Factors Associated with Extensive Cervical Lesions among HIV-infected Women Screening for ACTG Protocol A5282

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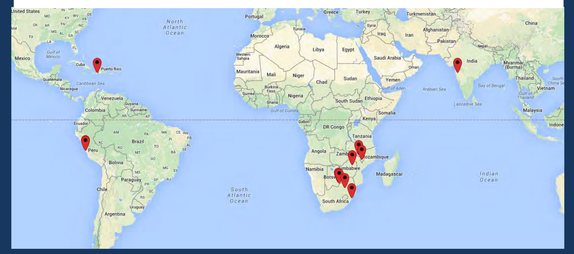
BACKGROUND

'Screen-and-treat' approaches for prevention of cervical cancer are used in many resource-constrained settings because of the challenges associated with cytology. Women are screened with: (1) visual inspection after acetic acid (VIA), or (2) testing for high-risk human papillomavirus (hrHPV), followed by treatment with cervical cryotherapy for those screening positive. However, women may have extensive cryotherapy-ineligible lesions that require excisional procedures such as Loop Electro-Excision Procedure (LEEP). We explored factors associated with these lesions to inform broad implementation of screen and treat programs.

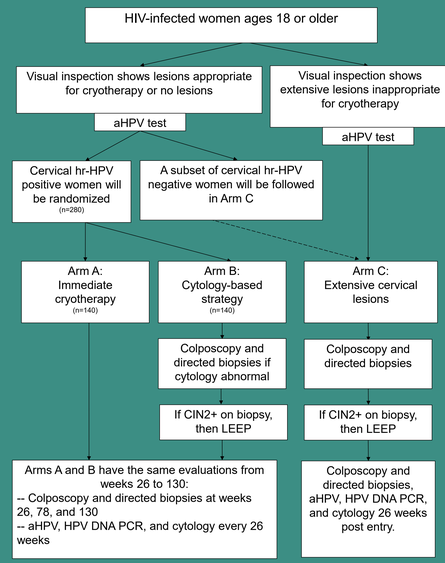
METHODS

Cross-sectional study of HIV-infected women screening for A5282, a randomized clinical trial comparing the HPV screen and treat approach to a cytology-based strategy for prevention of cervical cancer. Participants were screened with colposcopy (visual inspection after acetic acid wash using magnification without biopsy), HPV testing (Abbott® hrHPV PCR assay), and cytology. Abbott HR HPV testing yields 3 results: HPV 16, HPV 18, and the other 12 HR HPV types. Colposcopy results were categorized as no lesions, cryo-eligible lesions, and cryo-ineligible lesions according to WHO criteria. Participating sites included 8 in sub-Saharan Africa, 2 in India, 1 in Haiti, and 2 in Peru. Fisher's exact test was used to test for association.

A5282 STUDY SITES



OVERVIEW OF A5282



ACKNOWLEDGEMENTS

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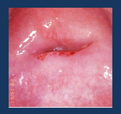
RESULTS

907 women who screened for A5282 had complete colposcopy, hrHPV, and cytology results. The median age (years) was 37 [IQR 32, 42]; median CD4 (cells/mm3) was 524 [IQR 386, 712]; 70% has plasma HIV-1 RNA <40 copies/mL. Cryo-ineligible lesions were not associated with CD4 count or plasma HIV-1 RNA. The prevalence of cryo-ineligible lesions was significantly higher in women with hrHPV than without (105/403, 26% vs. 44/504, 9%, P<0.001), and in those with abnormal cytology than with normal cytology (110/597, 18% vs. 39/310, 13%, P=0.024).

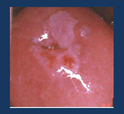
Table 1: Characteristics of Study Participants

Characteristic		Total (N=907)
Age (years)	Median (Q1, Q3)	37 (32, 42)
CD4 Count (cells/mm³)	Median [Q1, Q3]	524 [386, 712]
	N	865
	Missing	42
HIV RNA (copies/mL.)	< 40	602 (70%)
	≥ 40	261 (30%)
	Missing	44
Pap Smear Result	Normal	310 (34%)
	Abnormal	597 (66%)
Colposcopy Impression	No lesions seen	487 (54%)
	Lesions seen, appropriate for cryotherapy	271 (30%)
	Lesions seen, not appropriate for cryotherapy	149 (16%)
Abbott: HR HPV testing	Positive for any hr HPV type	403 (44%)
	HPV 16 positive	94 (10%)
	HPV18 positive	46 (5%)
	Other hr HPV positive	340 (37%)

No lesions



Cryo-eligible lesion



Cryo-ineligible lesion



Table 2: Summary of Cervical Cancer Screening Test Results and Cryo-eligibility among 907 HIV+ Women

Result	Screening Test: colposcopy	hrHPV	cytology
Screen negative	487 (54%)	504 (56%)	310 (34%)
Cryo-ineligible, N (%)	*N/A*	*44 (5%)*	*39 (4%)*
Screen positive, N (%)	420 (46%)	403 (44%)	597 (66%)
Cryo-ineligible, N (%)	*149 (16%)*	*105 (12%)*	*110 (12%)*

Colposcopy screen positive= lesions seen after acetic acid; Cytology screen positive=atypical squamous cells or greater; N/A=not applicable

Table 3: Association of Colposcopy Impression and hr HPV

Characteristic		Total (N=907)	hr-HPV: Not Detected (N=504)	hr-HPV: Positive (N=403)	P-Value*
Colposcopy Impression	No lesions seen	487 (54%)	339 (67%)	148 (37%)	<.001
	Lesions seen, appropriate for cryotherapy	271 (30%)	121 (24%)	150 (37%)	
	Lesions seen, not appropriate for cryotherapy	149 (16%)	44 (9%)	105 (26%)	

Table 4: Association of Colposcopy Impression and Baseline Cervical Cytology Results

Characteristic		Total (N=907)	Baseline Pap Smear Result: Normal (N=310)	Baseline Pap Smear Result: Abnormal (N=597)	P-Value*
Colposcopy Impression	No lesions seen	487 (54%)	162 (52%)	325 (54%)	0.012
	Lesions seen, appropriate for cryotherapy	271 (30%)	109 (35%)	162 (27%)	
	Lesions seen, not appropriate for cryotherapy	149 (16%)	39 (13%)	110 (18%)	

CONCLUSIONS

Extensive cervical lesions that are not eligible for treatment with cryotherapy are relatively common (~1 in 6) among HIV-infected women and are not associated with immune suppression or lack of virological control.

Adequate treatment for these lesions, such as loop electrosurgical excision procedure, should be readily available within 'screen-and-treat' implementation programs. Further studies are needed to define the optimal management of these lesions.