Prioritizing Anal Cancer Screening in PWH: Not All are at the Same Risk

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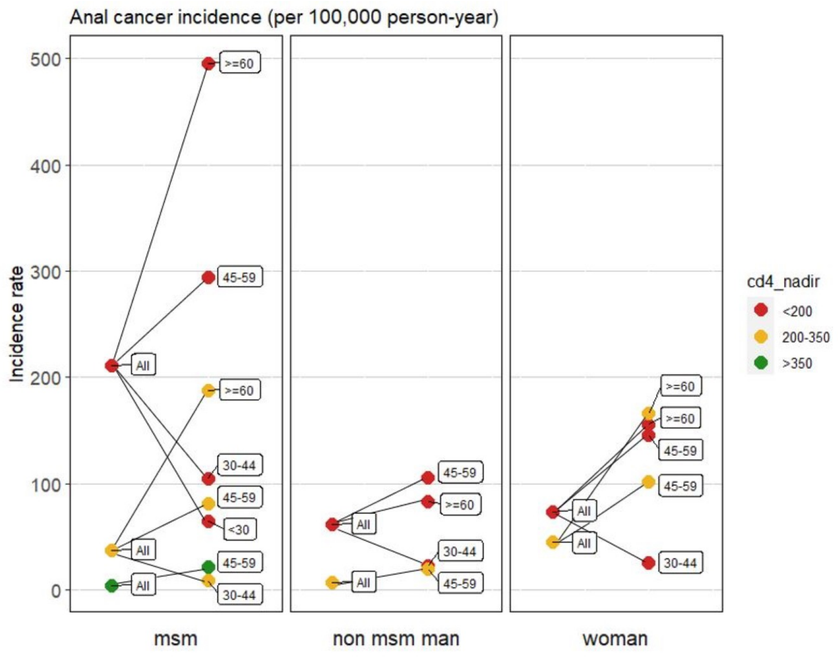
BACKGROUND

People with HIV (PWH) are up to 100 times more likely to develop anal cancer (AC) compared to the general population, where the overall incidence is 1.6/100,000 person-years (PY). Screening programs are efficient in preventing AC but are not accessible to all PWH. Identifying individuals at higher risk is crucial to implement effective and targeted screening strategies.

METHODS

In this PISCIS nested HIV cohort study, we included all treatment-naïve PWH ≥16 years from 16 hospitals in Catalonia/Balearic Islands, Spain, 1998-2022. The primary outcome was incidence rate (IR) of histologically-confirmed anal cancer. We used Poisson regression to identify risk factors, including age (time-updated), risk group, nadir CD4⁺ cell count, and calendar period of HIV diagnosis. The investigators at each participating centre validated the AC diagnosis and the nadir CD4+ values.

Figure 1. Anal cancer risk scale in the study population. Point estimates are shown for MSM, non-MSM men and women for age-groups (time-updated) <30, 30-44, 45-59, and ≥60 years.



PWH with nadir CD4+ count <200 cells/μL exhibit the highest anal cancer risk, especially MSM.

PWH with nadir CD4+ >350 cells/μL had a similar risk to the general population.

These findings provide important data to inform AC screening guidelines for PWH.

RESULTS

- We identified 107 events among 14,238 PWH, overall IR 72·4/100,000 PY (95%CI: 59·9-87·5), median follow-up 9·5 years (IQR: 4·4-15·7).
- The IR was highest with nadir CD4+ <200 cells/μL (105·0 [95%CI: 83·2-132·5]), followed by nadir CD4+ 200-350 cells/μL (29·3 [95%CI: 17·0-50·5]), and lowest with CD4+ >350 cells/μL (2·9 [95%CI: 0·4-20·3]). In these categories, men having sex with men (MSM) had IR of 211·4 (95%CI: 155·1-288·2), 37·6 (95%CI: 18·8-75·2), and 4·8 (95%CI: 0·7-34·2), respectively. Among PWH <30 years, there was only 1 case in MSM and none in the other groups, and no cases among women or non-MSM men with nadir >350 cells/μL (Figure 1).
- In multivariable analysis, nadir CD4+ <200 cells/μL had the highest risk compared to CD4+ >350, and CD4+ 200-350 cells/μL, with adjusted IR ratios (aIRR) of 29·1 (95%CI: 6·4-515·2), and 8·8 (95%CI: 1·7-159·8), respectively. Compared to those <30 years, PWH ≥60 had aIRR 27·6 [95%CI: 5·7-496·4], and 45-59 years had aIRR 21·6 [95%CI: 4·7-382·3]. An HIV diagnosis before 1998 had an aIRR 33·0 (95%CI: 10·0-203·5) (Figure 2)

Figure 2. Risk factors for anal cancer in the multivariable model.

Variable		N	Adjusted IRR	p-value
Age (time updated), years	<30	4171	Reference	
	30-44	10188	5.08 (1.03, 91.86)	0.116
	45-59	6836	21.59 (4.74, 382.30)	0.002
	>=60	1736	27.55 (5.67, 496.39)	0.001
Transmission group	Women	4603	Reference	
	MSM	10561	3.48 (1.99, 6.40)	<0.001
	Non-MSM men	7767	0.56 (0.29, 1.09)	0.081
Nadir CD4+ cell count	>350	6533	Reference	
	200-350	6723	8.78 (1.74, 159.76)	0.037
	<200	9675	29.05 (6.35, 515.15)	<0.001
Calendar period of HIV diagnosis	>=2015	4445	Reference	
	2009-2014	5612	2.90 (0.75, 19.04)	0.173
	2004-2008	4964	4.28 (1.20, 27.20)	0.054
	1998-2003	5323	3.00 (0.81, 19.39)	0.151
	<1998	2587	32.99 (10.04, 203.52)	<0.001

IRR adjusted for calendar time, age (time-updated), risk group and nadir CD4⁺ cell count

CONCLUSIONS

- **Age**, **MSM** and **nadir CD4+ cell count** had the strongest association with AC in PWH.
- Nadir CD4+ cell count <200 cells/μL exhibited the highest risk of AC, especially among MSM, whereas **PWH with nadir CD4+ count >350 cells/μL** had a similar risk to the general population.
- Nadir CD4+ cell count >350 cells/μL threshold can help identify PWH who should be prioritized during screening programmes.
- Tailored approaches for AC screening based on nadir CD4+ cell count, an easy surrogate marker, could optimize resources by prioritizing AC screening to those with the highest risk.

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