ADAPTING HPV DNA TESTS FOR CERVICAL CANCER SCREENING OF HIV-INFECTED WOMEN

Louise Kuhn[1], Rakiya Saidu[2], Ana Tergas[1], Roslind Boa[2], Jennifer Moodley[2], Cecilia Svanholm-Barrie[3], David Persing[4], Scott Campbell[4], Thomas C. Wright[1], Lynette Denny[2]

[1]Columbia University Medical Center, New York, NY; [2]University of Cape Town, South Africa; [3]Cepheid, Solna, Sweden; [4]Cepheid, Sunnyvale, CA

Background

HIV-infected women are at high risk of cervical cancer and its precursor lesions.

HIV-infected women have a high prevalence of HPV co-infection which complicates screening.

HPV DNA testing has excellent sensitivity but poor specificity for cervical cancer screening among HIV-infected women.

Objectives

We evaluated whether the point-of-care test, Xpert™ HPV, could be adapted to improve performance characteristics for screening HIV-infected women.

Study Population

We undertook a clinical study of:
- 586 HIV-uninfected women and
- 535 HIV-infected women,

aged 30-65 years,
in Cape Town, South Africa.

Women were recruited at Khayelitsha primary health care clinic to represent the general population of women seeking screening.

Women were also recruited at Groote Schuur Hospital Colposcopy Clinic to represent a referral population of high risk women.

Equal numbers of HIV-infected and uninfected women were recruited by design

HPV DNA test

All women had a cervical sample collected in 20ml of Preservcyt. 1ml was tested on-site with Xpert HPV.

Xpert HPV is a cartridge-based PCR assay that detects HPV DNA in 5 channels plus a sufficiency control:
HPV 16
HPV 18,45
HPV 31,33,35,52,58
HPV 51,59
HPV 39,56,66,68.







Study Endpoints

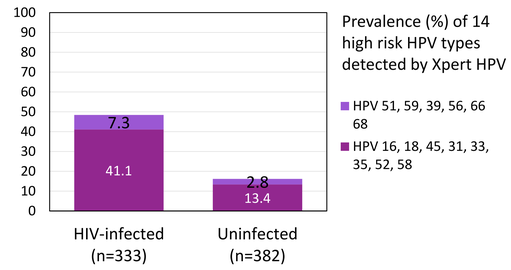
All women underwent colposcopy with histological sampling. Cervical intraepithelial neoplasia grade 2,3 or cancer (CIN2+) was diagnosed based on consensus pathology review.

Statistical Analysis

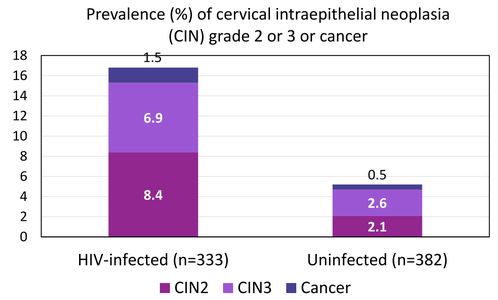
Sensitivity, specificity, positive and negative predictive values were calculated based on logistic regression and receiver operating characteristic (ROC) curves. Women from both populations contributed data to calculation of sensitivity. Only women recruited from the screening population contributed data to calculation of prevalence, specificity, PPV and screen-positive rates.

Results

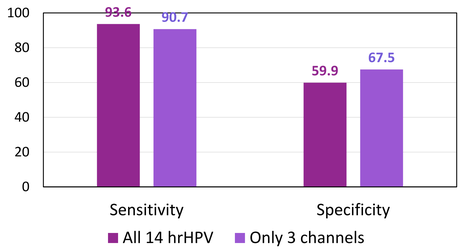
Prevalence of HPV was higher in HIV-infected (48.2%) compared to uninfected uninfected women (16.2%) (p<0.001).



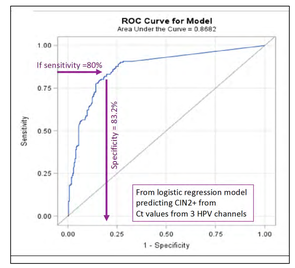
Prevalence of histology-confirmed CIN2+ was higher in HIV-infected (16.8%) compared to uninfected women (5.7%) (p<0.001).

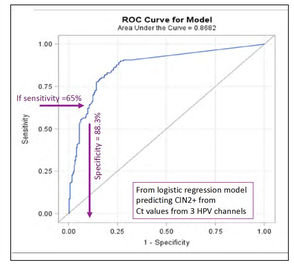


If the definition of screen-positive was limited to the 3 channels detecting HPV 16,18,45,31,33,35,52,58, sensitivity remained high and specificity improved vs. defining screen-positive as detection of any of the 14 high risk HPV types



Using logistic regression, we modelled CIN2+ from Ct values in the 3 channels detecting HPV 16,18,45,31,33,35,52,58. This allows us to determine effects of making cut-offs more stringent.





Sensitivity	Specificity	PPV	NPV	Screen-pos %
Any 14 high risk types				
93.6	59.9	31.7	97.0	48.4
3 channels detecting HPV 16, 18,45, 31,33,35,52,58				
90.7	67.5	35.0	95.9	41.1
Optimizing Ct on 3 channels detecting HPV 16, 18,45, 31,33,35,52,58				
85	77.0	43.1	96.2	33.5
80	83.2	49.4	95.3	27.5

Conclusions

Adapting Xpert HPV by:
- restricting to a limited set of high risk HPV types,
- making CT cut-offs more stringent (i.e. requiring higher levels of HPV DNA)

can greatly improve screening for HIV-infected women.

This approach limits the number of HIV-infected women who require further follow-up or treatment for cancer precursor lesions while targeting treatment for those who need it most.

Acknowledgements

❖Supported by the National Cancer Institute UH2/3 CA189908

printed by MegaPrint Inc. www.postersession.com