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Topic:	GYNAECOLOGICAL ONCOLOGY->Screening and prevention of gynaecological cancer, including HPV and colposcopy

Content English

Title:	HPV E4/p16INK4a immunohistochemistry for the prediction of CIN2 regression - a historical cohort study
Summary of Abstract:	p16INK4a immunohistochemistry is useful in clinical practice, possibly in addition to HPV typing and E4 testing.
Introduction/ Background:	CIN2 is a heterogenous diagnosis with a high likelihood of regression, suggesting that some women with CIN2 may benefit from undergoing active surveillance instead of an immediate excision.
Objectives:	We aimed to examine the performance of p16INK4a and HPV E4 immunohistochemistry for predicting CIN2 regression.
Methods:	We conducted a historical cohort study including women aged 23-40 undergoing active surveillance for CIN2 at Aarhus University Hospital, Denmark, from 2000 to 2010. Archived tissue samples were sectioned for H&E, HPV genotyping, and p16INK4a and HPV E4 immunohistochemestry We calculated absolute and adjusted relative risks (aRR) of regression by p16INK4a status, stratified by HPV E4, HPV type, cytology, and age. In a sensitivity analysis we restricted to women with an expert-confirmed CIN2.
Results/ Discussion:	Of 443 included women, most (73.8%) were aged <30 and half had a high-grade index cytology (48.8%). A total of 47.6% regressed to CIN1 or normal during the 2-year surveillance period. CIN2 regression rates were lower in p16INK4a-positive compared to p16INK4a-negative women (40.5% vs 63.3%, aRR: 0.77 ; 95%CI 0.64-0.94). In p16INK4a-positive women, risk of regression was significantly lower in HPV E4-negative compared to HPV E4-positive women (37.7% vs 53.8%, aRR 0.73; 95%CI 0.54-0.98) and in HPV16-positive compared to HPV16-negative women (27.9% vs 49.7%, aRR 0.54; 95%CI 0.40-0.75). Risks did not differ by cytology (<Low-grade vs high-grade: 40.6% vs 43.0%, aRR 0.78 ; 95%CI 0.60-1.02) or age at diagnosis (< 30 vs >30: 41.8% vs 36.7%; aRR 0.85; 95%CI 0.62-1.17).
Conclusion:	Our findings support the use of p16INK4a immunohistochemistry in clinical practice, possibly in addition to HPV typing and E4 testing.
Keywords:	Cervical precancer, HPV, diagnostics, cancer

Conflict of Interest Disclosure

- [x] I have a conflict of interest
  - [x] I declare the following conflict of interest

    I have received reagents for p16 staining for the current study from Roche Diagnostics. Roche had no role in the study design or the interpretation of results or the decision to submit