 82.43% | 113         | 84.96% | 174           | 84.06% |
| Integration- | 13         | 17.57% | 20          | 15.04% | 33            | 15.94% |

**Figure 1. Sensitivity of Different Screening Strategies for the Detection of AIS+ Lesions**



## Conclusions

HPV integration testing demonstrated high diagnostic sensitivity for cervical adenocarcinoma, complementing conventional screening and enabling earlier detection; its role in risk stratification warrants further validation in larger cohorts.

## Acknowledgments

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