ANAL PRECANCER SCREENING AMONG MSM: WHAT IS THE BEST STRATEGY?

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BACKGROUND

- Risk of non-AIDS defining cancers has increased among people with HIV (PWH). Anal cancer is rare in the general population, but men who have sex with men (MSM) have elevated risk.
- The gold standard of diagnosis for anal precancer using high-resolution anoscope ***(HRA)*** is costly and has high participant burden.
- Efficient screening strategies and early detection of anal precancer in high risk populations is still needed.

METHODS

- MSM from the Multicenter AIDS Cohort Study (MACS, part of the MACS/WIHS combined cohort study) were included.
- We evaluated ***three screening strategies*** (**single anal cytology** [aCyt], **sequential aCyt**, and **co-testing** [aCyt+oncogenic HPV]) and their ability to predict anal precancer among MSM.
- All men in the MACS were offered anal cytology tests (annually for 4 years for HIV+ and every other year for 4 years for HIV- men)
- Men with abnormal aCyt (aCyt+) and a subset with normal aCyt were referred for HRA procedure. Histological high grade squamous intraepithelial lesion, evaluated as anal intraepithelial neoplasia grade 2 or greater ***(AIN2+)*** were defined as anal pre-cancer.
- Oncogenic HPV (***oncHPV***) were defined as HPV genotypes 16, 18, 31, 33, 35, 59, 45, 51, 52, 56, 58, 59, 66, and 68 using Linear Array HPV genotyping.
- Multivariable logistic regression models evaluated risk of biopsy confirmed anal pre-cancer (AIN2+) within 5 years of screening using the three screening strategies adjusted for age, race, HIV status, number of anal sex partners, and study site.
- The diagnostic values of the screening strategies (sensitivity and specificity) were conducted within the subset of participants who had HRA testing, and the **verification bias was corrected** using weighted generalized estimating equation approach (see table for list of variables that was weighted in the correction).

Anal cytology screening had moderate predictive value for subsequent AIN2+ among HIV+ and HIV- MSM. Sequential anal cytology testing or adding oncogenic HPV co-test to anal cytology improved test performance.

Table. Comparison of tests characteristics for three anal precancer screening strategies in 430 MSM from the Multicenter AIDS Cohort Study

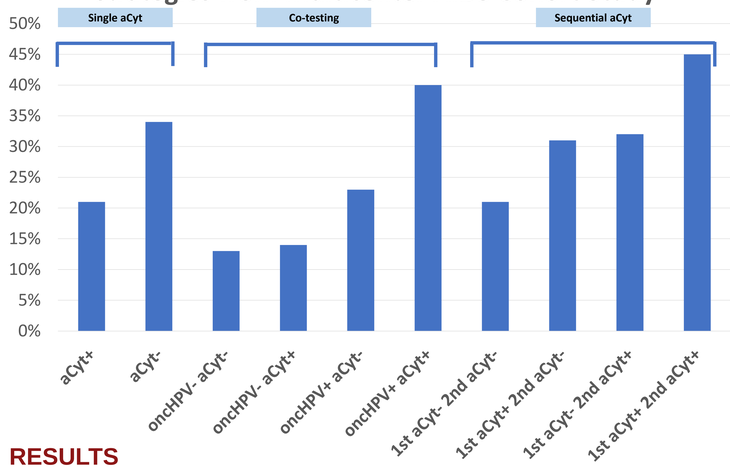
Screening result considered as positive	Crude Estimation		Verification Bias Correction[2]*	
	Sensitivity	Specificity	Sensitivity	Specificity
Single anal cytology (aCyt), N=430				
Abnormal aCyt (aCyt+)	67%	44%	51%	59%
Co-testing : anal cytology [aCyt] and oncogenic HPV [oncHPV], N=426				
oncHPV and/or aCyt positive	93%	17%	94%	23%
oncHPV DNA+	86%	34%	84%	36%
Both tests positive	61%	62%	47%	70%
Sequential anal cytology (aCyt), N=231				
1st and/or 2nd aCyt+	76%	35%	78%	41%
Only Second aCyt+	53%	62%	62%	74%
Both aCyt positive	36%	79%	39%	87%

*weighting was based on a model the probability of having anal HRA test controlled for age, race, number of male sex partners, college education, HIV status (for combined analysis), and study sites.

CONTACT INFORMATION & ACKNOWLEDGEMENT

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Figure. Probability of AIN2+ for three screening strategies from Multicenter AIDS Cohort Study



RESULTS

- Total of 430 MSM had HRA were included. Prevalence of AIN2+ was similar among HIV+ and HIV- MSM (31% vs. 24%, p=0.13).
- HIV+ MSM with low CD4 (<350 cells/mm^3) had higher prevalence of AIN2+ (41%, p=0.04).
- Odds of AIN2+ within 5 years was significantly higher in those with abnormal screening results with an 83% increase in those with a single aCyt+, a 3-fold increase following two aCyt+, and more than a 4-fold increase following oncHPV+/aCyt+ co-testing.
- Sensitivity and specificity was moderate (51% and 59%) in single aCyt. Sensitivity and specificity improved with adding sequential aCyt. Co-testing (aCyt and oncHPV) performed best among all screening tests.
- Results among HIV+ MSM and HIV- MSM were comparable. Screening strategies performed with higher sensitivity among HIV+ MSM than that in HIV- MSM.
- Results before and after correcting for verification bias had similar trend.

CONCLUSIONS

- Anal cytology screening only had moderate test performance to predict anal pre-cancer risk in HIV+ and HIV- MSM. Additional oncogenic HPV test improved test performance.
- Understanding different screening strategies and their ability to predict a future anal precancer event might guide clinical decision.
- Further research are needed to better understand the frequency of different screening tests to guide clinical recommendations.