Use of Highly Active Antiretroviral Therapy Is Associated With Lower Prevalence of Anal Intraepithelial Neoplastic Lesions and Lower Prevalence of Human Papillomavirus in HIV-Infected Men Who Have Sex With Men

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Background: The incidence of anal intraepithelial neoplasia (AIN) and anal cancer is increased in HIV-positive men who have sex with men (MSM). Persistent high-risk human papillomavirus (HPV) infection is an important etiologic agent.

Methods: In this study, a group of 250 HIV-positive MSM was included to determine the prevalence of AIN and to investigate the role of highly active antiretroviral therapy (HAART), high-risk HPV, and other risk factors possibly associated with this prevalence.

Results: Among patients included, 108 (43.2%) had lesions suspicious for AIN. Histologic analyses showed AIN 1 in 24 patients (22.2%), AIN 2 in 6 patients (5.6%), and AIN 3 in 10 patients (9.3%). In multivariable analyses, the use of HAART was associated with the absence of AIN (P = 0.045). In MSM without HAART, HPV infection was detected significantly more often compared with those who used HAART (P = 0.010). AIN was associated with HPV types 16 and 6.

Conclusions: In this cross-sectional study in 250 HIV-positive MSM, the use of HAART was associated with lower prevalence of AIN and a significantly lower prevalence of HPV. This association between the prevalence of AIN and the absence of HAART may contribute to the current debate on when to start HAART in HIV-infected individuals.

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associate with increased cervical HPV clearance but not with decrease of cervical intraepithelial neoplasia (CIN) in longitudi-
nal cohort studies.24,25

This cross-sectional study was performed to determine the prevalence of AIN in a group of 250 HIV-positive MSM in
Rotterdam and to investigate the values of several predictors of
AIN in the context of duration and response to HAART.

MATERIALS AND METHODS

Patients and Study Design
From February 2007 to March 2009, 250 individuals were included in a Rotterdam study on the screening of HPV-
related anal premalignancies in HIV-positive MSM. All pa-
tients were recruited from the outpatient clinics of 4 hospitals.
Participants gave written informed consent before start of the
study. The institutional review board of our hospital approved the
study.

Highly Active Antiretroviral Therapy
Antiretroviral therapy was started in patients with CD4

cell counts below 300 \( \times 10^3 \) cells/L or in case of symptoms consistent with the diagnosis of AIDS. This has been standard
treatment in The Netherlands for more than 5 years now.

HIV Viral Load Measurement
HIV RNA was in the majority of cases assessed quanti-
titatively with the Cobas Ampliprep/Cobas Amplicor version
1.5 (lower limit of detection: 50 copies/mL; Roche Molecular
Systems, Penzberg, Germany).

Data Collection
Behavioral data collected from all participants by means of a
questionnaire included age, current smoking habits, sexual ori-
entation, number of sex partners, including practice of anal sex
and earlier diagnosis of anogenital warts. From the medical
records, the following data were collected: length for known
HIV positivity, use and duration of HAART, recent CD4 cell

count, nadir CD4 cell count, HIV viral load, and the previous
(lifetime) occurrence of an AIDS-defining event. All partici-
pants were asked to report complaints in the anal region, such as intermittent itch, pain, and bloody or purulent discharge.

High-Resolution Anoscopy
Anal examination was performed at the department of
dermatology by the same experienced dermatologist in all
patients. The examination consisted of visual inspection of the
perianal and intra-anal area before and after acetic acid (5%)
application. Acetic acid application increases visibility of HPV-
related lesions and intra-anal area. The swabs were immediately placed into standard collecting tubes without transport medium and stored at \(-20\)°C before being sent to the Department of Virology for
further processing. Total nucleic acids were isolated at the
MagnaPureLC Isolation Station (Roche Applied Science).

Detection and Typing of HPV
Detection and typing of HPV DNA was performed using the
INNO-LiPa HPV Genotyping Extra assay (Innogenetics, Ghent, Belgium). The INNO-LiPa HPV Genotyping Extra
assay is a polymerase chain reaction-based line hybridization
assay that utilizes several biotinylated consensus primers
(SPF10) to amplify a region of the L1 gene of HPV types.26

The assay covers all currently known high-risk HPV (HR-HPV)
genotypes and probable HR-HPV genotypes (16, 18, 26, 31, 33,
35, 39, 45, 51, 52, 53, 56, 58, 59, 68, 73, 74, 82), as well as a
number of low-risk HPV (LR-HPV) genotypes (6, 11, 40, 43,
44, 54, 70) and some additional types (69, 71, 74). Fully
automated processing of the strips was executed by using
Auto-LiPA, and automated interpretation of the strips was
performed with LiRAS for LiPA HPV (Innogenetics).26

We used the epidemiologic classification according to
Munoz et al27 and Miyashita et al,28 which groups HPV types
16, 18, 31, 33, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 as
high-risk and considered types 26, 53, 66, 70 or 69, 71, and
“unclassified” (X) as “unknown” with regard to risk.

Statistical Analyses
Data were compared in order to assess statistically sig-
nificant differences in several characteristics (Tables 1 and 2),
including the prevalence of HPV (Table 3) between the groups
with and without dysplasia. Prevalence was calculated as the
number of positive tests per 100 tested individuals. For testing
differences between the groups, the exact \( \chi^2 \) test was used, after
all explanatory variables had been dichotomized. Age, number
of lifetime sexual partners, length for known HIV positivity,
and CD4 cell count and viral load count were tested as contin-
uous variables. Statistical significance was defined as a \( P \) value
of less than 0.05.

Next, the variables age, length for known HIV positivity,
and use of HAART were compared between groups (Table 2).
To adjust for confounding variables, logistic regression analy-
sis was used. The primary selection of covariates for entering
in the model, along with group, was based on univariable
analysis in 2 by 2 tables; an exact \( P \) value below 0.05 was used.
Analyses were done using SPSS 18.0.

RESULTS
A total of 250 males were included in this study, 210
without and 40 with AIN. Patients’ characteristics are summa-
rized in Table 1. The median age of all males included was 46.5
years (interquartile range [IQR]: 40.0–53.3). The median
length of known HIV positivity was 8.0 years (IQR: 4.0–13.0).
Of the cohort, 201 patients (80.4%) were on HAART. The median length of use of HAART was 7.0 years (IQR: 3.0–10.0). The median CD4 cell count was 490.0/\muL (IQR: 357.5–640.0), and the median nadir CD4 cell count was 229.0/\muL (IQR: 120.0–310.0). Of all patients, 67.1% had HIV RNA below the limit of 50 copies/mL. The median number of copies of those with detectable (>50 copies/mL) HIV RNA was 6285.0 (IQR: 322.5–38125.0).

Of all males, 247 (98.8%) had had sex with men only, in the preceding 6 months. Other patients were bisexual.

### Table 1. Characteristics of 250 HIV-Positive Man Who Have Sex With Men

<table>
<thead>
<tr>
<th>Total</th>
<th>No Dysplasia</th>
<th>AIN 1, 2, or 3</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 (100.0)</td>
<td>210 (84.0)</td>
<td>40 (16.0)</td>
<td>0.011</td>
</tr>
<tr>
<td>Median age (yr; IQR)</td>
<td>46.5 (40.0–53.3)</td>
<td>47.0 (40.0–54.3)</td>
<td>43.5 (36.3–49.0)</td>
</tr>
<tr>
<td>Circumcision before age of 10 yr</td>
<td>26 (10.4)</td>
<td>21 (10.0)</td>
<td>5 (12.8)</td>
</tr>
<tr>
<td>Age at sexual debut (median; IQR)</td>
<td>18.0 (15.0–21.0)</td>
<td>18.0 (15.0–21.0)</td>
<td>18.0 (16.0–21.0)</td>
</tr>
<tr>
<td>Bisexual orientation</td>
<td>3 (1.2)</td>
<td>3 (1.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No. lifetime sexual partners (median; IQR)</td>
<td>100.5 (50–500)</td>
<td>101 (45–500)</td>
<td>100 (50–400)</td>
</tr>
<tr>
<td>Receptive anal intercourse in previous 12 mo</td>
<td>174 (69.6)</td>
<td>144 (68.6)</td>
<td>30 (76.9)</td>
</tr>
<tr>
<td>Receptive anal intercourse ever</td>
<td>222 (88.8)</td>
<td>185 (88.5)</td>
<td>37 (94.9)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>90 (36.0)</td>
<td>77 (36.7)</td>
<td>13 (33.3)</td>
</tr>
<tr>
<td>History of anal warts</td>
<td>111 (44.4)</td>
<td>92 (43.8)</td>
<td>19 (48.7)</td>
</tr>
<tr>
<td>Complaints in anal area (pain, itch, pus/blood)</td>
<td>86 (34.4)</td>
<td>68 (32.4)</td>
<td>18 (45.0)</td>
</tr>
</tbody>
</table>

### Table 2. Statistical Analysis for All 250 HIV-Positive Man Who Have Sex With Man

<table>
<thead>
<tr>
<th></th>
<th>All Males</th>
<th>Univariable OR (95% CI)</th>
<th>P*</th>
<th>Multivariable OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (yr; IQR)</td>
<td>46.5 (40.0–53.3)</td>
<td>1.05 (1.01–1.09)</td>
<td>0.011</td>
<td>1.03 (0.99–1.07)</td>
<td>0.17</td>
</tr>
<tr>
<td>Circumcision before age of 10 yr</td>
<td>26 (10.4)</td>
<td>0.76 (0.27–2.14)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Age at sexual debut (median; IQR)</td>
<td>18.0 (15.0–21.0)</td>
<td>0.98 (0.92–1.04)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Bisexual orientation</td>
<td>3 (1.2)</td>
<td>—</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>No. lifetime sexual partners (median; IQR)</td>
<td>100.5 (50–500)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Receptive anal intercourse in previous 12 mo</td>
<td>174 (69.6)</td>
<td>0.66 (0.29–1.46)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Receptive anal intercourse ever</td>
<td>222 (88.8)</td>
<td>0.42 (0.09–1.84)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Recent smoker</td>
<td>90 (36.0)</td>
<td>1.16 (0.56–2.39)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>History of anal warts</td>
<td>111 (44.4)</td>
<td>0.82 (0.41–1.63)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Complaints in anal area (pain, itch, pus/blood)</td>
<td>86 (34.4)</td>
<td>0.59 (0.30–1.16)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Median length for known HIV positivity (yr; IQR)</td>
<td>8.0 (4.0–13.0)</td>
<td>1.06 (1.00–1.13)</td>
<td>0.040</td>
<td>0.97 (0.91–1.04)</td>
<td>0.38</td>
</tr>
<tr>
<td>Years of known HIV positivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5 yr</td>
<td>97 (38.8)</td>
<td>1.34 (0.96–1.87)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>6–10 yr</td>
<td>54 (21.6)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>11–15 y</td>
<td>63 (25.2)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt;15 yr</td>
<td>36 (14.4)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Recent CD4 cell count (median; IQR)</td>
<td>490 (358–640)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Nadir CD4 cell count (median; IQR)</td>
<td>229 (120–310)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Recent HIV viral load (median; IQR)</td>
<td>50 (50–305)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>HIV viral load ≤50 log copies/mL</td>
<td>167 (66.8)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Previous occurrence of AIDS defining event</td>
<td>89 (35.6)</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
<tr>
<td>Use of HAART</td>
<td>201 (80.4)</td>
<td>3.11 (1.49–6.50)</td>
<td>0.004</td>
<td>2.28 (1.02–5.09)</td>
<td>0.045</td>
</tr>
<tr>
<td>Use of HAART for &gt;8 yr</td>
<td>95 (38.0)</td>
<td>1.16 (0.50–2.70)</td>
<td>NS</td>
<td>1.00 (1.00–1.00)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Only P values <0.10 are fully given.

OR indicates odds ratio; CI, confidence interval; NS, not significant.
TABLE 3. Results HPV-PCR in Intra-Anal Swabs of 247 HIV-positive Man Who Have Sex With Men

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>No Dysplasia</th>
<th>AIN 1, 2, or 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>N = 208 (84.2)</td>
<td>N = 39 (15.8)</td>
</tr>
<tr>
<td>HPV-6</td>
<td>27 (13.0)</td>
<td>12 (30.8)</td>
</tr>
<tr>
<td>HPV-11</td>
<td>23 (11.1)</td>
<td>9 (23.1)</td>
</tr>
<tr>
<td>HPV-16</td>
<td>27 (13.0)</td>
<td>12 (30.8)</td>
</tr>
<tr>
<td>HPV-18</td>
<td>18 (8.7)</td>
<td>6 (15.4)</td>
</tr>
<tr>
<td>No HPV</td>
<td>21 (10.1)</td>
<td>2 (5.1)</td>
</tr>
<tr>
<td>Single infection</td>
<td>49 (23.6)</td>
<td>8 (20.5)</td>
</tr>
<tr>
<td>Multiple infections</td>
<td>138 (66.3)</td>
<td>29 (74.4)</td>
</tr>
<tr>
<td>Only high-risk HPV</td>
<td>64 (30.8)</td>
<td>10 (25.0)</td>
</tr>
<tr>
<td>No. types (median; IQR)</td>
<td>2 (1–4)</td>
<td>3 (1–5)</td>
</tr>
</tbody>
</table>

In 3 of 250 HPV specimens, analysis could not be performed. *Only P <0.10 are fully given. IQR indicates interquartile range; NS, not significant.

TABLE 4. Results of Biopsies Taken in Patients With Lesions Suspicious for HPV-Related Intraepithelial Lesion (N = 108)

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>N %</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIN 3</td>
<td>10</td>
</tr>
<tr>
<td>AIN 2</td>
<td>6</td>
</tr>
<tr>
<td>AIN 1</td>
<td>24</td>
</tr>
<tr>
<td>AIN 0</td>
<td>1</td>
</tr>
<tr>
<td>Perianal wart</td>
<td>32</td>
</tr>
<tr>
<td>Granulomatous tissue of unknown origin</td>
<td>19</td>
</tr>
</tbody>
</table>

In this large cross-sectional study in a group of 250 HIV-positive MSM, the prevalence of AIN was 16.0%, which is in line with data from German and French studies. Our study supports the data of the longitudinal cohort study by De Pokomandy et al that usage of HAART may lower the risk on AIN.

DISCUSSION

Among all 250 patients, 108 (43.2%) had lesions suspicious for HPV-related intraepithelial lesion. A total of 122 biopsies were taken. Of all these biopsies, 60 (49.2%) were taken from the perianal area and 62 (50.8%) from the intra-anal area. In 14 patients, both perianal and intra-anal biopsies were taken. Histologic analyses showed AIN 1 in 24 patients (22.2%), AIN 2 in 6 patients (5.6%), and AIN 3 in 10 patients (9.3%). AIN 3 was observed equally often at the perianal and intra-anal area. Of 10 males with AIN 3, 4 had clinically Bowenoid AIN 3. Bowenoid lesions are characterized by pigmented papules, which are histologically similar to Bowen disease (i.e., severe dysplasia) and may have a less aggressive nature than other AIN 3 in HIV-positive MSM. These males were significantly younger than the patients with non-Bowenoid clinical expression of their AIN 3 (median age, 27.0 vs. 50.0 years; P = 0.019). The results of all biopsies taken are summarized in Table 4. In univariable analysis, age (P = 0.011), length for known HIV positivity (P = 0.040), and use of HAART (P = 0.004) were significantly associated with AIN. Neither CD4 cell count, nadir CD4 cell count nor HIV viral load were associated with the prevalence of AIN. All other characteristics in Table 1 were not related with AIN.

In multinivariable analyses, the use of HAART was associated with the absence of AIN (Table 2). This was the case when age, length for known HIV positivity, and use of HAART were used in the analyses.

Intermittent anal itch was reported by 59 (23.6%) patients and pain in the anal region on a regular basis by 34 (13.6%) patients. Sporadic bloody or purulent discharge was reported by 51 (20.4%) patients. None of these complaints were significantly more frequent in those diagnosed with AIN.

HPV types were identified in 224 of 247 samples (90.7%). Data are summarized in Table 3. In only 3 specimens (1.2%), no detection could be performed. A median number of 3 HPV types were detected in positive specimens (IQR: 1–4; maximum number: 13). Of those males with HPV, 171 of 224 (76.3%) had one or more HR-HPV type. LR-HPV was detected in only 27 of 224 (12.1%) positive specimens. HPV types most often detected were HPV-52 (43.8%; HR-HPV), HPV-39 (24.1%; HR-HPV), HPV-74 (21.9%; unknown risk), HPV-54 (21.0%; LR-HPV), and HPV-51 (18.3%; HR-HPV). Well-known HR-HPV types 16 and 18 were detected in 17.4% and 10.7% of positive specimens, respectively. The LR-HPV types 6 and 11 were detected in 17.4% and 14.3% of positive specimens, respectively.

In MSM with AIN, the HPV types 6 and 16 were detected significantly more often compared with those with no dysplasia (P = 0.009 and 0.009) in the sentence “In MSM with AIN, the HPV…” are OK as given.—. No differences were found regarding high-risk types, number of types, or multiple infections.

In MSM with HAART, the absence of any HPV infection was found significantly more often compared with those who did not use HAART (11.5% vs. 0%; P = 0.010). Multiple infections were detected more often in those who did not use HAART (80.9% vs. 64.5%; P = 0.037).

Minority of 69.6% reported to have had receptive anal sex in the preceding 12 months. In all, 111 patients (44.4%) reported a previous history of anogenital warts. Ninety patients (36.0%) had a history of circumcision before the ones without HAART with regard to circumcision before age of 10 years, age at sexual debut, sexual orientation, number of lifetime sexual partners, (recent) practice of receptive anal intercourse, complaints in the anal area, or smoking habit. Those who used HAART were significantly older (median, 48 vs. 39 years; P < 0.0005) and were longer known as being HIV-positive (median, 10 vs. 4 years; P < 0.0005).

In 3 of 250 HPV specimens, analysis could not be performed. *Only P <0.10 are fully given. IQR indicates interquartile range; NS, not significant.
Use of HAART

Data on the impact of HAART on the prevalence of AIN are scarce. Earlier studies did not report this association. This maybe due to small numbers of patients or due to recent introduction of HAART. In a more recent longitudinal study in a cohort of 357 HIV seropositive gay men in San Francisco, Palefsky et al did not assess the effect of antiretroviral therapy possibly because some of the patients in his study were still not using a full HAART regimen. A single longitudinal cohort study on the effect of HAART on CIN showed that women on HAART were 40% more likely to demonstrate regression and less likely to demonstrate progression. Another group confirmed a higher regression rate of CIN in HAART-treated women in a prospective longitudinal study. In contrast, in a recent longitudinal cohort study in women with HIV and at-risk women without HIV by Paramothyth et al, HAART was associated with enhanced cervical HPV clearance, but not with Pap test regression. In this study, only 20% of the women on HAART had HIV RNA <500 copies/mL due to low adherence, which may have underestimated the effects associated with HAART.

Data of the longitudinal cohort study by De Pokomandy et al suggest that receiving HAART for more than 4 years may contribute to some benefit against AIN 2 or 3.

The prevalence of AIN in this study was not associated with duration of known HIV infection, (nadir) CD4 counts, HIV viral load, or the previous occurrence of AIDS-defining events. This may be explained by the high percentage of patients successfully using HAART, with normal median recent CD4 cell counts in both groups.

HPV infection, the etiologic agent of AIN, was detected significantly more often in treatment-naive patients compared with those who used HAART (100% vs. 88.5%; P < 0.010). Differences regarding prevalence of HPV infections in both groups are in agreement with data from several previous studies. Although this difference in our study is significant, a percentage of 88.5%, it is still a high rate of (probably persistent) HPV infections.

Despite potent anti-HIV therapy, with suppression of HIV replication and an increase of CD4 cell counts, this may not be sufficient to reduce HPV persistence but it may be helpful to induce regression of newly acquired acute HPV infection. Our cross-sectional study cannot answer that question. Longitudinal studies on the effect of HAART on HPV persistence in women indeed do report significantly enhanced clearance of HPV after starting HAART. One may hypothesize that longer duration of successful HAART could eventually diminish the risk of AIN.

In this study, the prevalence of AIN was significantly related with the prevalence of both HPV types 16 and 6. HPV type 16 has been linked to different types of anogenital cancers. There was no association between prevalence of AIN and other HR-HPV types or the number of high-risk types. This can be explained by the high prevalence (90.7%) of HPV in this group of patients, of which 76.3% had at least one high-risk type. The prevalence of at least one high-risk type was detected equally often in those with and without AIN.

In contrast to other studies, we did not find an association with nadir CD4 cell count. The nadir CD4 counts in our study were relatively high. This may explain the lower prevalence of AIN 2 or 3 in this study. In contrast to the study by De Pokomandy et al, duration of HAART regimen was not related with the prevalence of AIN.

The strength of this study is the combination of the assessment of AIN and HPV in a group of patients with a high rate of successful HAART, with detailed clinical and laboratory parameters, such as the previous occurrence of AIDS-defining events, recent and nadir CD4 counts, and HIV viral load. Furthermore, the same physician evaluated all patients.

This study was limited by the cross-sectional design. No anal cytology has been used as screening method for the detection of AIN. This limitation might explain the lower percentage of AIN found in this group of HIV-positive MSM compared with other groups where both histology and cytology were used. Due to these small numbers of AIN, it was not possible to separately examine data of AIN 1 versus AIN 2/3.

In conclusion, in this cross-sectional study in 250 HIV-positive MSM, the use of HAART was associated with a significantly reduced prevalence of AIN (OR = 2.28; P = 0.045) and a significantly lower prevalence of HPV (P = 0.010). AIN was associated with HPV types 6 and 16. This association between the prevalence of AIN and the absence of HAART may contribute to the current debate on when to start HAART in HIV-infected individuals. Current European guidelines advice initiation of HAART in case of CD4 cell counts between 350 and 500 × 10^6 cells/L. In patients coinfected with hepatitis B or C, HAART should be initiated even when CD4 cell counts are 500 × 10^6 cells/L or above. Because HPV infection can be considered coinfection, earlier introduction in these patients may be useful, as it may influence its clinical course and related burden.

REFERENCES


