

FACTORS RELATED WITH PERSISTANCE AND CLEARANCE OF ANAL HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS IN MEN WHO HAVE SEX WITH MEN LIVING WITH HIV

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INTRODUCTION and OBJECTIVES

- Anal squamous cell carcinoma has a high incidence in certain groups, with the highest incidence in men who have sex with men (MSM) living with HIV, in whom it can reach to 78-402 cases /100000 person-years.
- It is preceded by a precursor lesion, the high-grade-intraepithelial lesions (HSIL). The detection and treatment of HSIL reduce the incidence of anal cancer.
- There is evidence that spontaneous regression of HSIL can occur.

The aim of the study was to describe the cumulative anal HSIL incidence and clearance rate and factors related in a cohort of MSM living with HIV.

METHODS

STUDY PARTICIPANTS

The ELAVI cohort is a prospective cohort of MSM living with HIV, following an anal screening programme from June 2016 to March 2021 in the Bellvitge University Hospital of Barcelona. The ELAVI cohort includes 354 participants. For the present study 291 participants with ≥ 2 years of follow-up were included. Participants with HSIL did not receive treatment during the follow-up.

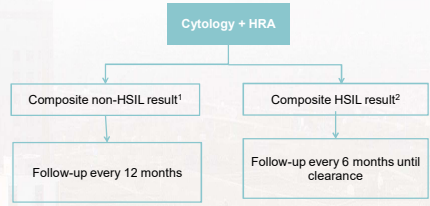
OUTCOME DEFINITIONS

- Incident HSIL:** HSIL new diagnosis after a baseline visit without HSIL.
- Clearance of HSIL:** no HSIL in 2 consecutive visits after an HSIL diagnosis.
- Persistent HSIL:** not cleared HSIL after ≥ 2 years of follow-up.

PROCEDURES

At the same visit:

Anal smear for anal cytology and human papillomavirus (HPV) biomarkers and high resolution anoscopy (HRA) with biopsy of suspicious lesions



¹ Non-HSIL cytological result and HRA with no biopsy or non-HSIL histological result.

² Cytological HSIL result and/or histological HSIL result.

HPV biomarkers:

- Aptima® E6/E7 mRNA test (E6/7 mRNA): detection of 14 HR-HPV genotypes*.

- Hybrid Capture 2® (HC2) HPV DNA test: detection of 13 HR-HPV genotypes*.

- Linear Array® (LA) HPV DNA test: detection of 37 HPV genotypes.

*HPV-16/-18/-33/-35/-39/-45/-51/-52/-56/-58/-59/-66/-68

STATISTICAL ANALYSIS

Independent Cox proportional hazards models were performed for each outcome, including baseline demographic and HIV factors, anal cytology, and HPV biomarkers.

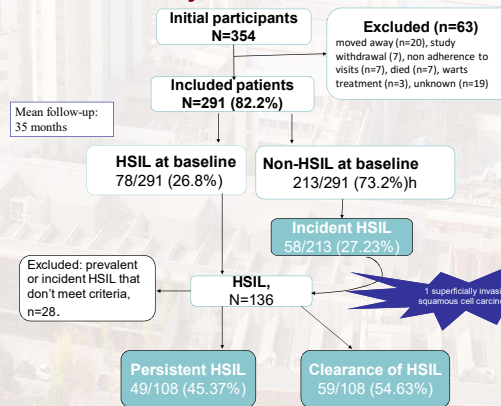
RESULTS

Baseline characteristics

	All participants	N	HSIL (n=78)	Non HSIL (n=213)	p-value
Age (years)	45.6 (10.9)	291	44.94 (10.51)	45.89 (11.03)	0.498
Current smokers	107 (38.2%)	280	31 (40.79%)	76 (37.25%)	0.719
HIV infection related variables					
Nadir CD4 T-cell count, cells/μL	322.9 (258.1)	291	323.4 (233.9)	322.8 (267)	0.831
Current CD4 T-cell count, cells/μL	793.70 (332.7)	291	759.3 (344.4)	806.3 (328.2)	0.114
Nadir CD4 T-cell count < 200	91 (31.3%)	291	23 (29.49%)	68 (31.92%)	0.776
Undetectable HIV-1 RNA viral load, n (%)	255 (87.6%)	291	68 (87.2%)	187 (87.8)	0.776
Sexual behaviour					
Age at first sexual intercourse	17.9 (4.0)	275	17.7 (3.2)	17.9 (4.3)	0.557
Lifetime sexual partners					
<30, n (%)	96 (34.66%)	277	27 (36.00%)	69 (34.16%)	
30-50, n (%)	66 (23.83%)	19 (25.33%)	47 (23.27%)		
50-100, n (%)	40 (14.44%)	13 (17.33%)	27 (13.4%)	0.555	
>100, n (%)	75 (27.08%)	16 (21.33%)	59 (29.21%)		
Receptive anal sexual intercourse, n (%)	212 (75.7%)	51 (67.11%)	161 (78.92%)	0.059	
HPV biomarkers					
LA HPV DNA test	258 (89.5%)	287	74 (98.67%)	184 (86.79%)	0.002
14 assessed by E6/E7 mRNA test	205 (71%)	71 (94.67%)	134 (63.21%)	<0.001	
HPV-16	47 (16.4%)	34 (45.33%)	32 (15.09%)	<0.001	
HC2 HPV DNA test	121 (42.16%)	287	57 (76.00%)	64 (30.19%)	<0.001
E6/E7 mRNA test	147 (51.40%)	286	64 (86.49%)	83 (39.15%)	<0.001
HPV-16	47 (16.4%)	31 (41.89%)	16 (7.55%)	<0.001	
Cytology results, n (%)					
Benign	150 (52.63%)	13 (16.67%)	137 (66.18%)		
ASCUS	48 (16.84%)	10 (12.82%)	38 (18.36%)		
LSIL	43 (15.09%)	17 (21.79%)	26 (12.56%)		
ASC-H	37 (12.98%)	1 (1.28%)	6 (2.90%)		
HSIL	7 (2.46%)	37 (47.44%)	0 (0.00%)		

HSIL: composite HSIL; LA: Linear array; HC2: Hybrid capture; HPV: human papillomavirus; ASCUS: atypical squamous intraepithelial lesion; LSIL: low-grade squamous intraepithelial lesion; ASC-H: atypical squamous intraepithelial lesion that cannot exclude HSIL; HSIL: high-grade squamous intraepithelial lesion.

Natural history

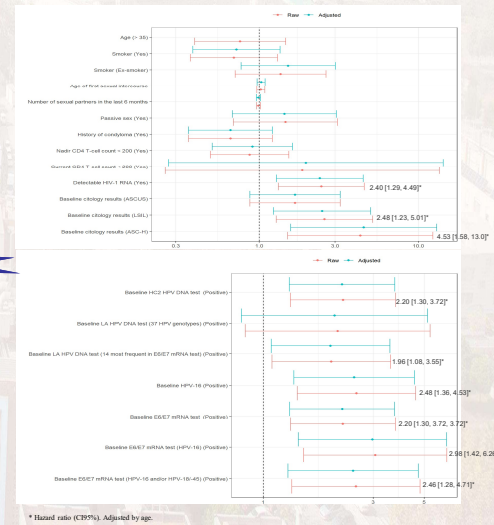


Incidence rate for each outcome

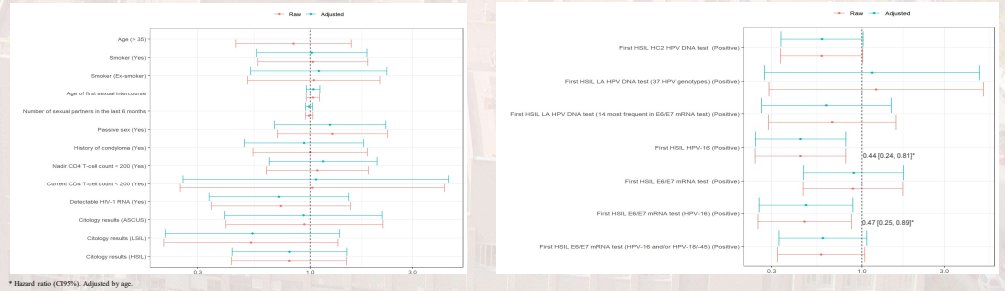
	N(%)	Person-years	Rate (per 100 PY)
Incident HSIL	58/213 (27.23%)	540.49	10.73 (8.15; 13.87)
Persistent non-HSIL	155/213 (72.77%)	540.49	28.68 (24.34; 33.56)
Persistent HSIL	49/108 (45.37)	235.75	20.78 (15.38; 27.48)
Clearance of HSIL	59/108 (54.63%)	238.20	24.77 (18.86; 31.95)

Variables related with incident HSIL

(Incident HSIL vs persistent non-HSIL)



Variables related with clearance of HSIL (Clearance of HSIL vs persistent HSIL)



HPV prevalence in each outcome

	Persistent non-HSIL N=155	Incident HSIL N=58	Persistent HSIL N=49	Clearance of HSIL N=59
LA HPV DNA test	132 (85.16%)	52 (91.23%)	74 (98.67%)	55 (96.49%)
14 assessed by E6/E7 mRNA test	92 (59.35%)	42 (73.68%)	71 (94.67%)	50 (87.23%)
HPV-16	17 (10.97%)	15 (26.32%)	34 (45.33%)	15 (26.32%)
HC2 HPV DNA test	39 (25.16%)	25 (43.86%)	57 (76.00%)	33 (57.89%)
E6/E7 mRNA test	52 (33.55%)	31 (54.39%)	64 (86.49%)	40 (70.18%)
HPV-16	7 (4.52%)	9 (15.79%)	31 (41.89%)	14 (24.56%)

CONCLUSIONS

Incident HSIL occurred in 10.7 per 100 PY and was associated with HIV-1 RNA viral load, anal cytology and HPV-biomarkers. More than half of HSIL cleared spontaneously during follow-up. Detection of the HPV-16, could help determine if HSIL treatment is necessary.