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Background

Squamous cell carcinoma of anus (SCCA) is strongly associated with Human Papilloma Virus (HPV) infection and in particular with high-risk HPV genotypes (**HR-HPV**)

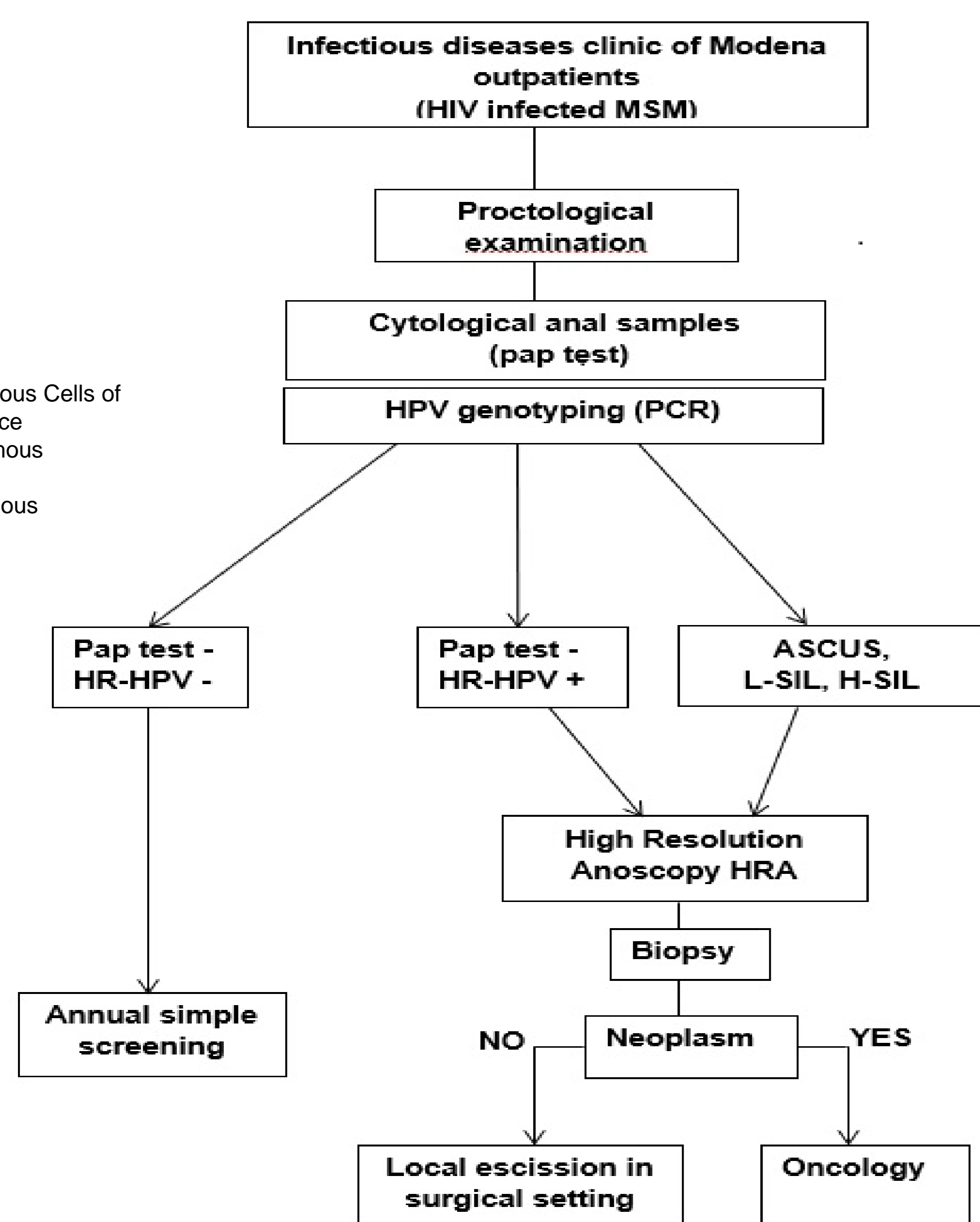
SCCA is one of the most frequent **non-AIDS defining malignancies** in HIV patients, especially MSM; the relative risk of anal cancer among HIV seropositive MSM is 59-fold higher than in the general population

According to **international** guidelines, MSM patients with HIV infection should yearly undergo an anal pap test with cytology. Then, an **High-Resolution Anoscopy (HRA)** is suggested with positive cytology.

Aims of the study: to retrospectively establish the **prevalence of HPV infection**, the **distribution of HPV genotypes** and the **prevalence of pre-cancer lesions** in Modena HIV+ MSM cohort, and to evaluate **epidemiological and viro-immunological risk factors** associated with HPV infections/lesions

Material and methods

We retrospectively analysed HIV data, anal pap test, HPV genotypes and High-Resolution Anoscopy (HRA) results of a cohort of 121 HIV-infected MSM patients accessing our clinic between December 2015 and January 2018, The screening program is explained in this flowchart:



ASCUS: Atypical Squamous Cells of Undetermined Significance
L-SIL: Low-grade Squamous Intraepithelial Lesion
H-SIL: High-grade Squamous Intraepithelial Lesion

Results

Characteristics of patients

Characteristics	Number of patients n=121
Age ±SD	47.2 ±11
<30 y, n, %	6 (4.9)
30-50 y, n, %	71 (58.7)
>50 y, n, %	44 (36.4)
Previous Syphilis, %	53 (43.8)
Previous Hepatitis A, %	18 (14.8)
Previous Condylomatosis, %	33 (27.2)
Previous AIDS-defining events, %	15 (12.3)
Coinfections (HBV, HCV), %	8 (6.6)
Nadir CD4, cells/μL ±SD	326 ± 199
Nadir CD4<200/μL, %	30 (24.8)
HIV NR, months ±SD	75 ± 134
Current CD4 count, cells/μL ±SD	793 ± 297
CD4<200/μL, %	2 (1.6)
Current VL, copies/mL ±SD	19 ±122
VL>40 copies/mL, %	4 (3.3)
CD4/CD8 ratio < 0.8, %	53 (43.8)

Pap test and genotyping

- 50 out of 121 swabs (41.3%) resulted positive to cytological analysis for HPV-related lesions
- HPV genotype known in 72 (59.5%) patients
- HR-HPV genotype were detected in 67% of analyzed samples
- Among negatives pap-test (71), 42 resulted positive for at least one HPV genotype (59%)
- 65.2% of the screened outpatients resulted eligible to HRA (pap-test+/HR-HPV+)
- Focusing on HR HPV, HPV-16 was the most frequent genotype in L-SIL e H-SIL, meanwhile HPV-52 and HPV-58 were the most frequent in negative pap tests.

HRA

- 19 patients performed HRA and biopsies and 14/19 (73.7%) resulted positive for HPV-related alterations
- HRA was determinant for H-SIL diagnosis in two cases (one case detected for the first time)
- In a patient previously diagnosed and treated for H-SIL an anal CIS was diagnosed within 4-months-follow up thanks to HRA
- In a patient previously positive for L-SIL (due to HPV-16) an anal CIS was diagnosed within 6-months-follow up thanks to HRA

Univariate analysis: risk factors for HPV infections/lesions

22 patients with positive pap test suffered from condylomatosis (44%, p=0.0006). None of HIV related features appeared linked to HPV screening positivity.

Characteristics	Total (121)	Positive pap test (50)	HR HPV genotype (48)	HSIL (3)
Condylomatosis, n (%)	33 (27.2%)	22 (44%)	9 (18.7%)	2 (67%)
Previous Syphilis, n (%)	53 (43.8%)	26 (52%)	26 (54.1%)	0 (0%)
Previous Hepatitis A, n (%)	18 (14.8%)	10 (20%)	2 (4.2%)	0 (0%)
AIDS, n (%)	15 (12.3%)	5 (10%)	8 (16.6%)	1 (33%)
Coinfections, n (%)	8 (6.6%)	3 (3.6%)	3 (6.2%)	1 (33%)
Mean nadir CD4	326	337	329	170
HIV NR, mean months	75	79.8	55.6	82
Mean current CD4 count	793	844	698	345
CD4/CD8 ratio < 0.8, n (%)	53 (43.8%)	25 (50%)	24 (50%)	2 (67%)
Mean age	47,2	47	47,6	61

Conclusions

Our results show similar rates of HPV-related lesions to those reported in literature, and stress the importance of HR-HPV genotyping in subjects with no evident lesions at a first level evaluation (pap test)

In our population the occurrence of HPV-related infections **does not correlate with immuno-virological characteristics**, emphasizing the importance of primary prevention.

Limits of the study are: small sample size, **HRA eligibility** (we started HPV genotyping later than the first pap tests), no data on number of different sexual partners.