Clinical Predictors and Outcomes of Invasive Anal Cancer for People with HIV in an Inception Cohort

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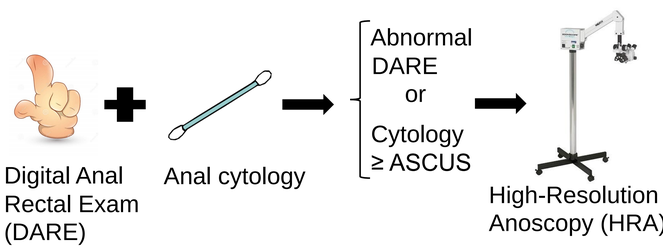
BACKGROUND

- The heterogeneity of risk for invasive anal cancer (IAC) among People with HIV (PWH) underscores the importance of identifying clinical predictors to inform a shared decision-making framework for screening.
- We investigated predictors of IAC and described outcomes among those diagnosed with cancer.

METHODS

- Longitudinal cytology-based inception cohort of anal cancer screening of PWH as part of routine clinical care.

- **UCSD screening protocol**:



- PWH diagnosed with histological anal high-grade squamous intraepithelial lesions (aHSIL) were offered ablative treatments.
- Patients were eligible if they were at least 18 years, underwent ≥ 2 anal cytology examinations.
- Cohort analysis: 30 November 2006 to 3 March 2021. This was to provide over two years of follow-up time to assess IAC after the last screening.
- We accounted for variations in screening rates across sociodemographic and risk categories using inverse probability weighting (IPW).
- Time-at-risk for anal cancer development began on the date of the initial anal cytology and ended at the earliest of initial diagnosis of IAC, the patient's last clinic visit, death, or July 31, 2023.
- We estimated 5 &10-year adjusted probabilities of anal cancer since the initial anal cytology using IPW Cox proportional hazards models.
- Evaluation of additive and multiplicative interaction in the final main effects model was conducted.
- Primary outcome: Development of incident IAC. Secondary outcome: Mortality attributable to IAC.

"PWH with both aHSIL cytology and nadir CD4≤200 have 9 to 13-fold increased anal cancer risk compared to those lacking both. Mortality due to IAC was 21% and occurred when diagnosed with stages ≥ IIIA"

RESULTS

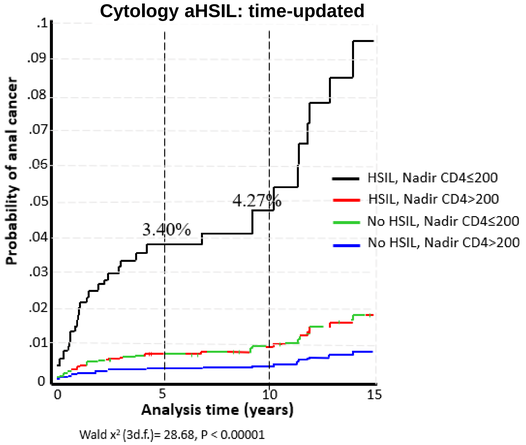
Screened Cohort: 30 November 2006 to 3 March 2021

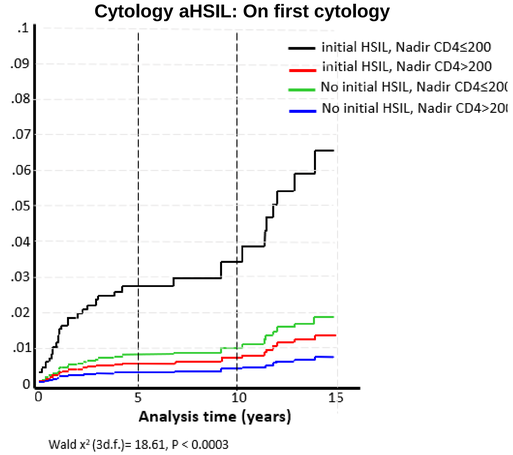


Five and 10-year risks of IAC:

A. Cohort unadjusted 0.63% and 0.80%, respectively
B. Nadir CD4 ≤200 and initial aHSIL cytology: 2.75% and 3.42%
C. Nadir CD4 ≤200 and Time-updated aHSIL cytology: 3.40% and 4.27%

Joint Effects of Cytological aHSIL and Nadir CD4 on Time to Incident IAC on Cox Regression Models By Cytological aHSIL Metric (initial and time-updated)





Only cytological aHSIL and nadir CD4≤ 200 predicted risk of IAC

Hazard Ratio (HR) using Inverse Probability Weighted (IPW) Cox Models for Incident IAC		
Cytology/CD4	**Unadjusted HR** (95% CI)	**Adjusted HR** (95% CI)
aHSIL (baseline)	3.86 (1.79–8.34)*	
aHSIL (time-updated)	5.08 (2.43–10.61)*	4.54 (2.19–9.43)*
Nadir CD4 ≤ 200	3.32 (1.48–7.45)**	2.99 (1.35–6.62)**

*P < 0.001 ,** P <0.0001

Having aHSIL cytology & nadir CD4 ≤ 200 increased IAC risk 13-fold

IPW Cox Models for Anal Cancer: Joint Effects of Initial and Time-updated cytological aHSIL and CD4 Nadir				
Covariate	**Baseline HSIL[a] HR (95% CI)**	**P**	**Time-updated HSIL[a] HR (95% CI)**	**P**
Never cytology aHSIL, Nadir CD4 >200	1.00		1.00	
Cytology aHSIL, Nadir CD4 >200	1.83 (0.38–8.93)	0.45	2.35 (0.48–11.54)	0.29
Never cytology HSIL, Nadir CD4 ≤200	2.54 (0.99–6.51)	0.05	2.38 (0.92–6.18)	0.07
Cytology aHSIL, Nadir CD4 ≤200	**9.05 (3.23–25.40)**	0.00	**13.03 (4.78–35.38)**	0.00

[a] Estimates of RERI, the attributable proportion due to interaction, and the synergy index from both joint effect models met criteria for super-additive interaction

RESULTS CONT'D

- PWH with IAC were diagnosed at median age of 50 years and 830 days after their 1st cytology. They were older at cohort entry and had a higher prevalence of cytology aHSIL on initial or subsequent follow-up.
- HRA refusal was observed in 23 of 33 PWH diagnosed with IAC, including eight who had opted out of secondary HRA surveillance.
- Mortality due to IAC was 21% (7 of 33). Also, five PWH (15%) died due to unrelated conditions after their cancer was cured.
- All PWH who died due to IAC had clinical stages IIIA or higher

CONCLUSIONS

- Nadir CD4 cell count and cytological aHSIL independently predict the IAC risk among PWH. The effect of low nadir CD4 is strongly amplified by the occurrence of aHSIL cytology.
- All patients who died due to IAC progression had clinical stages IIIA or higher at diagnosis, highlighting the importance of screening and early diagnosis.

ACKNOWLEDGMENTS

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