Persistent anal hrHPV as biomarker for predicting HGAIN in HIV-infected MSM

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Background

High-grade AIN (HGAIN) is a precursor stage of anal cancer and is diagnosed with high-resolution anoscopy (HRA) and histopathology. HRA is a time-consuming, specialized procedure which can be burdensome for the patient. Therefore, it would be beneficial to pre-select those at high risk of HGAIN.

Objectives

- Objective 1: To study if persistent anal hrHPV infection predicts the risk of HGAIN among HIV-positive MSM.
- Objective 2: To study if the HPV-type of a persistent anal hrHPV infection predicts the presence of HGAIN.

Conclusions

Based on this longitudinal study we showed that persistent anal hrHPV infection(s) are predictive of HGAIN. Specifically

- A persistent anal high-risk HPV infection(s) of at least one HPV type was found to be a predictor of HGAIN.
- A persistent HPV-16 and persistent HPV-35 infection were significant predictors of HGAIN.

However, the sensitivity of persistent hrHPV infections as a predictor for HGAIN is too low to be used as a triage tool for HIV-positive MSM prior to HGAIN screening.

Results

Among 195 MSM (median age 50 years [IQR]:45-56) 60 (31%) were diagnosed with HGAIN. In total, 132 participants (68%) had a persistent infection with at least one hrHPV-type, of whom 45 (34%) were diagnosed with HGAIN.

Table 1: Characteristics of the study population (N=195)

	N (195)	%
Median age in years [IQR]	50	[45 – 56]
Smoking status (at first HRA)		
Never smoked	64	33%
Ever smoked / quit smoking	64	33%
Current smoking	43	22%
Median nadir CD4 cell count (cells/µl) [IQR]	235	[150 – 320]
Nadir CD4 cell count (cells/µl)		
<200	75	39%
200-349	80	42%
≥ 350	37	19%
Persistent infection of at least one HPV type	132	68%
HGAIN	60	31%

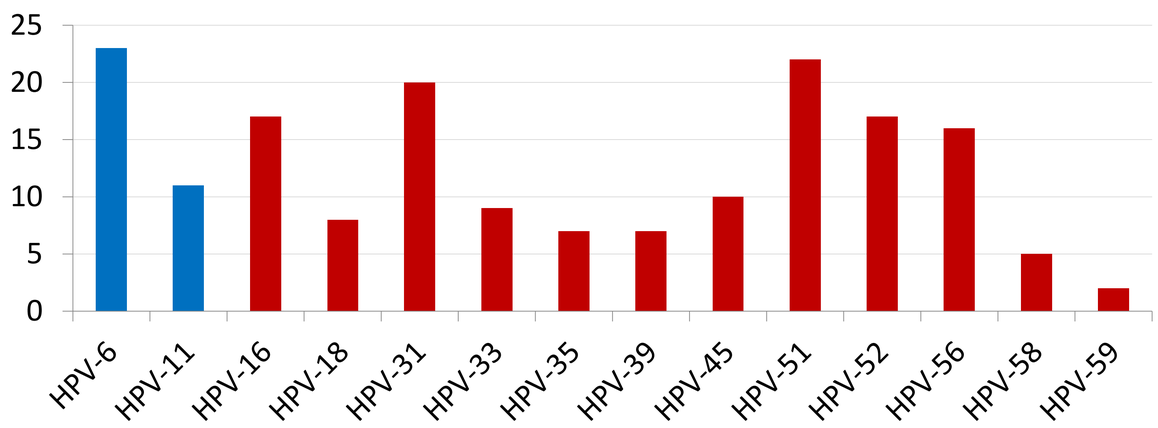

Figure 1: Number of participants with a persistent HPV infections per HPV-type

Table 2: Univariable and multivariable logistic regression of persistent type-specific HPV infection with HGAIN (N=195)

	Univariable logistic regression		Multivariable logistic regression		
HPV type	**OR**	**95% CI**	**aOR**	**95% CI**	***p***
6	2.05	**1.01 - 4.18**	1.90~	0.92 - 3.93	0.083
16	2.70	**1.26 - 5.76**	2.47~	1.14 - 5.34	**0.022**
35	3.18	**1.12 - 8.99**	4.14~	1.38 - 12.47	**0.012**
No. of persistent HPV infections					
0 infections	REF	REF	REF	REF	REF
1 infection	1.12	0.49 - 2.57	1.03*	0.44 - 2.43	0.941
2-3 infections	1.45	0.64 - 3.29	1.48*	0.64 - 3.41	0.354
≥ 4 infections	3.99	**1.45 - 10.94**	3.91*	1.41 - 10.87	**0.009**

~ Adjusted for nadir CD4 cell count (cells/µl)
* Adjusted for type of sexually transmitted infection

Persistent HPV-16 and HPV-35 infection were found to be predictors of HGAIN. However, sensitivity and specificity were limited for both HPV-16 infections as well as at least one persistent hrHPV infection.

	HPV-16	≥1 hrHPV
Sensitivity	28%	75%
Specificity	87%	35%
PPV	50%	23%
NPV	73%	25%
AUC	0.58	0.55

PPV= positive predictive value; NPV= negative predictive value; AUC= area under the curve

Table 3: Parameters of usability of HPV-16 and at least one persistent hrHPV infection as a predictor of HGAIN

Methods

HIV-positive participants of the longitudinal HIV&HPV in MSM study (H2M) who had at least two visits and an HRA, were included in this analysis. Anal-self swabs were collected in 2010-2013, and typed using the SPF_{10}-PCR-DEI-$LIPA_{25}$-system v1. HRAs done after the last H2M visit were included in this analysis. Persistence was defined as ≥3 positive anal samples for the same hrHPV-type. Univariable and multivariable logistic regression was used to study whether persistent HPV infection with (at least) one of 12 hrHPV-types was a predictor of HGAIN.

Discussion

HPV-16 infection has been found to cause most of the anal cancers worldwide. HPV-16 is also proven to be a risk factor for HGAIN, the pre-stage of anal cancer. We showed that persistent HPV-16 is a predictor of HGAIN among HIV-positive MSM.
A strength of this study is that only HIV-positive MSM were included, the population with the highest risk of anal cancer. A limitation of this study is the relatively small sample size for type-specific analyses.