

Role of low-risk HPV PCR mono-infection in screening for HSIL and anal cancer in MSM living with HIV

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Objectives: To determine: the value of low-risk human papillomavirus (HPV) PCR to screen for “high-grade anal squamous intraepithelial lesion and anal cancer” (HSIL-plus), rate of patients with low-grade anal squamous intraepithelial lesion (LSIL) progressing to HSIL-plus, and progression-related factors.

Design: Prospective, longitudinal study of consecutive MSM-LHIV attended between May 2010 and December 2021 and followed for 43 months (IQR: 12-76). **Methods:** HIV-related variables were gathered at baseline, performing anal cytology for HPV detection/genotyping, thin-layer cytological study, and high-resolution anoscopy (HRA). Follow-up was annual when HRA was normal or LSIL, and post-treatment when HSIL-plus, re-evaluating sexual behavior, viral-immunological status, and HPV infection of anal mucosa.

Table 1. Epidemiological characteristics of the cohort.	Cohort N=493
Age, mean (years), (± SD)	36.48 (±10.434)
Nationality, n (%)	
European	464 (94.1)
Central/South American	27 (5.5)
African	2 (0.4)
Median NPT (IQR)	50 (20-200)
Median NP12m (IQR)	2 (1-8)
Median age at start of sexual relations ((IQR)	18 (16-20)
Use of condom, n (%)	329 (66.7)
Median % of use of condom (IQR)	100 (0-100)
Relationships during the previous year, n (%)	442 (89.7)
Occupation (%)	
Non-retired (including students, actively employed, and unemployed, etc.)	434 (88)
Schooling level, n (%)	
No schooling	5 (3.5)
Primary	24 (16.9)
Secondary	40 (28.2)
University	69 (48.6)
Smoking, n (%)	237 (48.1)
Ex-smoker, n (%)	45 (9.1)
Median packs/year, (IQR)	1.65 (0-15)
Alcohol, n (%)	210 (42.6)
Median SDUs, (IQR)	0 (0-4)
Ex-IDU, n (%)	4 (0.8)
Polypharmacy, n (%)	55 (11.2)
HPV vaccination, n (%)	74 (15)
Chronic hepatopathy by HBV, n (%)	16 (3.2)
Chronic hepatopathy by HCV, n (%)	14 (2.8)
Syphilis in baseline visit, n (%)	154 (31.2)
Other STIs at baseline visit, n (%)	144 (29.2)
Total number of STIs at baseline visit, n (%)	
-None	288 (58.4)
-One	196 (39.8)
-Two	6 (1.2)
-Three	2 (0.4)
Positive Mantoux at baseline visit, n (%)	33 (6.7)
Comorbidities, n (%)	60 (12.2)
Condylomas in inclusion visit, n (%)	105 (21.3)
History of genital condylomas, n (%)	149 (30.2)

Table 2. Variables related to HIV infection.	Cohort N=493
Risk for acquiring HIV infection	
-MSM	485 (98)
-IDU	1 (0.2)
-Unknown	6 (1.2)
Median months since diagnosis of HIV infection (IQR)	30.5 (10-105)
Median age at diagnosis of HIV infection (IQR)	31 (25-37)
AIDS (A3, B3, C), n (%)	114 (23.1)
CD4 at diagnosis, mean (± SD)	444.58 (± 288.8)
CD8 at diagnosis, mean (± SD)	1115.57 (± 749.9)
VL at diagnosis, (log10) mean (± SD)	5.5 (± 6.1)
Nadir, n (%)	
<200	114 (23.1)
200-500	231 (46.9%)
>500	129 (26.2)
CD4 baseline visit, mean (± SD)	689.8 (± 450.5)
CD8 baseline visit, mean (± SD)	1954.4 (± 528.7)
CD4/CD8 baseline visit, mean (± SD)	3.3 (± 14.8)
VL (log10) baseline visit, mean (± SD)	3.6 (± 4.2)
VL < 50 cop/mL baseline visit, n (%)	344 (70.9)
Naive, n (%)	53 (10.8)
Median ART lines from initiation (IQR)	1 (1-2)
Median months with ART up to V0 (IQR)	20 (7-73)
ART line baseline visit, median, (IQR)	1 (1-2)
Adherence to ART at V0, median % adherence (IQR)	100 (100-100)
Virological failure, n (%)	20 (4.1)
Reason for ART abandonment, n (%)	
- Adverse effects	8 (1.6)
- Other causes	5 (1)
ART, n (%)	
- NRTI	393 (79.7)
- NNRTI	162 (32.9)
- PI	129 (26.2)
- INSTI	190 (38.5)

Cytology	N = 493
Normal, n (%)	201 (40.8)
-Normal, without HR genotypes, n (%)	42 (8.5)
- Normal, with HR genotypes, n (%)	149 (30.2)
ASCUS, n (%)	38 (7.7)
LSIL, n (%)	230 (46.7)
HSIL, n (%)	13 (2.6)
High resolution anoscopy (HRA)	N = 493
Abnormal, n (%)	235 (47.7)
LSIL (AIN1), n (%)	190 (38.5)
HSIL (AIN2/3), n (%)	54 (11)
Anal carcinoma	3 (0.6)
HR-HPV, n (%)	365 (74)
Number of HR-HPV serotypes, median (P25-P75)	1 (1-3)
LR-HPV, n (%)	351 (71.2)
Number of LR-HPV serotypes, median (P25-P75)	1 (0-2)
Coinfection HPV (HR and LR), n (%)	276 (56)
A9 subspecies HPV 18, 39, 45, 59, 60, n (%)	206 (41.8)
A7 subspecies 16, 31, 33, 35, 52, 58, 67, n (%)	238 (48.3)
Simultaneous infection oncogenic HPV branch A7 and A9, n (%)	119 (24.1)
HPV 6, n (%)	82 (16.6)
HPV 11, n (%)	130 (26.4)
HPV 16, n (%)	64 (13)
HPV 18, n (%)	8 (1.6)
HPV 26, n (%)	67 (13.6)
HPV 31, n (%)	36 (7.3)
HPV 33, n (%)	48 (9.7)
HPV 35, n (%)	61 (12.4)
HPV 39, n (%)	12 (2.4)
HPV 40, n (%)	88 (17.8)
HPV 42, n (%)	20 (4.1)
HPV 43, n (%)	63 (12.8)
HPV 45, n (%)	71 (14.4)
HPV 51, n (%)	63 (12.8)
HPV 52, n (%)	42 (8.5)
HPV 53, n (%)	36 (7.3)
HPV 54, n (%)	83 (16.8)
HPV 55, n (%)	40 (8.1)
HPV 56, n (%)	35 (7.1)
HPV 58, n (%)	50 (10.1)
HPV 59, n (%)	35 (7.1)
HPV 61, n (%)	84 (17)
HPV 62, n (%)	40 (8.1)
HPV 66, n (%)	55 (11.2)
HPV 68, n (%)	16 (3.2)
HPV 69, n (%)	38 (7.7)
HPV 70, n (%)	31 (6.3)
HPV 72, n (%)	44 (8.9)
HPV 73, n (%)	79 (16)
HPV 81, n (%)	25 (5.1)
HPV 82, n (%)	5 (1.0)
HPV 83, n (%)	33 (6.7)
HPV 84, n (%)	13 (2.6)
HPV 108, n (%)	

Table 4. Sensitivity, specificity, PPV, and NPV for anal cytology and HPV PCR in diagnosis of HSIL-plus.	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Normal Cytology (n= 202)	27.3	56.3	7.4	85.7
Abnormal Cytology (n=281)	72.7	43.7	14.2	82.4
LSIL (n=230)	61.8	54.2	14.8	91.7
HSIL (n= 13)	12.7	98.6	53.8	89.7
ASCUS (n=38)	1.8	91.3	2.6	87.8
HPV- High-risk (n=368)	85.7	25.4	13	93.2
HPV-Low-risk (n=43)	79.6	27.9	12.7	91.6
HPV-High and low-risk (n=277)	66.1	43.9	13.4	90.8
HPV-Low-Risk positive and normal cytology (n=125)	14.8	72.3	6.4	86.9
HPV-Low-Risk positive, HPV-High-risk negative and normal cytology (n=35)	100	91.9	2.9	100
HPV-Low-Risk negative and normal cytology (n=75)	9.4	83.4	6.7	88
HPV-High risk negative and normal cytology (n=61)	100	90.2	87.5	100

Progression from LSIL to HSIL-plus occurred in 4.27% of patients within 12 months (IQR: 12-12); risk factors were acquisition of high-risk (HR: 4.15; 95%CI: 1.14-15.03) and low-risk (HR: 3.68; 95%CI: 1.04-12.94) HPV genotypes, specifically genotype 6 (HR: 4.47; 95%CI: 1.34-14.91), and history of AIDS (HR: 5.81 95%CI: 1.78-18.92).

Conclusions: Mono-infection by LR-HPV genotypes in patients with normal cytology is not associated with anal cancer or precursor lesions. Progression from LSIL to HSIL-plus, observed in <5% of patients, was related to acquisition of HR and LR HPV genotypes, especially 6, and a history of AIDS.