Nadir CD4 and Anal Cytology Predict Development of Invasive Anal Cancer

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BACKGROUND

- The long-term natural history of anal high-grade squamous intraepithelial lesions (HSIL) is incompletely characterized.
- We aimed to evaluate the effects of readily available patient characteristics on the risk of developing invasive anal cancer (IAC) in a longitudinal cohort of people with HIV (PWH).

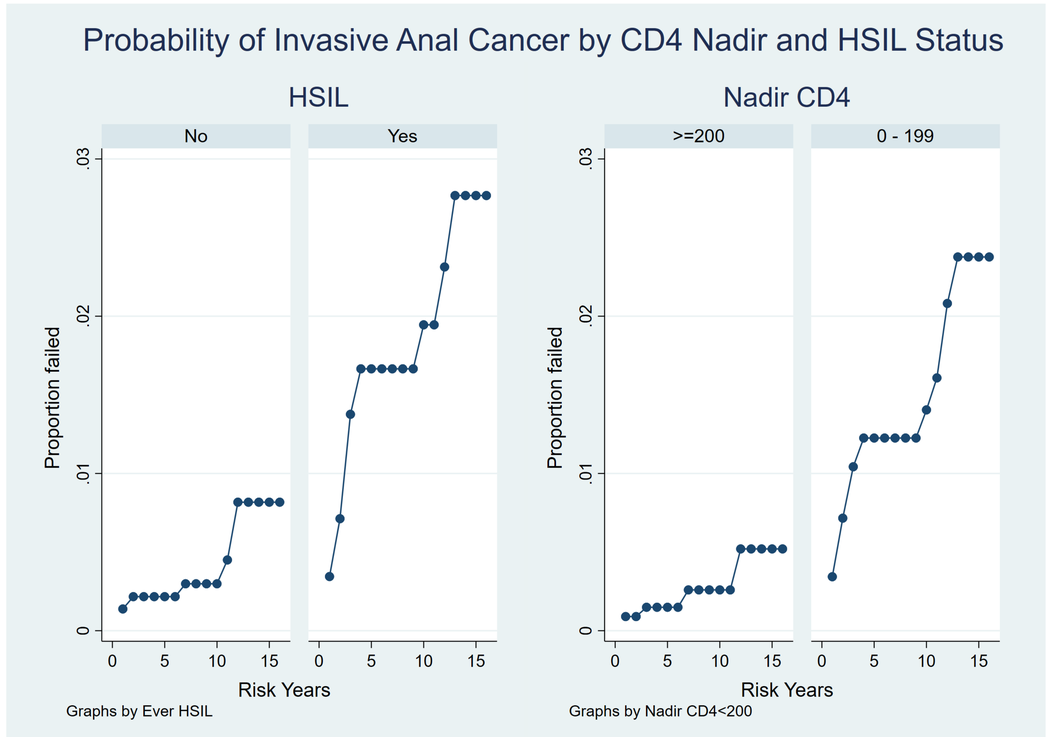
METHODS

- We performed a retrospective inception cohort analysis of PWH between 2006-2021 who received care at the UCSD Owen Clinic.
- Patients were eligible if they were 18 years or older, underwent ≥ 1 anal cytology examinations as part of routine care, and provided informed consent.
- Validation of IAC was conducted through review of surgical pathology reports.
- We estimated the risk of developing IAC using Kaplan-Meier analysis and inverse probability of screening weighted (ipw) Cox proportional hazards modeling.
- Covariates included sociodemographics, HIV risk factors, smoking, antiretroviral therapy (ART), CD4 and HIV viral load (VL) results.
- Time-at-risk began on the date of the initial anal cytology and was censored on the date of initial diagnosis of IAC, the last clinic visit, or the end of the study period (31 Dec 2021), whichever occurred first.

RESULTS

- Our cohort included 3,967 PWH followed for a median of 5.5 years (up to 13.8 years).
- The median age was 44, 10% were females, 36% non-white, 78% MSM and 33% smokers.
- Most were on ART (91%). Those with VL< 400 copies/ml at the beginning and end of follow-up were 68% and 89%, respectively.
- PWH had a median nadir CD4 count of 267 cells/mm3 (IQR: 102, 454) and 39% had a CD4 count nadir < 200.
- In our cohort PWH had a median of 2 anal cytologies.

In a **15-year longitudinal inception cohort**, having an **anal cytology HSIL** and a **nadir CD4 less than 200** independently predicted the risk of developing anal cancer.



RESULTS CONT'D

- At the first cytology test, 12 % had HSIL, while cumulatively 23% developed HSIL during follow-up.
- Twenty-six PWH 26 develop incident IAC during follow-up.
- In weighted Cox models, independent predictors of developing IAC were **ever having HSIL (HR:3.92, 95% CI:1.76-8.75, P=0.001)** and **nadir CD4 < 200 (HR:4.56, 95% CI: 1.54-12.8145, p=0.004).**
- Neither age, sex assigned at birth, race, smoking status, VL or HIV risk factor predicted incident IAC, Harrell's C = 0.77.
- The 5-year predicted probabilities of IAC were 1.67% and 0.22% for PWH with HSIL and those with less than HSIL, respectively (Figure, left-sided panel).
- Comparing PWH with nadir CD4<200 to those ≥200, the 5-year IAC probabilities were 1.23% and 0.15% (Figure, right-sided panel).

CONCLUSIONS

- In this 15-year longitudinal inception cohort, anal cytology HSIL and nadir CD4 count were independent predictors of IAC.
- Given limited access to high-resolution anoscopy (HRA) across the USA, HRA triage should be given priority to those with HSIL cytology or nadir CD4 cell count less than 200 with an abnormal anal cytology result..
- Unbiased estimates of the natural history of IAC observed in inception cohorts should inform shared decision-making discussions regarding anal cancer screening.

LIMITATIONS

- HSIL effect on incident IAC did not taken into account effects of ablative treatment.
- Additional studies need to investigate the effect of non-modeled risk factors such as current time-updated tobacco use and other patient risk behaviors.

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