8° WORKSHOP NAZIONALE CISAI

Prevenzione e gestione delle co-morbidità associate all'infezione da HIV

PRESIDENTI: PAOLO BONFANTI, GIUSEPPE DI SOCIO, TIZIANA QUIRINO

PERUGIA, 30-31 MARZO 2017

PROGRAMMA PRELIMINARE

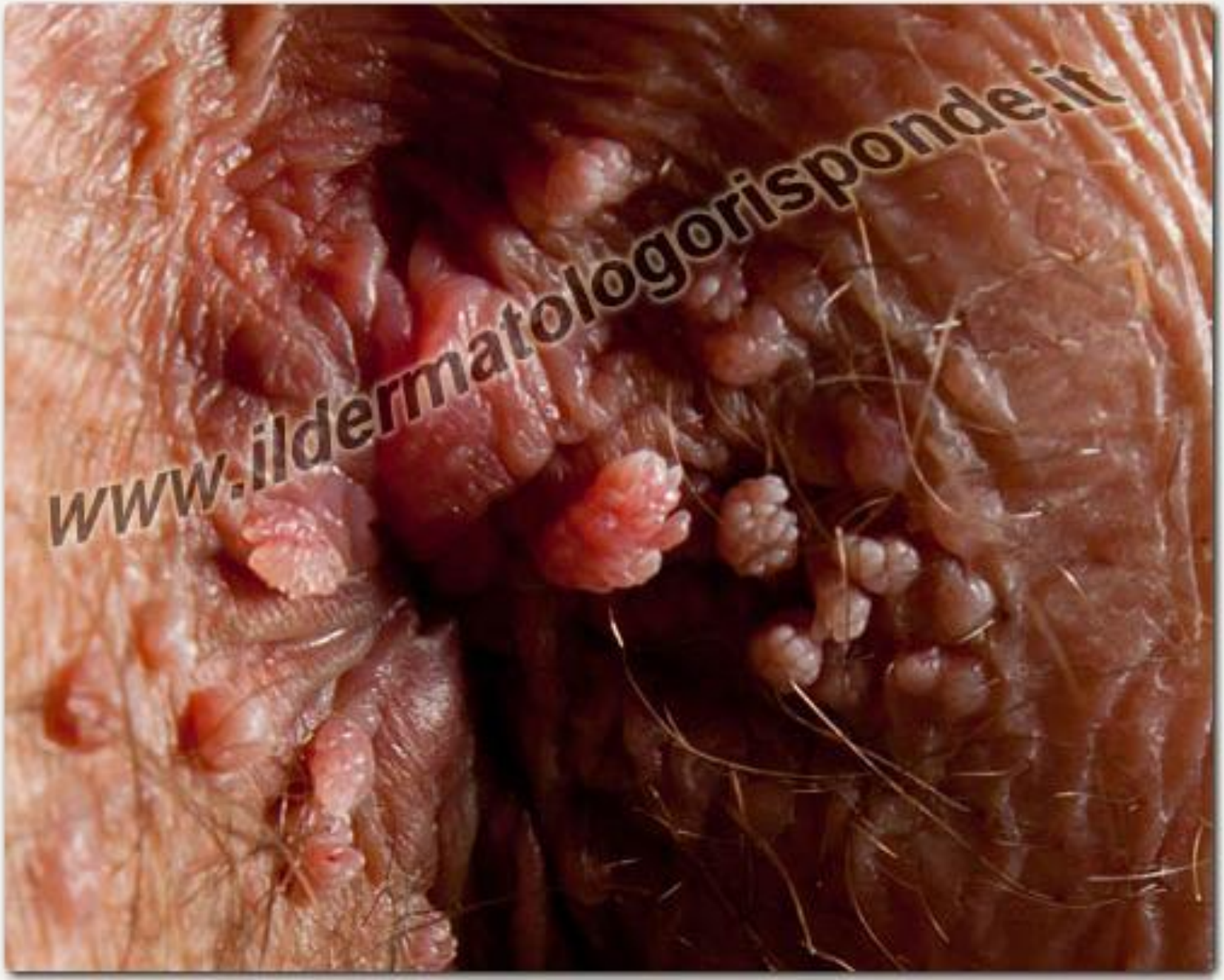
Fondazione A.S.I.A.

CISAI Coordinamento Italiano Studio Allergie e Infezione da HIV

Le neoplasie anali HPV-correlate

Giustino Parruti
UOC Malattie Infettive
AUSL Pescara

Perugia, 31 marzo 2017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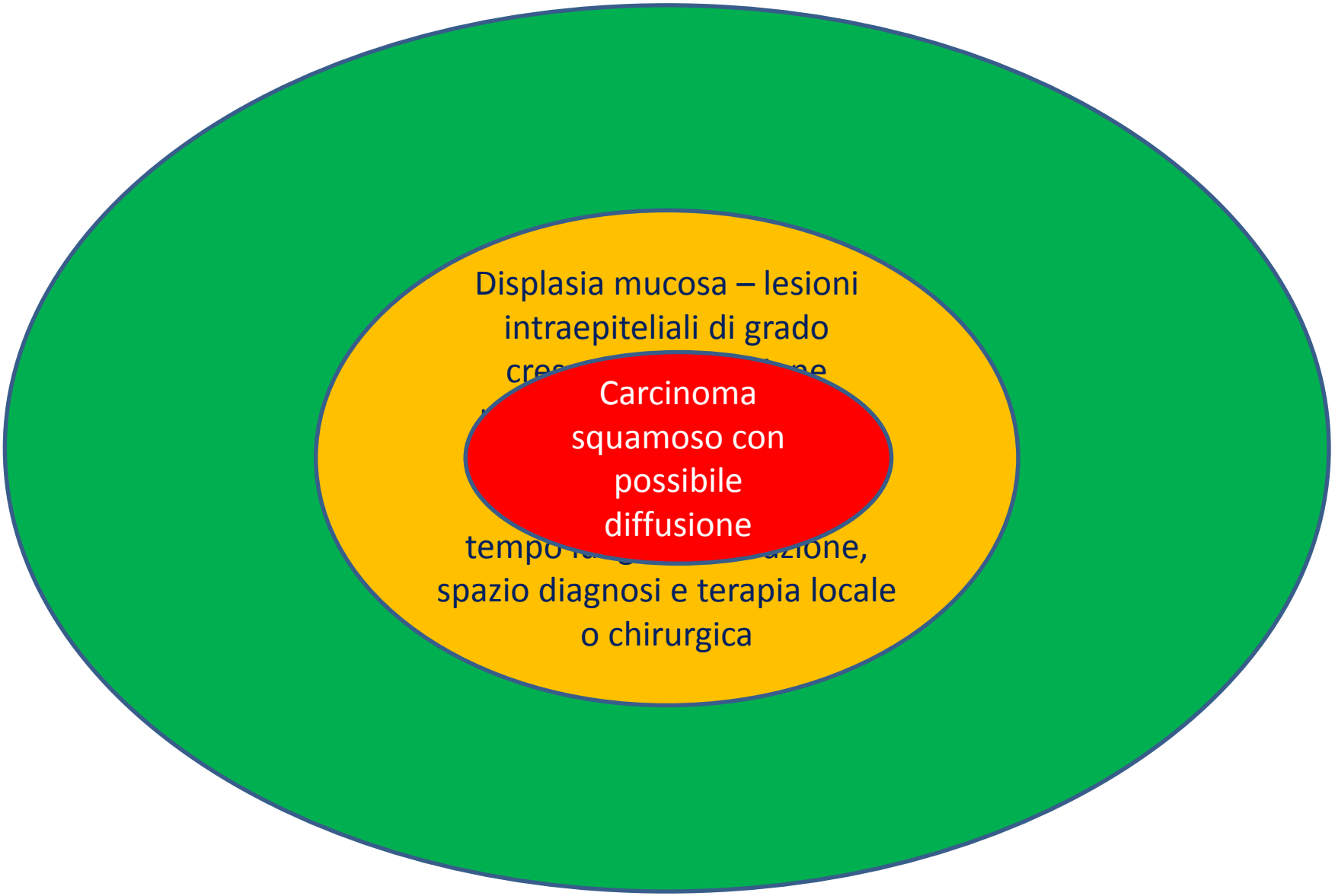

Papillomatosi genitale:
fenomeno frequente e spontanemante reversibile nella maggioranza degli immunocompetenti, conseguente a *disadattato* mescolamento dei viriomi nella promiscuità

Anal canal and rectal condylomatosis: exhaustive proctological examination and STD patients

A. Delbello, C. Colli, T. del Rosario Martínez, and G. Trevisan

SUMMARY

Infection of the anorectal area with some subtypes of HPV virus results in local involvement that appears as warty, papillary, condylomatous lesions. Patients exposed to high-risk HPV types, such as HPV-16, -18, and -31, are at risk for developing high-grade dysplasias or carcinomas. We reviewed 15 years (1991–2006) of patient records from our proctological unit and STD center and found 1,122 patients affected by anorectal condylomatosis. This study supports the importance of an exhaustive proctological examination in patients suffering from condylomatosis of the genital area, especially of the perianal zone, and in patients examined in the STD clinic, even for other reasons. An unknown anorectal condylomatosis is a frequent cause of relapse of anogenital warts. Anal warts should be examined by proctoscopy to assess the full extent of the lesions and prevent possible complications.

Results

We observed that 142 patients (12.6%) suffered from endoanal (anorectal) condylomatosis only, 362 patients (32.3%) from endoanal and perianal condylomatosis, and 618 patients (55.1%) from perianal condylomatosis only, which means that 504 patients (44.9%) were suffering from anal and/or rectal HPV infection. Almost half of the patients had condyloma

examination.

Seventy-seve

been treated for

other anogenital

other areas.

Primo punto: queste lesioni vano cercate proattivamente in tutti i pazienti con condilomatosi genitale, oltre le lesioni evidenti

Two-thirds of the patients' sexual partners developed the infection themselves. Ten percent of the patients reported an infected partner and 20.2% at least one unknown partner in the last year.

Only 10.2% of the males with endoanal localization identified as homosexual; 0.8% were HIV+, 2% were HBV+, and 1.8% were HCV+.

Original article

doi:10.1111/j.1463-1318.2009.01902.x

Extensive anal condylomatosis: prognosis in relation to viral and host factors

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Abstract

Objective To evaluate the clinical course of extensive anal condylomatosis in relation to treatment modalities, patient comorbidity and immune function, and associated papillomavirus (HPV) sequences.

Method Clinical data, treatment modalities and follow-up were recorded and analysed in relation to host and viral type. Histology, immunohistochemistry and molecular analyses for HPV search and typing were performed on formalin-fixed paraffin-embedded samples.

Results Sixteen patients [14 males, median age 41.8 years (range 19–66)] affected by extensive anal condylomatosis [10 Buschke-Lowenstein Tumors (BLT) and 6 condylomatosis] treated in three different Italian institutions were included. There was associated preoperative anal intraepithelial neoplasia grade 3 (AIN3) in one and invasive carcinoma in three patients. After radical resection (n = 16) recurrence occurred in 4/10 (40%) BLT patients. Malignancy before or after treatment developed in 5/16 (31.25%) patients. HPV sequences were present in all the samples of 15 evaluable patients (types 6 or 11, 9 patients; type 16, 6 patients). A statistically significant association was found between presence of HPV type 16 and both malignancy and recurrence. Viral variant L83V was present in 3/4 HPV 16 positive recurrent cases.

Conclusion Radical resection resulted in a favourable clinical course. Typing of HPV sequences in the management of patients affected by extensive anal condylomatosis may be useful.

Keywords Anal condylomatosis, Busckhe-Lowenstein Tumor, HPV type

Original article

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Table 2 Association of patient and viral characteristics with lesion grade and recurrence.

	Lesion grade			Recurrence		
Characteristic	AIN2+	≤ AIN1	*P*	YES	NO	*P*
Mean age, years (range)*	42.6 (19–66)	41.3 (24–57)	0.84	35.2 (19–48)	44.1 (24–66)	0.20
Concurrent infections†	3/7 (42.9%)	2/9 (22%)	0.377	2/4 (50%)	3/12 (25%)	0.350
HPV type 16†,‡	5/7 (71.4%)	1/8 (12.5%)	0.020	4/4 (100%)	2/11 (18.2%)	0.004

*Student's *t*-test.

†Chi-square test.

‡Patient 12 excluded because HPV status could not be determined.

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Transplant Infectious Disease . ISSN 1398-2273

Case report

Giant anal condylomatosis after allogeneic bone marrow transplantation: a rare complication of human papilloma virus infection

N. Ganguly, S. Waller, C.J. Stasik, B.S. Skikne, S. Ganguly. Giant anal condylomatosis after allogeneic bone marrow transplantation: a rare complication of human papilloma virus infection.
Transpl Infect Dis 2008: **10**: 56–58. All rights reserved

Abstract: Condyloma acuminata or genital warts are caused by human papilloma virus (HPV). Ongoing proliferation of HPV in patients with congenital or acquired immunodeficiency states leads to the development of rapidly progressive and sometimes locally invasive tumor with or without dysplasia. Aggressive treatment, diagnostic immuno-typing, and follow-up are necessary in patients with ongoing immunosuppression. We report a case of giant ano-genital condylomatosis due to HPV types 6 and 11 in a patient with chronic myeloid leukemia after allogeneic bone marrow transplantation. The tumor was successfully treated with surgical excision and local application of 5% imiquimod cream.

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Key words: condyloma acuminata; human papilloma virus; bone marrow transplantation

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Received 8 November 2006, revised 2 January 2007, accepted for publication 7 January 2007

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Transplant Infectious Disease . ISSN 1398-2273

Case report

Giant anal condylomatosis after allogeneic bone marrow transplantation: a rare complication of human papilloma virus infection

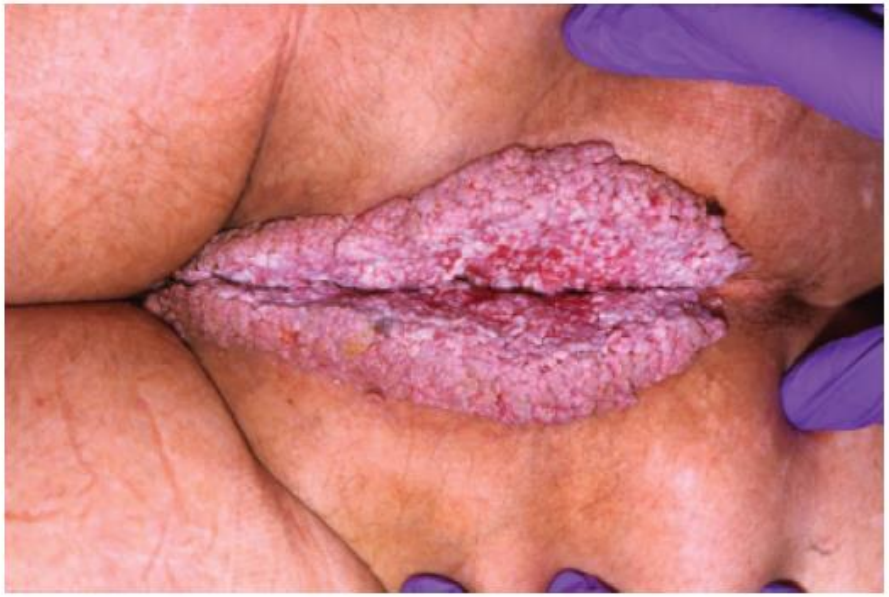
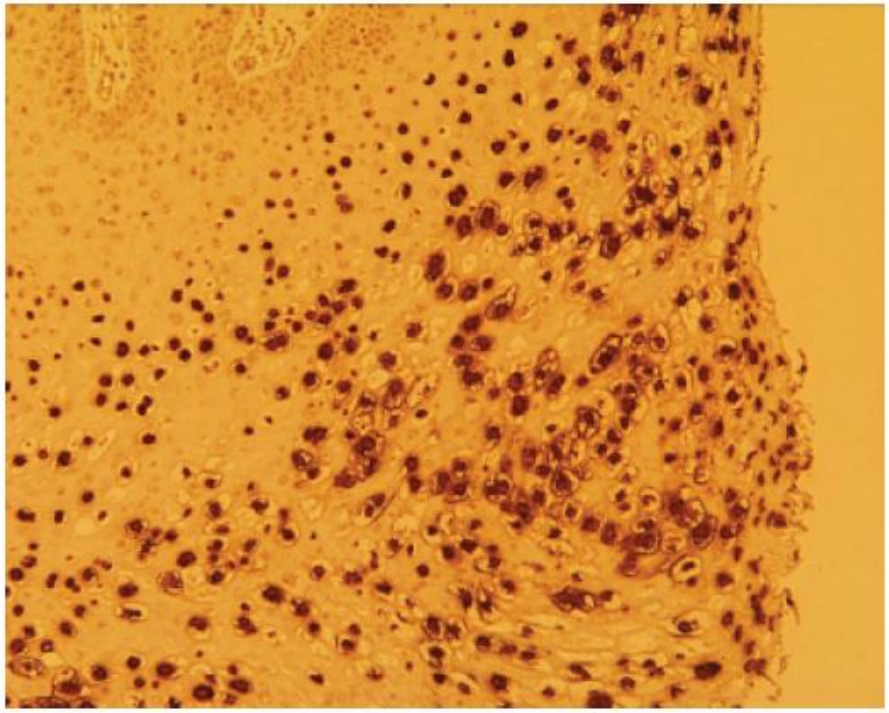


Fig. 1. Peri-anal giant condyloma.



Diagnosi di Tumore in Pazienti HIV: Trend 1980-2002

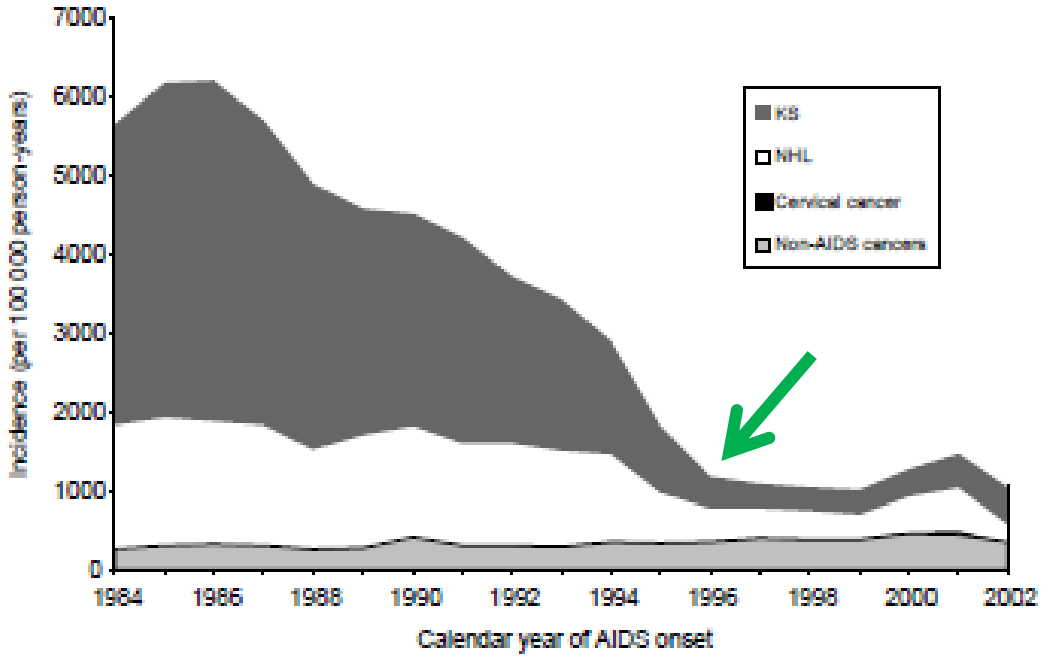


Fig. 3. Cancer incidence among people with AIDS in the United States (1984–2002). Incidence is shown as a function of calendar year of AIDS onset for Kaposi sarcoma (KS), non-Hodgkin lymphoma (NHL), cervical cancer, and non-AIDS-defining cancers. Incidence estimates for each cancer are stacked on top of each other to depict the proportion of total cancer incidence contributed by each cancer type. Analysis was restricted to the 2-year period 4–27 months after AIDS onset.

AIDS 2006, **20**:1645–1654

Cancer Risk and Use of Protease Inhibitor or Nonnucleoside Reverse Transcriptase Inhibitor–Based Combination Antiretroviral Therapy: The D:A:D Study

Mathias Bruyand, MD, PhD, Lene Ryom, MD, PhD,† Leah Shepherd, MBiostat,‡ Gerd Fatkenheuer, MD, PhD,§‖ Andrew Grulich, MD, PhD,¶ Peter Reiss, MD, PhD,#** Stéphane de Wit, MD, PhD,†† Antonella d'Arminio Monforte, MD, PhD,‡‡ Hansjakob Furrer, MD, PhD,§§ Christian Pradier, MD, PhD,‖‖ Jens Lundgren, MD, PhD,† and Caroline Sabin, PhD,‡ for the D:A:D study group*

Background: The association between combination antiretroviral therapy (cART) and cancer risk, especially regimens containing protease inhibitors (PIs) or nonnucleoside reverse transcriptase inhibitors (NNRTIs), is unclear.

Methods: Participants were followed from the latest of D:A:D study entry or January 1, 2004, until the earliest of a first cancer diagnosis, February 1, 2012, death, or 6 months after the last visit. Multivariable Poisson regression models assessed associations between cumulative (per year) use of either any cART or PI/NNRTI, and the incidence of any cancer, non–AIDS-defining cancers (NADC), AIDS-defining cancers (ADC), and the most frequently occurring ADC (Kaposi sarcoma, non-Hodgkin lymphoma) and NADC (lung, invasive anal, head/neck cancers, and Hodgkin lymphoma).

Results: A total of 41,762 persons contributed 241,556 person-years (PY). A total of 1832 cancers were diagnosed [incidence rate: 0.76/100 PY (95% confidence interval: 0.72 to 0.79)], 718 ADC [0.30/100 PY (0.28–0.32)], and 1114 NADC [0.46/100 PY (0.43–0.49)]. Longer exposure to cART was associated with a lower ADC risk [adjusted rate ratio: 0.88/year (0.85–0.92)] but a higher NADC risk [1.02/year (1.00–1.03)]. Both PI and NNRTI use were associated with a lower ADC risk [PI: 0.96/year (0.92–1.00); NNRTI: 0.86/year (0.81–0.91)]. PI use was associated with a higher NADC risk [1.03/year (1.01–1.05)]. Although this was largely driven by an association with anal cancer [1.08/year (1.04–1.13)], the association remained after excluding anal cancers from the end point [1.02/year (1.01–1.04)]. No association was seen between NNRTI use and NADC [1.00/year (0.98–1.02)].

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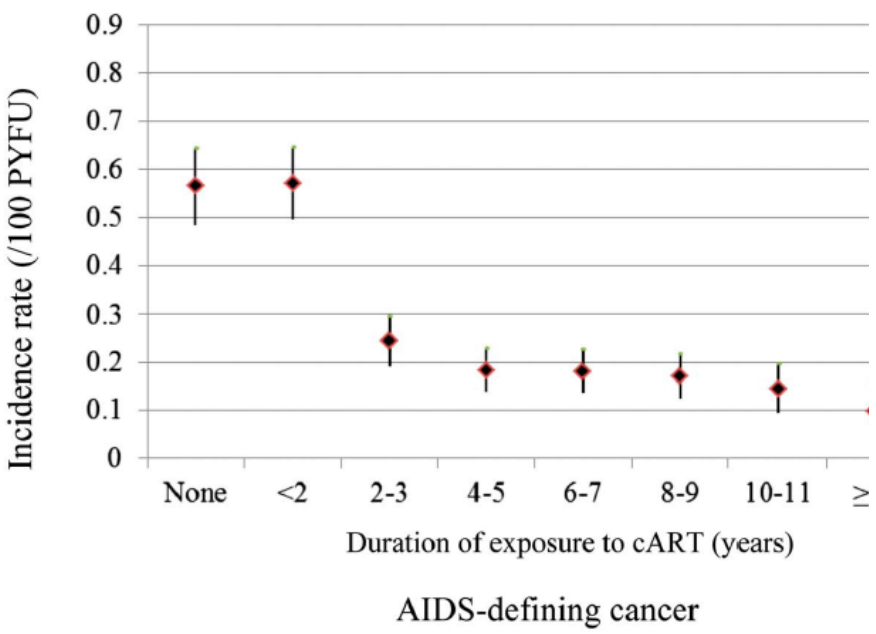
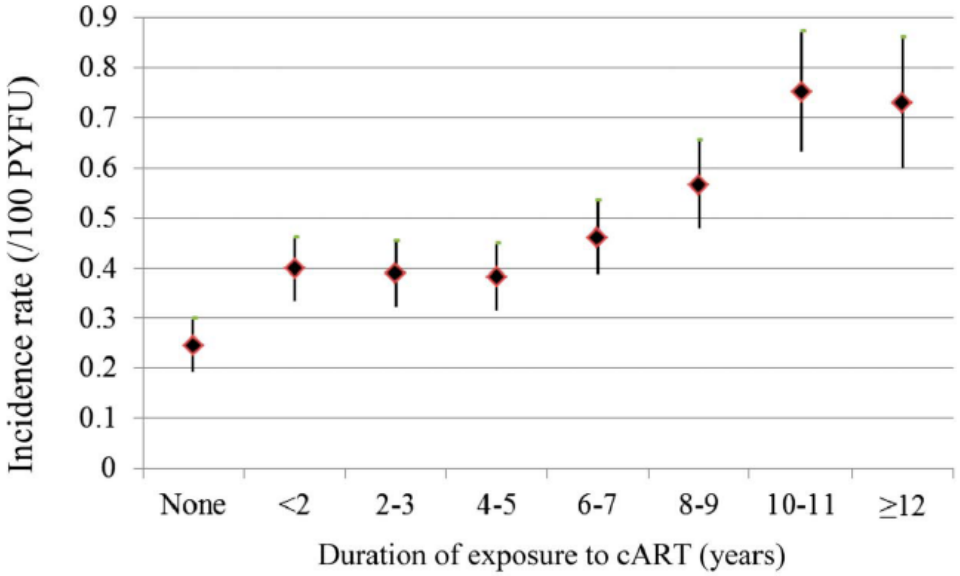
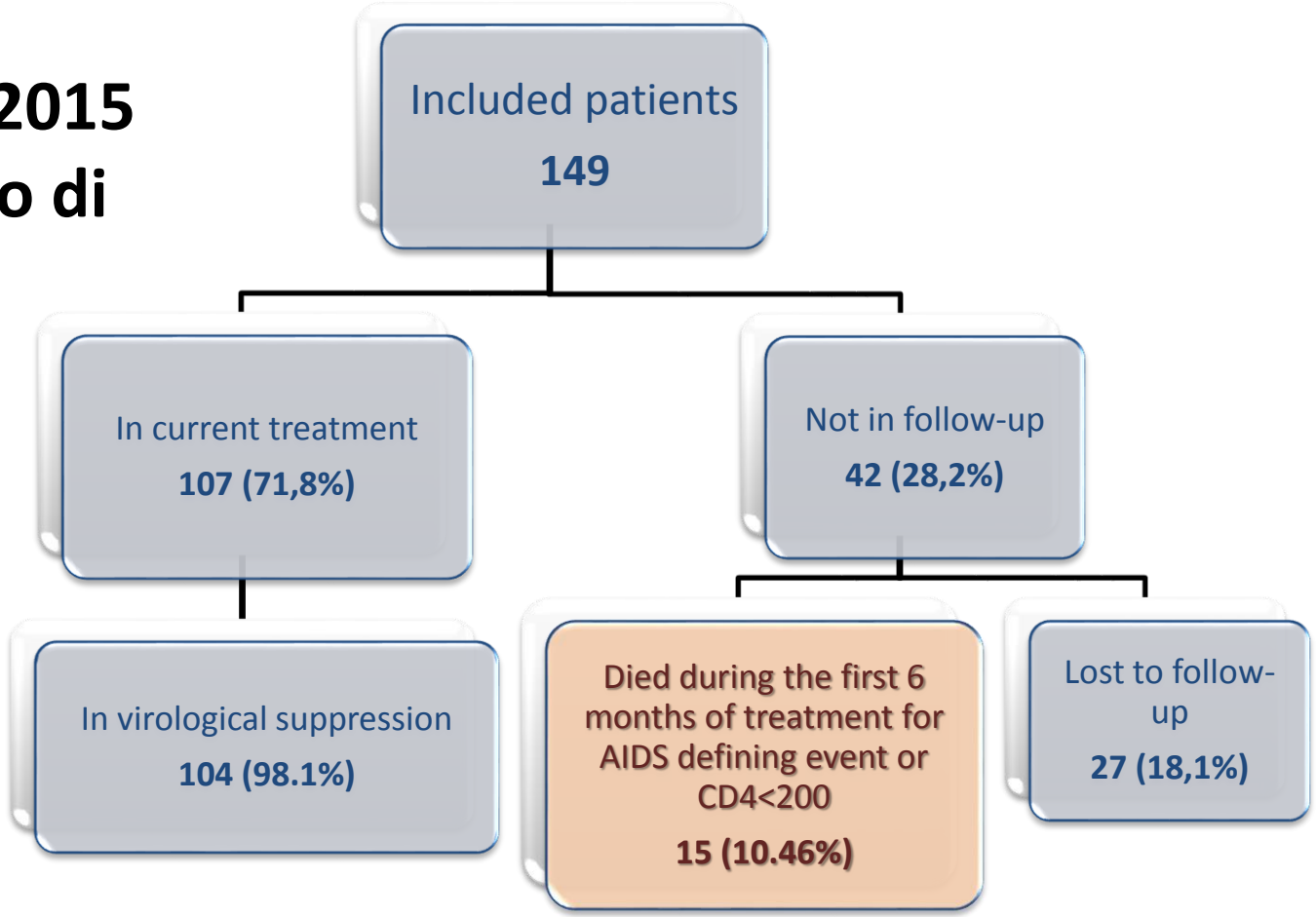


AIDS-defining cancer



Non-AIDS-defining cancer

L'esperienza recente 2013-2015 presso il centro di Pescara



- **107 pazienti (71.8%) risultavano in trattamento**
- **il 98,1% in soppressione virologica**
- **15 (10,6%) è morto durante i primi 6 mesi di trattamento**
- **5 (33%) dei deceduti ha presentato una neoplasia alla diagnosi**

Malignancies in HIV/AIDS: from epidemiology to therapeutic challenges

Paul G. Rubinstein[a,b,*], David M. Aboulafia[c,*] and Andrew Zloza[b,d]

The incidence of AIDS-defining cancers (ADCs) – Kaposi sarcoma, primary central nervous system lymphoma, non-Hodgkin lymphoma, and cervical cancer – although on the decline since shortly after the introduction of HAART, has continued to be greater even in treated HIV-infected persons than in the general population. Although the survival of newly infected people living with HIV/AIDS now rivals that of the general population, morbidity and mortality associated with non-AIDS-defining cancers (NADCs) such as lung, liver, anal, and melanoma are significant and also continue to rise. Increasing age (i.e. longevity) is the greatest risk factor for NADCs, but longevity alone is not sufficient to fully explain these trends in cancer epidemiology. In this review, we briefly review the epidemiology and etiology of cancers seen in HIV/AIDS, and in this context, discuss preclinical research and broad treatment considerations. Investigation of these considerations provides insight into why malignancies continue to be a major problem in the current era of HIV/AIDS care.

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AIDS 2014, **28**:453–465

Table 1. Standard incidence ratios for common AIDS-defining and non-AIDS-defining cancers in the early and later HAART era and in the context of tumor-associated oncogenic viruses.

HIV-associated malignancies	SIR pre-HAART (1990–1995)	SIR early-HAART era (1996–2002)
ADCs		
Kaposi sarcoma	22 100	3640
PCNSL	5000	>1020
Burkitt's lymphoma	52	49
DLBCL	64	29.6
All NHLs	79	22.6
Cervical carcinoma	4.2	5.3
NADCs		
Hodgkin lymphoma	8.1	14
Anal carcinoma	18.3	33
Lung carcinoma	2.5	2.2–6.6
Head and neck carcinoma	1.2	1–4
Prostate cancer	N/A	4
Hepatocellular carcinoma	19	7–35
Melanoma	N/A	3
All NADCs	1.8	1.7–2

ADCs, AIDS-defining cancers; DLBCL, diffuse large B-cell lymphoma; EBV Epstein–Barr virus; HPV, human papillomavirus; N/A, not available; NADCs, non-AIDS-defining cancers; NHL, non-Hodgkin lymphoma; PCNSL, primary central nervous system lymphoma; SIR, standard incidence ratio.

Diagnosi di Tumore in Pazienti HIV: Standard Incidence Ratios

AIDS 2014, **28**:453–465

Table 3. Common AIDS-defining and non-AIDS-defining and tumor-associated oncogenic viruses.

HIV-associated malignancies	Associated oncogenic virus
Kaposi sarcoma	100% HHV-8 [53]
PCNSL	100% EBV [26]
Burkitt's lymphoma	20–40% EBV [26]
DLBCL	Centroblastic 30% EBV [26]
	Immunoblastic 90% EBV [26]
PEL	100% HHV-8 [27]
	100% EBV [25,27]
Plasmablastic	50% HHV-8 [25,26]
	50% EBV [25,26]
Cervical	100% HPV [53]
Hodgkin lymphoma	80–100% EBV [25,26]
Anal carcinoma	100% HPV [52]
Head and neck carcinoma	HPV [53]
	EBV [53]
Hepatocellular	HBV [53]
Carcinoma	HCV [53]

DLBCL, diffuse large B-cell lymphoma; EBV, Epstein–Barr virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV-8, human herpesvirus 8; HPV, human papillomavirus; NADC, non-AIDS-defining cancer; NHL, non-Hodgkin lymphoma; PCNSL, primary central nervous system lymphoma; PEL, primary effusion lymphoma.

TUMORI ED EZIOLOGIA VIRALE

AIDS 2014, **28**:453–465

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POSTER FOR YOU

Prevalence of anal HPV infection in a cohort of HIV+ MSM patients

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Results

- The median age of the study population was 42,3 years.
- The majority was caucasians (92.2%).
- The median age at which partecipants first had sexual intercourse was 17,5 years.
- 17.6% of our population has more than 100 lifetime sexual partners .
- 82% of patients had at least another sexually trasmitted disease in his life.
- 41% of study population is smoker.

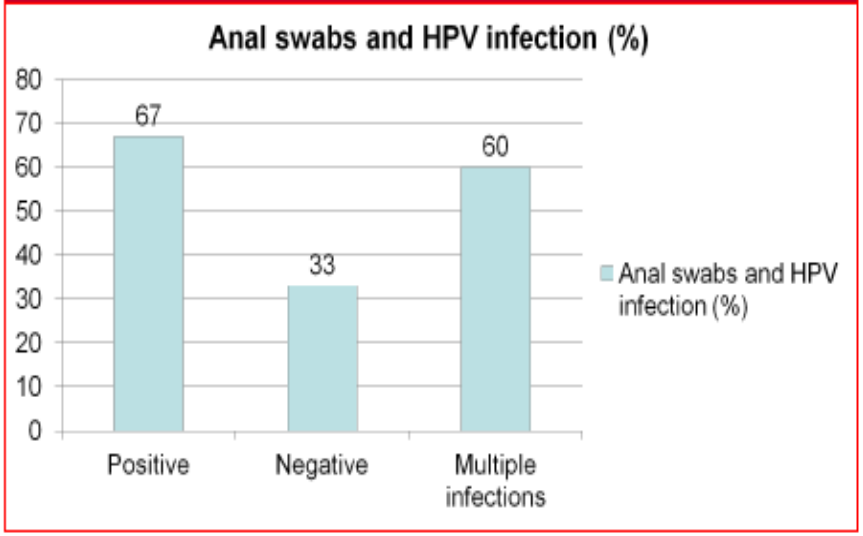
Results 2

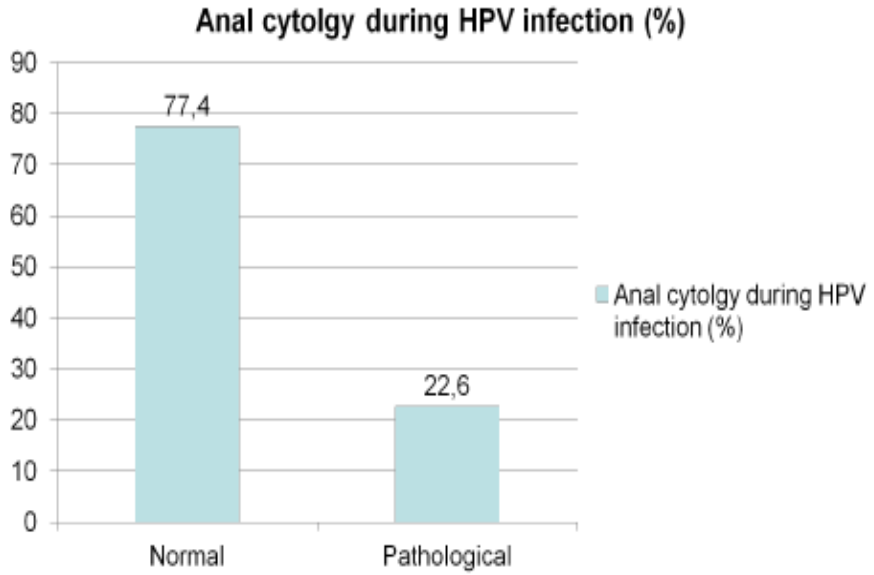
- Overall HPV prevalence is 67%.
- The prevalence of HPV 16/18 infection is 32.3%.
- In this subgroup of patients the prevalence of multiple HPV infection is 60%.
- In patients with HPV anal infection abnormal cytology is found in 22.6% (5 ASCUS and 2 LSIL).
- Median duration of HIV infection is 7.5 years. Median CD4+ count at the screening is 734/mmc, 7.8% has a prior AIDS diagnosis, 74.5 % of patients is in HAART, 94.7% of whom are virologically suppressed.
- At the beginning of our screening none patients was vaccinated for HPV.

Table 1 **Baseline characteristics of patients at the screening**

Median Age (year)	42,3
Caucasians (%)	92,2
Median age of first sexual intercourse (years)	17,5
Patients with > 100 lifetime sexual partners (%)	17,6
Patients with at least another sexual trasmitted disease (%)	82
Smokers (%)	41
Median duration of HIV infection (years)	7,5
Median CD4+ count at the screening (cell./mmc)	734
Prior AIDS diagnosis (%)	7,8
Patients on HAART (%)	74,5
Patients on HAART virologically suppressed (%)	94,7

Figure 1 **Overall prevalence of HPV infection (%)**





Conclusion

HIV+ MSM show a very high rate of HPV infection in the anal canal. In our cohort the type distribution of incident infection is similar to that seen in prevalence studies. HIV–positive MSM should be counseled about anal cancer and risk factor for incident HPV infection. They also should be counseled about primary prevention measures such as condom use and the HPV vaccine that was recently approved for the prevention of anal HPV infection and associated disease in men aged 9-26 years.

Reference

1. « *Incidence of and risk factors for type-specific anal human papillomavirus infection among HIV-positive MSM*» Alexandra L. Hernandez et al., AIDS 2014, 28:1341-1349

ICAR SETTIMO CONGRESSO NAZIONALE Italian Conference on AIDS and Retroviruses
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P46
POSTER FOR YOU

Association between HPV infection and related disease with other sexually transmitted infections (STIs) in a cohort of Italian male and female HIV-positive patients

Barco A[1], Pandolfo A[1], Bai F[1], Suardi E[1], Rovati M[2], Marchetti G[1], Bini T[1], d'Arminio Monforte A[1]
[1]Institute of Infectious and Tropical Diseases, Department of Health Sciences, "San Paolo Hospital", University of Milan [2]Surgery Chair, Department of Health Sciences, "San Paolo Hospital", University of Milan

Results

466 HIV-positive pts were studied:

- Females: 140 pts (31%), males 326 (69%)
- Median age: 41 years (IQR 34-47)
- Median CD4+ T cell count: 501 cells/mmc (IQR 361-654)
- Pts on HAART: 325 (70%)
  - undetectable HIV-RNA: 252 (77%)

STIs infection

- 341 (73%) pts had HPV infection, of these 268 (79%) harboured HR-HPV and 158 (46%) showed multiple genotypes.
- 73 (16%) pts showed syphilis infection, 92 (20%) were HBV-positive and 57 (12%) were HCV-positive; 27 pts (6%) resulted positive for all the 3 STIs investigated.
- HPV-positive pts had more frequently syphilis (p=.0001), compared to HPV-negative pts, but not HBV (p=.136) and HCV (p= 0.95).

Figure 1. Prevalence of STIs infection according to HPV positivity

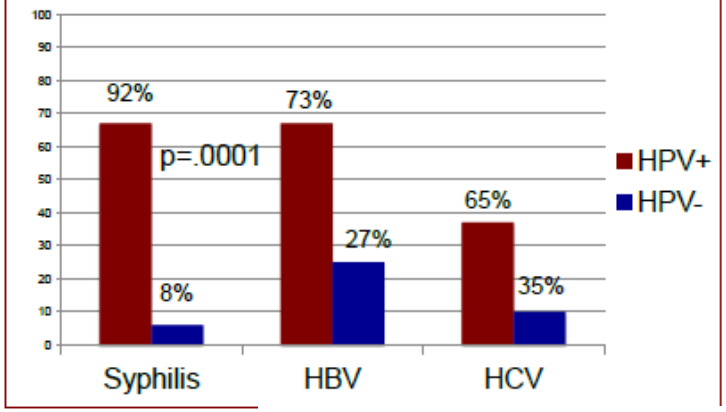

Table 1. Risk of HPV infection according to other STIs

	Univariate			Multivariate*		
Parameters	**OR**	**95%CI**	**p**	**AOR**	**95%CI**	**p**
HBV+ (vs HBV-)	0.98	0.59-1.64	0.95	0.71	0.35-1.45	0.35
HCV+ (vs HCV-)	0.64	0.36-1.15	0.14	0.89	0.39-2.04	0.78
Syphilis+ (vs Syphilis-)	4.97	2.1-11.8	**0.0001**	2.5	0.95-6.53	0.06

ICAR Settimo Congresso Nazionale Italian Conference on AIDS and Retroviruses
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P46
Poster For You

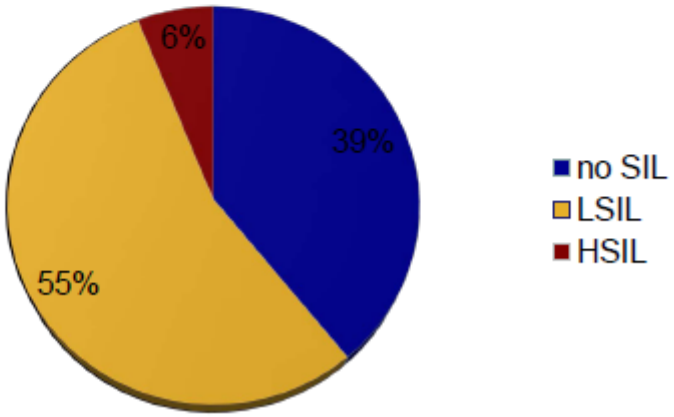
Association between HPV infection and related disease with other sexually transmitted infections (STIs) in a cohort of Italian male and female HIV-positive patients

Barco A[1], Pandolfo A[1], Bai F[1], Suardi E[1], Rovati M[2], Marchetti G[1], Bini T[1], d'Arminio Monforte A[1]
[1]Institute of Infectious and Tropical Diseases, Department of Health Sciences, "San Paolo Hospital", University of Milan [2]Surgery Chair, Department of Health Sciences, "San Paolo Hospital", University of Milan

HPV related disease

- Among HPV-positive pts, 198/325 (61%) showed SIL, while 127 (39%) had a normal cytology (no SIL).
- 20 (10%) of SIL pts showed HSIL and 178 (90%) had LSIL

Figure 2. Prevalence of cytologycal abnormalities among HPV+ patients



- In multivariate analysis, only HCV infection resulted significantly associated to the presence of cytological dysplasia. HIV+/HCV+ pts showed an independent 3.4 higher risk of SIL than HCV- pts.

Table 2. Risk of cytological abnormalities in HPV-positive patients accordinf to other STIs

	Univariate			Multivariate*		
Parameters	**OR**	**95%CI**	**p**	**AOR**	**95%CI**	**p**
HBV+ (vs HBV-)	0.86	0.5-1.48	0.58	1.02	0.54-1.93	0.95
HCV+ (vs HCV-)	1.88	0.85-4.17	0.12	3.39	1.26-9.08	**0.015**
Syphilis+ (vs Syphilis-)	1.26	0.43-1.26	0.43	1.2	0.64-2.25	0.57

*Adjusted for variables <0.1 in univariate: age, gender, MSM, duration of HIV infection

Alpha, beta and gamma Human Papillomaviruses in the anal canal of HIV-infected and uninfected men who have sex with men

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Accepted 10 February 2015
Available online 16 February 2015

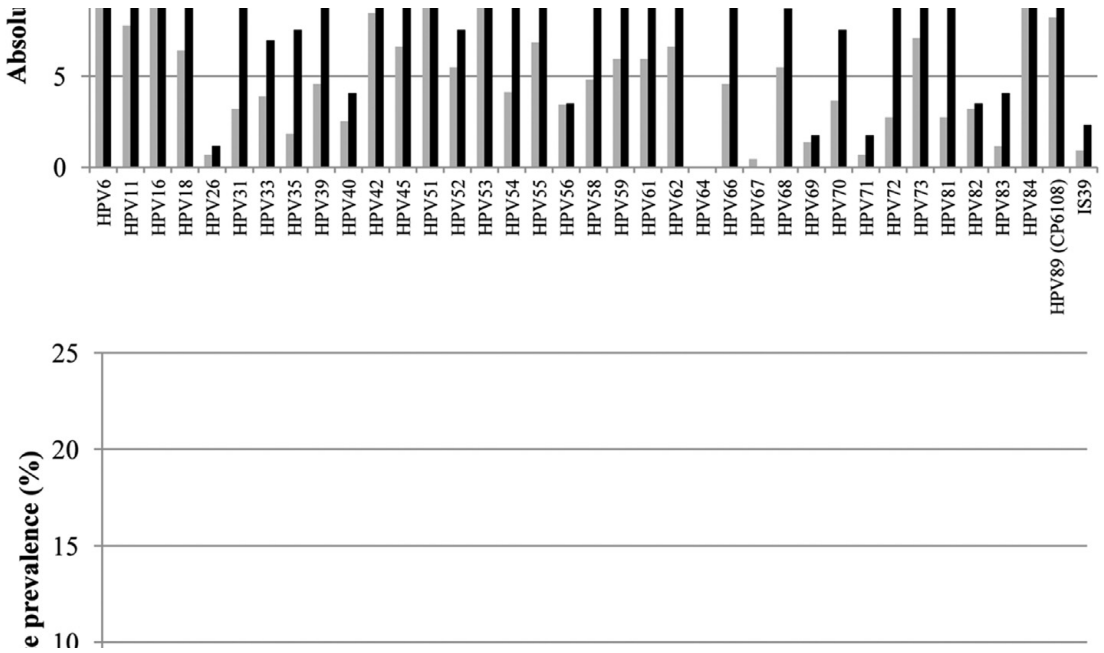
KEYWORDS
Human Papillomavirus;
Infection;
Cutaneous;
Mucosal;
Anal canal;
HIV;
Men who have sex with men

Summary *Objectives:* Anal infection by cutaneous Human Papillomaviruses (HPV) has been rarely investigated. We aimed to assess the prevalence, genotype diversity, and determinants of mucosal (alpha) and cutaneous (beta and gamma) anal HPV infection in men who have sex with men (MSM).
Methods: Anal samples were collected with a Dacron swab. Alpha HPVs were detected using the Linear Array HPV genotyping test, while beta and gamma HPVs using a PCR combined with Luminex technology.
Results: A total of 609 MSM (437 HIV-uninfected and 172 HIV-infected, most of which were undergoing cART) were enrolled. Alpha, beta, and gamma HPVs were detected in 78.0%, 27.6% and 29.3% of the participants. Only alpha HPV prevalence was significantly higher among HIV-infected compared to uninfected MSM (93.0% vs. 72.1%, $p < 0.0001$). Beta2 and gamma10 represented the most frequent cutaneous HPV species, with no significant differences between HIV-infected

Table 2 Prevalence of infection by alpha (N = 609), beta (N = 602) and gamma (N = 597) HPV types by HIV status among the individuals with a valid HPV genotyping test result for the respective genus.

HPV genus		HIV-uninfected MSM	HIV-infected MSM	p value
		n/N (%)	n/N (%)	
Alpha	at least 1 alpha HPV	315/437 (72.1)	160/172 (93.0)	**<0.0001**
	>1 alpha HPV[a]	211/315 (67.0)	129/160 (80.6)	**0.002**
Beta	at least 1 beta HPV	118/434 (27.2)	48/168 (28.6)	0.73
	>1 beta HPV[a]	32/118 (27.1)	8/48 (16.7)	0.15
Gamma	at least 1 gamma HPV	119/430 (27.7)	56/167 (33.5)	0.16
	>1 gamma HPV[a]	28/119 (23.5)	20/56 (35.7)	0.09

p values < 0.05, i.e., indicating statistically significant differences, have been highlighted in bold.
[a] Percentages were calculated considering the number of individuals positive for the respective HPV genus.



High Prevalence of Human Papillomavirus Type 58 in HIV Infected Men Who Have Sex With Men: A Preliminary Report in Central Italy

Michela Lucia Sammarco,[1] Claudio Ucciferri,[1,2] Manuela Tamburro,[1] Katia Falasca,[2] Giancarlo Ripabelli,[1]* and Jacopo Vecchiet[2]

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Human papillomavirus (HPV) infection and type-specific prevalence at anal, oral, coronal sulcus, and urethral mucosa in fifty HIV positive men having sex with men (MSM) were evaluated; patients were enrolled in a non-metropolitan area of Central Italy. Clinical and socio-demographic information, drug, and sexual behaviors were obtained for each participant. HPV was detected by PCR from an overall of 200 specimens, and genotyping was performed by both Restriction Fragment Length Polymorphism analysis and sequencing. HPV DNA was found in 60.0% (n = 30) of HIV positive MSM, and prevalence was higher at anal canal (n = 28, 56.0%) compared to all the other anatomical sites (χ^2 test $P < 0.01$) of coronal sulcus (n = 11, 22.0%), oral (n = 8, 16.0%), and urethral mucosa (n = 5, 10.0%). We found 63.3% (n = 19) of MSM with at least one high-risk genotype, and HPV-58 was more frequently detected (n = 9, 47.4%) respect to HPV-16 (n = 6, 31.6%). This is the first report on HPV detected at four anatomical sites involved in sexual practices in HIV positive MSM. We found an unusual distribution of oncogenic genotypes with an exceeding prevalence of HPV-58 respect to HPV-16. Hence, the recently licensed nonavalent vaccine should be suitable to prevent a larger number of infections caused by potentially emerging high-risk genotypes. ***J. Med. Virol. 88:911–914, 2016.*** © 2015 Wiley Periodicals, Inc.

and risk of HIV acquisition [Rositch et al., 2013; Videla et al., 2013]. Moreover, the incidence of anal cancer increased in men who have sex with men (MSM) compared to heterosexual men and in HIV infected individuals despite highly active antiretroviral treatment [Houlihan et al., 2012; Lawton et al., 2013; Hernandez et al., 2014]. Among these risk population groups, where life expectancy is reduced by non-HIV related morbidities [Ucciferri et al., 2012, 2013], HPV infections are generally caused by high-risk (HR) genotypes [De Vuyst et al., 2009; Ripabelli et al., 2010], particularly HPV-16. Therefore, in order to design and develop successful preventive protocols for HIV infected MSM, it is necessary to assess the prevalence of HR HPV genotypes, including those targeted by available vaccines, in order to estimate the potential impact of the vaccination strategies on types circulation and to monitor their relative frequencies [Sammarco et al., 2013].

To date, there are two licensed HPV vaccines showing high efficacy to prevent HPV infections or precancerous lesions caused by two HR genotypes. Particularly, the bivalent vaccine offers active protection against HPV-16 and 18 associated to vaginal, vulvar, and anal cancers, as well as the quadrivalent vaccine which is also used to prevent low-risk (LR) HPV-6 and 11 genotypes, associated with anogenital warts. Schiller et al. [2012] reviewed the results of large scale clinical trials and reported that both vaccines provide significant protection against HR genotypes similar to HPV-16, such as 39, 45, 59, and 68, and also against

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TABLE I. HPV Prevalence Per Anatomical Site in fifty HIV Positive MSM

HPV	n	%
Infection by anatomical site		
Anal canal	28/50	56.0
Oral cavity	8/50	16.0
Urethra	5/50	10.0
Coronal sulcus	11/50	22.0
HR type at anatomical site		
Anal	11/28	39.3
Oral	6/8	75.0
Urethral	3/5	60.0
Coronal sulcus	7/11	63.6
Multiple site-infection in HPV positive individuals		
One site	15/30	50.0
Two sites	9/30	30.0
Three sites	5/30	16.7
All sites	1/30	3.3

TABLE II. HR HPV Types Prevalence and Site-Specific Proportion in HIV Positive MSM

		HR type proportion per anatomical site[c]			
HR type	HR type prevalence[b] n (%)	Anal n (%)	Oral n (%)	Urethral n (%)	Coronal sulcus n (%)
16[a]	6 (31.6)	4 (36.3)	2 (33.3)	–	–
31[a]	1 (5.3)	1 (9.1)	–	–	–
39	1 (5.3)	1 (9.1)	–	–	–
58[a]	9 (47.4)	2 (18.2)	3 (50.0)	2 (66.7)	5 (71.4)
59	1 (5.3)	–	1 (16.7)	–	1 (14.3)
66	2 (10.6)	1 (9.1)	–	1 (33.3)	–
68	1 (5.3)	1 (9.1)	–	–	1 (14.3)
82	1 (5.3)	1 (9.1)	–	–	–

[a]HR HPV types included in the nonavalent vaccine (16/30, 53.3%).
[b]Prevalence of HPV HR types was calculated on the number of HIV positive (n = 19) MSM who had detectable HR type at least at one anatomical site.
[c]Site-specific proportion of HR HPV type was calculated on the number of patients with anal (n = 11), oral (n = 6), urethral (n = 3), and coronal sulcus (n = 7) harboring at least one HR type.

Human Papillomavirus and Genital Warts: A Review of the Evidence for the 2015 Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines

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To provide updates for the 2015 Centers for Disease Control and Prevention sexually transmitted diseases treatment guidelines on human papillomavirus (HPV) and anogenital warts (AGWs), a review of the literature was conducted in key topic areas: (1) epidemiology and burden of disease; (2) transmission and natural history; (3) diagnosis and management of AGWs; (4) occupational exposure of healthcare workers; (5) anal cancer screening among men who have sex with men (MSM); and (6) HPV vaccine recommendations. Most sexually active persons will have detectable HPV at least once in their lifetime; 14 million persons are infected annually, and 79 million persons have prevalent infection. HPV is transmitted frequently between partners; more frequent transmission has been reported from females to males than from males to females. A new formulation of imiquimod (3.75% cream) is recommended for AGW treatment. Appropriate infection control, including performing laser or electrocautery in ventilated rooms using standard precautions, is recommended to prevent possible transmission to healthcare workers who treat anogenital warts, oral warts, and anogenital intraepithelial neoplasias (eg, cervical intraepithelial neoplasia). Data are insufficient to recommend routine anal cancer screening with anal cytology in persons living with human immunodeficiency virus (HIV)/AIDS or HIV-negative MSM. An annual digital anorectal examination may be useful for early detection of anal cancer in these populations. HPV vaccine is recommended routinely for 11- or 12-year-olds, as well as for young men through age 21 years and young women through age 26 years who have not previously been vaccinated. HPV vaccine is also recommended for MSM, people living with HIV/AIDS, and immunocompromised persons through age 26 years.

Keywords. HPV; genital warts; treatment; HPV vaccine.

SUPPLEMENT ARTICLE

Human Papillomavirus and Genital Warts: A Review of the Evidence for the 2015 Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines

Ina U. Park,[1,2] Camille Introcaso,[3] and Eileen F. Dunne[3,a]

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geal cancers. Based on data from the Surveillance Epidemiology and End Results and National Program of Cancer Registries, it is estimated that 34 788 new HPV-associated cancers occurred in the United States in 2009 [3]. Overall annual direct medical costs for HPV-associated diseases in the United States are an estimated $8 billion US dollars, including $6.6 billion (82.3%) for routine cervical cancer screening and follow-up, $1.0 billion (12.0%) for cancer treatment, $300 million (3.6%) for AGW treatment, and $200 million (2.1%) for recurrent respiratory papillomatosis treatment [4].

Human Papillomavirus and Genital Warts: A Review of the Evidence for the 2015 Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines

Ina U. Park,[1,2] Camille Introcaso,[3] and Eileen F. Dunne[3,a]

Diagnosis and Treatment of Anogenital Warts

Diagnosis and Indications for Biopsy

AGWs are most often diagnosed based on their clinical appearance, and tests for the presence of HPV are not recommended for diagnosis of AGWs. Histologic examination of biopsy specimens can be performed to rule out intraepithelial or invasive squamous cell carcinomas (SCCs), which can coexist with or appear similar to AGWs. A Danish study of nearly 50 000 people with AGWs found an elevated risk of HPV-associated cancers in people with AGWs compared with the general population.

men (SIR, 21.5) [18]. A retrospective series of MSM with AGWs requiring surgical removal found high-grade intraepithelial neoplasms or SCCs in the excised AGW tissue of 47% (75/159) of MSM living with HIV/AIDS and 26% (42/160) of HIV-negative MSM [19]. Another study of immunosuppressed women with both vaginal intraepithelial neoplasia (VIN) and AGWs reported that in all 11 subjects, VIN occurred admixed with or directly adjacent to the site of AGWs [20].

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Anal Cancer Screening and Treatment of Anal Intraepithelial Neoplasia

Epidemiology

Though anal cancer is rare in the general population (1–2 cases/100 000 PY), anal cancer burden is much higher among certain populations, including MSM. Anal cancer incidence among HIV-negative MSM is estimated at 5 cases/100 000 PY; for MSM living with HIV/AIDS, this estimate is 45.9 cases/100 000 PY overall and 77.8 cases/100 000 PY in the post–highly active antiretroviral therapy era [40]. Anal HPV infection is nearly ubiquitous in MSM living with HIV/AIDS (93% prevalence), with high-risk HPV prevalence estimated to be 73.5% for MSM living with HIV/AIDS and 37.2% for HIV-negative MSM. A systematic review concluded that more than half of MSM living with HIV/AIDS have abnormal cytology (57%), and 29% have high-grade anal intraepithelial neoplasia (HGAIN) [40]. The incidence of HGAIN among MSM living with HIV/AIDS has been estimated by 2 studies [41, 42] and ranges from 8.5% to 15.4% per year.

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Table 1. Recommended and Alternative Regimens for Treatment of External Anogenital Warts

Recommended Patient-Applied Regimen	Dosing
Imiquimod 5% cream	Topically every night at bedtime for 3 times/wk up to 16 wk
Imiquimod 3.75% cream	Topically every night at bedtime up to 16 wk
Podofilox 0.5% solution or gel	Topically twice daily × 3 d followed by 4 d off for up to 4 cycles
Sinecatechins 15% ointment	Topically 3 times daily, for up to 16 wk
Bichloracetic acid 80%–90%	Applied once every 1–2 wk
Cryotherapy	Applied once every 1–2 wk
Surgical removal	
Trichloroacetic acid 80%–90%	Applied once every 1–2 wk

Source: CDC, MMWR Recomm Rep 2015; 64(No. RR-3):1–137.

Table 2. Recommended and Alternative Regimens for Treatment of Mucosal Warts (Intra-anal, Urethral Meatus, Intravaginal)

Recommended Provider-Administered Regimen	Dosing/Route
Bichloracetic acid 80%–90%	Applied once every 1–2 wk (anal, vaginal)
Cryotherapy	Applied once every 1–2 wk (anal, urethral meatus, vaginal)
Surgical removal	
Trichloroacetic acid 80%–90%	Applied once every 1–2 wk (anal, vaginal)

Source: CDC, MMWR Recomm Rep 2015; 64(No. RR-3):1–137.

Data are insufficient to recommend anal cancer screening with anal cytology in people living with HIV, MSM without HIV infection, and the general population based on the available evidence. More evidence is needed concerning the natural history of AIN, the best screening methods and target populations, potential harms of screening, safety of, and response to treatments, and other programmatic considerations before screening can be routinely recommended. There is currently an ongoing trial of anal cancer screening (NCT02135419), which may address many of these outstanding issues.

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HPV Vaccine Recommendations

The ACIP recommends routine HPV vaccination at age 11–12 years; the vaccination series can be started beginning at age 9 years [67] (Table 3). Vaccination is also recommended for females aged 13–26 years and for males aged 13–21 years who have not been vaccinated previously or who have not completed the 3-dose series [67]. Men aged 22–26 years may be vaccinated. Vaccination of females is recommended with bivalent HPV vaccine, Cervarix (2vHPV), quadrivalent HPV vaccine, Gardasil (4vHPV) (as long as this formulation is available), or nonavalent HPV vaccine, Gardasil9 (9vHPV). Vaccination of males is recommended with 4vHPV (as long as this formulation is available) or 9vHPV [68].

The 2vHPV, 4vHPV, and 9vHPV vaccines all protect against HPV 16 and 18, types that cause about 66% of cervical cancers and the majority of other HPV-attributable cancers in the United States; 9vHPV targets 5 additional cancer-causing types, which account for about 15% of cervical cancers. 4vHPV and 9vHPV also protect against HPV 6 and 11, types that cause anogenital warts [68]. MSM, people living with HIV, and immunocompromised persons should be vaccinated through age 26 years [68].

Table 3. Human Papillomavirus Vaccine Recommendations From the Advisory Committee on Immunization Practices

Population	Age Group, y	Recommendation
Females	11-12 (may start at 9)	Routine vaccination with either 2vHPV, 4vHPV, or 9vHPV
	13–26	Routine vaccination with either 2vHPV, 4vHPV, or 9vHPV[a]
Males	11–12 (may start at 9)	Routine vaccination: 4vHPV or 9vHPV
	13–21	Routine vaccination: 4vHPV or 9vHPV
	22–26	4vHPV or 9vHPV may be administered
MSM and HIV$^+$	22–26	Routine vaccination: 4vHPV or 9vHPV

Sources: CDC, Morb Mortal Wkly Rep 2010; 59:626–32. CDC, Morb Mortal Wkly Rep 2011; 60:1705–8. CDC, Morb Mortal Wkly Rep 2015; 64:300–4.

Abbreviations: 2vHPV, bivalent HPV vaccine; 4vHPV, quadrivalent HPV vaccine; 9vHPV, nonavalent HPV vaccine; HIV, human immunodeficiency virus; HPV, human papillomavirus; MSM, men who have sex with men; PLHA, people living with HIV/AIDS.

[a] Vaccination should be given respective of history of abnormal Pap, HPV, genital warts.

Original Paper

Intervirology

Intervirology 2016;59:118–122
DOI: 10.1159/000452710

Received: April 19, 2016
Accepted: October 19, 2016
Published online: December 7, 2016

Feasibility and Acceptability of Anal Self-Sampling for Human Papillomavirus Screening in HIV-Infected Patients

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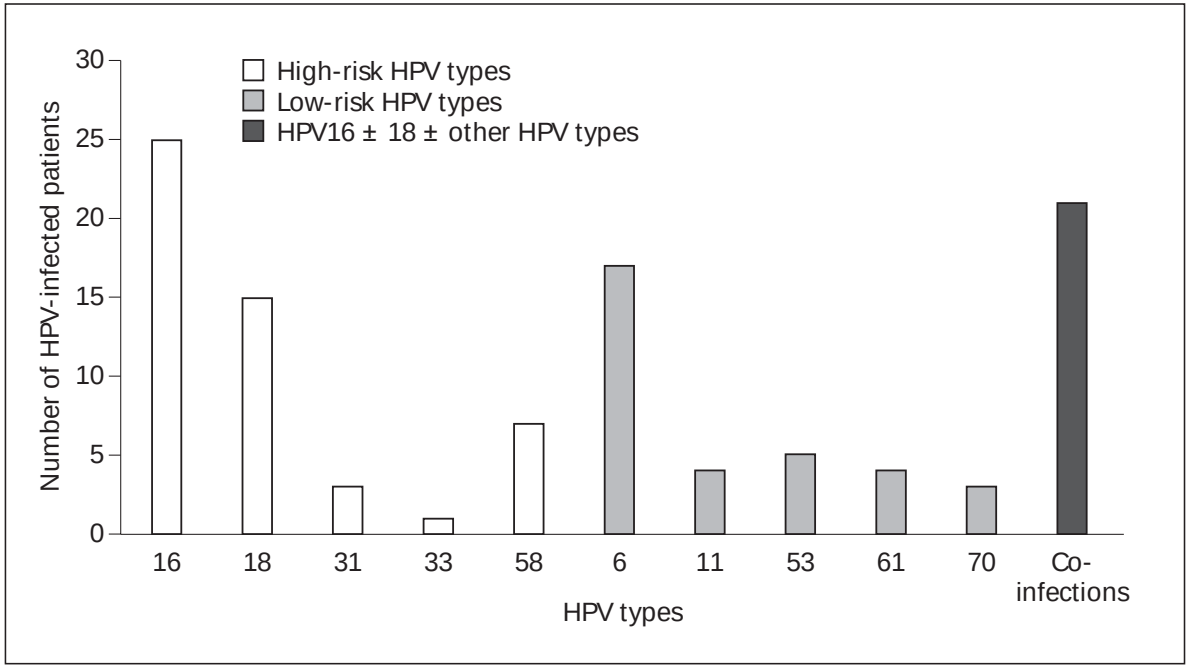
Table 1. Patients' characteristics and HPV results

Parameters	Results
Sex (M/F)	89/17
Median age, years	46
CD4 cell count, cells/mm^3	642 ± 286
HIV RNA load, $\log_{10}$ copies/mL	4.5 ± 5.1
Interpretable samples[1]	94/106 (89)
HPV-negative samples (positive/tested)	23/94 (24)
HPV-positive samples (positive/tested)	71/94 (76)
HPV16	25 (35)
HPV18	15 (21)
HPV16 + 18	10 (14)
≥2 HPV types other than 16 + 18	21 (30)
HR HPV types	38 (54)
LR HPV types	38 (54)

Values are given as *n* (%) or means ± SD, unless otherwise indicated. HR, high-risk; LR, low-risk. [1] Accurate cellular assessment for HPV detection.



World Journal of Gastrointestinal Oncology

Submit a Manuscript: http://www.wjgnet.com/esps/ World J Gastrointest Oncol 2017 February 15; 9(2): 50-61

DOI: 10.4251/wjgo.v9.i2.50 ISSN 1948-5204 (online)

Anal intraepithelial neoplasia: A review of diagnosis and management

Table 3 Progression rates of anal intraepithelial neoplasia to squamous cell carcinoma

Progression	No. patients	Rate of progression	Median or average progression time	Ref.
AIN II/III to SCC	72	11%	42 mo	[33]
AIN III to SCC	35	8.6%	53 mo	[34]
AIN I to AIN III	199	12.6% (8.1/100 person-years)	18 mo	[35]
ASCUS/AIN I to AIN II/III	556	24.5% (10.5/100 person-years)	36 mo	[36]
HSIL to SCC	138	19.6%	57 mo. w/prevalent HSIL; 64 mo. w/ incident HSIL	[37]

ASCUS: Atypical squamous cells of undetermined significance; LSIL: Low-grade squamous intraepithelial lesion; HSIL: High-grade squamous intraepithelial lesion; AIN: Anal intraepithelial neoplasia; SCC: Squamous cell carcinoma.

Table 2 Rates of anal cancer among various populations compiled from various sources

Anal cancer rates among select populations, per 100000 person-years	
General population	2[1]
General population, female	0.55-2.4[13]
HIV positive women	3.9-30[13]
HIV negative MSM	5.1[12]
Solid organ transplant	10-15[66]
Prior HPV related malignancy	0.8-63.8[13]
HIV positive MSM	49.5[12]
Colon cancer in general population	41[2]

HIV: Human immunodeficiency virus; MSM: Sex with men; HPV: Human papilloma virus.

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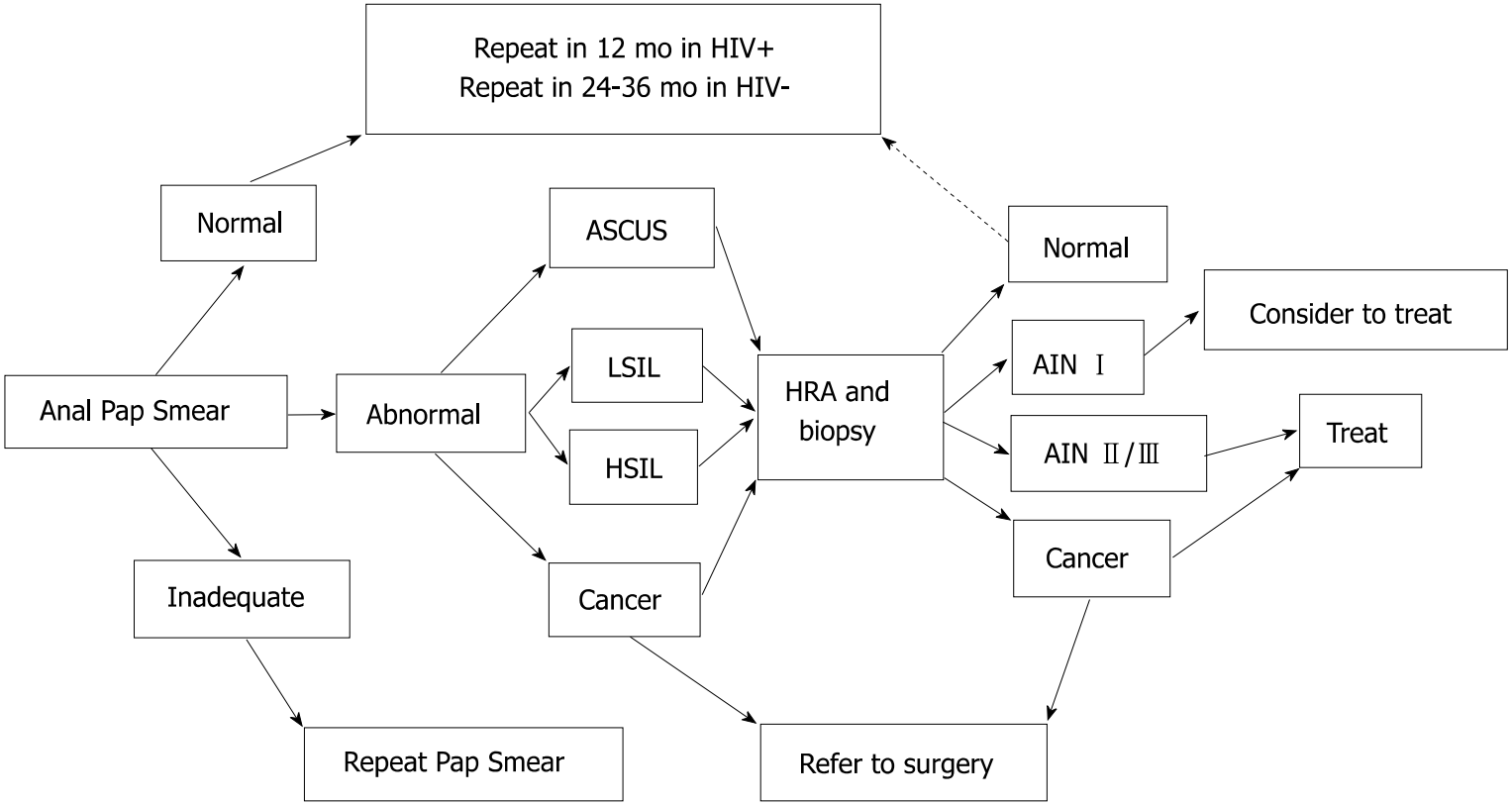
Anal intraepithelial neoplasia: A review of diagnosis and management



Screening to Prevent Anal Cancer: Current Thinking and Future Directions

Joel M. Palefsky, MD, CM, FRCP(C), Professor of Medicine, University of California San Francisco

Joel M. Palefsky, MD, CM, FRCP(C), is Professor of Medicine at the University of California San Francisco. He is an internationally recognized expert on the molecular biology, treatment, pathogenesis, and natural history of anogenital human papillomavirus (HPV) infections, particularly in the setting of human immunodeficiency virus (HIV) infection. He is director of the world's first clinic devoted to the prevention of anal cancer: the University of California San Francisco Anal Neoplasia Clinic, Research, and Education Center. He has pioneered diagnostic and treatment methods for anal squamous intraepithelial lesions. He is also chair of the HPV Working Group of the US National Cancer Institute-supported AIDS Malignancy Consortium and Principal Investigator of the ANal Cancer/HSIL Outcomes Research (ANCHOR) study. He is founder of the International Anal Neoplasia Society and president of the International Papillomavirus Society.

Anal cancer is biologically similar to cervical cancer in its relationship to human papillomavirus (HPV) and, like cervical cancer, is preceded by high-grade squamous intraepithelial lesion (HSIL). Using techniques adapted from cervical cancer prevention programs, anal HSIL can readily be identified using high-resolution anoscopy (HRA), with the goal of providing histopathologic confirmation of the level of disease and guiding therapy.

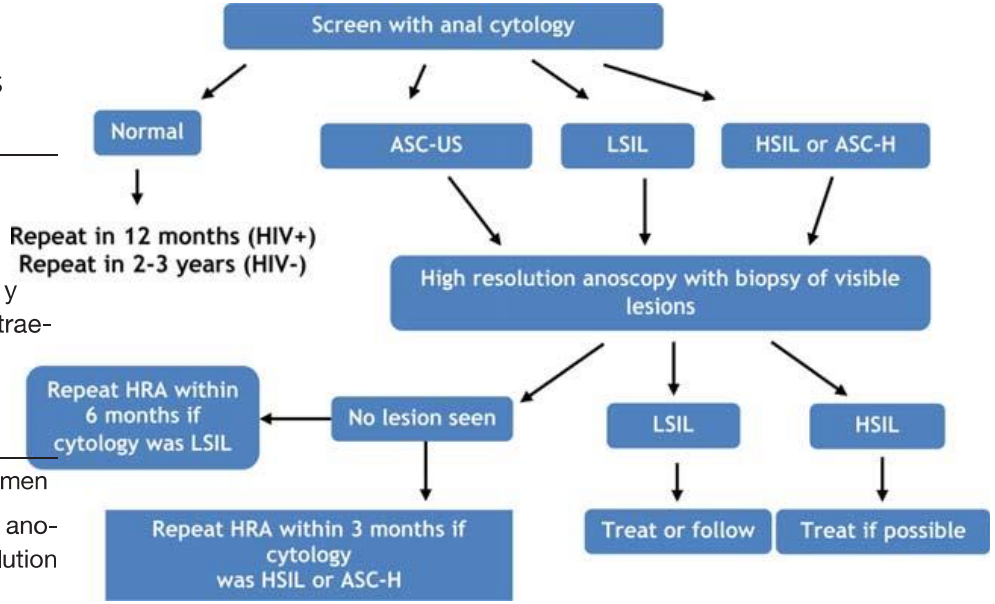
guidelines recommending screening for anal HSIL. In this era of evidence-based medicine, evidence of the efficacy of anal screening to reduce the incidence of anal cancer is needed. To date, data do not exist demonstrating the success of screening the anus for HSIL. Fortunately, such a study to acquire the necessary data recently was initiated. Known as the ANCHOR (ANal Cancer/HSIL Outcomes Research)

TABLE 1. List of Populations That Should Be Considered for Anal Cancer/High-Grade Squamous Intraepithelial Lesion Screening[a]

- All HIV-positive men aged >25 y regardless of sexual orientation
- All HIV-positive women aged >25 y
- All HIV-negative MSM aged >40 y
- Women with high-grade cervical or vulvar lesions or cancer aged >40 y
- All men and women with perianal condyloma/high-grade squamous intraepithelial lesion aged >25 y
- Solid organ transplantation recipients and patients with other forms of immunosuppression aged >25 y

HIV indicates human immunodeficiency virus; MSM, men who have sex with men

[a] All men and women at risk of anal cancer should have an annual digital anorectal examination to palpate masses, even if anal cytology and high-resolution anoscopy services are not available to them.



Leeds *et al. World Journal of Surgical Oncology* (2016) 14:208
DOI 10.1186/s12957-016-0970-x

World Journal of Surgical Oncology

RESEARCH Open Access

Outcomes of abdominoperineal resection for management of anal cancer in HIV-positive patients: a national case review

Ira L. Leeds[1*], Hasan Alturki[2], Joseph K. Canner[2], Eric B. Schneider[2], Jonathan E. Efron[1], Elizabeth C. Wick[1], Susan L. Gearhart[1], Bashar Safar[1] and Sandy H. Fang[1]

Background: The incidence of anal cancer in human immunodeficiency virus (HIV)-positive individuals is increasing, and how co-infection affects outcomes is not fully understood. This study sought to describe the current outcome disparities between anal cancer patients with and without HIV undergoing abdominoperineal resection (APR).

Methods: A retrospective review of all US patients diagnosed with anal squamous cell carcinoma, undergoing an APR, was performed. Cases were identified using a weighted derivative of the Healthcare Utilization Project's National Inpatient Sample (2000–2011). Patients greater than 60 years old were excluded after finding a skewed population distribution between those with and without HIV infection. Multivariable logistic regression and generalized linear modeling analysis examined factors associated with postoperative outcomes and cost. Perioperative complications, in-hospital mortality, length of hospital stay, and hospital costs were compared for those undergoing APR with and without HIV infection.

Results: A total of 1725 patients diagnosed with anal squamous cell cancer undergoing APR were identified, of whom 308 (17.9 %) were HIV-positive. HIV-positive patients were younger than HIV-negative patients undergoing APR for anal cancer (median age 47 years old versus 51 years old, $p < 0.001$) and were more likely to be male (95.1 versus 30.6 %, $p < 0.001$). Postoperative hemorrhage was more frequent in the HIV-positive group (5.1 versus 1.5 %, $p = 0.05$). Mortality was low in both groups (0 % in HIV-positive versus 1.49 % in HIV-negative, $p = 0.355$), and length of stay (LOS) (10+ days; 75th percentile of patient data) was similar (36.9 % with HIV versus 29.8 % without HIV, $p = 0.262$).
Greater hospitalization costs were associated with patients who experienced a complication. However, there was no difference in hospitalization costs seen between HIV-positive and HIV-negative patients ($p = 0.66$).

Conclusions: HIV status is not associated with worse postoperative recovery after APR for anal cancer as measured by length of stay or hospitalization cost. Further study may support APRs to be used more aggressively in HIV-positive patients with anal cancer.

Keywords: Anal cancer, Abdominoperineal resection, Human immunodeficiency virus infection, Surgical outcomes

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Table 4 Generalized linear modeling (gamma distribution) of total hospitalization costs after APR for anal cancer

Variables	Adjusted exp:coefficient[a] (95 % CI)	Mean difference in cost (2011$)	*P* value
HIV	1.03 (0.86–1.22)	670	0.78
Any complication	1.29 (1.11–1.51)	6914	0.001
Tissue flap	1.20 (0.98–1.49)	5008	0.082
Age (years)			
<40	Reference	Reference	
41–50	1.03 (0.83–1.29)	859	0.76
51–60	1.12 (0.89–1.50)	2923	0.33
Sex			
Male	Reference	Reference	
Female	0.89 (0.77–1.03)	−3128	0.125
Teaching status			
Non-teaching	Reference	Reference	
Teaching	1.23 (1.08–1.41)	5662	<0.001
Extended LOS	2.20 (1.88–2.57)	21,162	<0.001

[a]Exponential coefficients

Critical Reviews in Oncology/Hematology 101 (2016) 131–138

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Treatment that follows guidelines closely dramatically improves overall survival of patients with anal canal and margin cancers

Jean-Baptiste Delhorme[a], Delphine Antoni[b,c], Kimberley S. Mak[d,e], François Severac[f], Kelle C. Freel[g], Catherine Schumacher[b], Serge Rohr[a], Cécile Brigand[a], Georges Noel[b,c,*]

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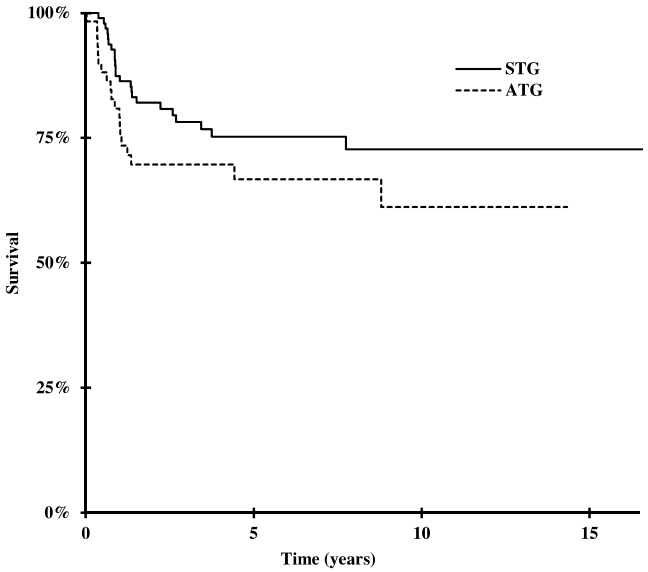

Table 2
Treatments implemented for the patients.

	Standard treatment n (%)	Altered treatment n (%)	p
First treatment sequence	95 (100)	60 (100)	
RT1			
– External beams	1	43 (71.7) 2	<0.001 0.15
– Brachytherapy	0		
CRT1	94 (98.9)	15 (25)	<0.001
Dose per fraction			<0.001
– 1.8 Gy	83 (87.3)	32 (53.3)	
– 2 Gy	9 (9.5)	18 (30)	
– Others	1	10 (16.7)	
Immediate surgery after radiation	0	6	0.003
Median time gap (weeks)	4.0 (range 1–14)	3.0 (range 2–6)	<0.001
– 3D-RT/IMRT	4.0	3.0	
– Brachytherapy	4.0	3.0	
Second treatment sequence	95 (100)	37 (61.7)	<0.001
RT2			<0.001
- External beams	13 (13.7)	9 (15)	0.80 <0.001
- Brachytherapy	72 (75.8)	28 (46.7)	
CRT2			0.007
Dose per fraction			0.096
- 1.8 Gy	11 (47.8)	2	
- 2 Gy	11 (47.8)	4	
- Others	0	2	
- 1.8 and 2 Gy	1	0	
Treatment-induced early toxicity			0.21
0	11 (11.6)	14 (23.3)	
1	16 (16.8)	14 (23.3)	
2	32 (33.7)	16 (26.7)	
3	27 (28.4)	11 (18.3)	
4	2	2	
5	0	1	
x	7 (7.4)	2	
Use of platinum in CRT1 or CRT2	54 (56.8)	7 (11.6)	<0.001
Use of 5FU—Mitomycin C	38 (40)	7 (11.6)	<0.001
Median duration of first sequence (Days)	39	38	0.49
Median total cumulative dose (Gy)	65 (range 52–82)	61 (range 40–76)	<0.001
- <T3	65.2	64.5	
- ≥T3	65.0	50.2	

Gy: Gray, p: p-value, CRT: chemoradiation, RT: radiation, n: numbers, IMRT: Intensity-Modulated Radiation Therapy, 5FU: 5-Fluorouracil.

GYNECOLOGY

Prevalence of anal human papillomavirus infection and anal HPV-related disorders in women: a systematic review

Elizabeth A. Stier, MD; Meagan C. Sebring, BBA, BA; Audrey E. Mendez, PhD, MS; Fatimata S. Ba, MPH; Debra D. Trimble, PhD, RN; Elizabeth Y. Chiao, MD, MPH

selection criteria, and 23 anal cancer publications met the selection criteria. Among HIV-positive women, the prevalence of high-risk (HR)—HPV in the anus was 16—85%. Among HIV-negative women, the prevalence of anal HR-HPV infection ranged from 4% to 86%. The prevalence of anal HR-HPV in HIV-negative women with HPV-related pathology of the vulva, vagina, and cervix compared with women with no known HPV-related pathology, varied from 23% to 86% and from 5% to 22%, respectively. Histological

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lower genital tract pathology. The incidence of anal cancer among HIV-infected women ranged from 3.9 to 30 per 100,000. Among women with a history of cervical cancer or cervical intraepithelial neoplasia 3, the incidence rates of anal cancer ranged from 0.8 to 63.8 per 100,000 person-years, and in the general population, the incidence rates ranged from 0.55 to 2.4 per 100,000 person-years. This review provides evidence that

ranged from 0.55 to 2.4 per 100,000 person-years. This review provides evidence that anal HPV infection and dysplasia are common in women, especially in those who are HIV positive or have a history of HPV-related lower genital tract pathology. The incidence of anal cancer continues to grow in all women, especially those living with HIV, despite the widespread use of combined antiretroviral therapy.

Prevalence of anal human papillomavirus infection and anal human papillomavirus–related disorders in women: a systematic review

TO THE EDITORS: Stier et al[1] bring focus to the growing incidence of squamous cell cancer of the anus (SCCA) in women over the last 4 decades, which has doubled from 1975 through 2008. Moreover, human papillomavirus (HPV) has been detected in 80–90% of SCCA with types 16 and 18 found in 80% of anal cancers.[1] The current increase in the incidence of SCCA among women dictates that more attention is needed on women's risk factors and the mechanism of transmission of SCCA.

Stier et al[1] proposes that, while a reported history of anal intercourse among women was not a consistent risk factor for acquiring anal HPV, there is a "field effect" on the lower genital tract in women. However, we suggest that the prevalence of anal intercourse may be underreported in this study. Receptive anal intercourse among heterosexual partners has become common in the United States. There is less condom use during heterosexual anal intercourse (HAI) than reported with vaginal intercourse.[2] In a study of 10,463 sexually active heterosexual women, Benson et al[2] reported that 13.2% and 36.3% study participants had a recent or lifetime HAI experience, respectively. It is postulated that women of all ages and ethnicities are engaging in more HAI than providers may have previously realized and the prevalence of HAI has steadily increased since the early 1990s.[3] Further, it may be helpful to report the percentage of women in the study that were vaccinated against HPV strains 16 and 18 and still acquired SCCA.

If receptive HAI is a risk factor for SCCA, there is clearly a need to develop and distribute targeted education for patients and health care professionals. Increasing awareness by all stakeholders may be particularly important as reports indicate decreased condom use during HAI. ■

disorders in women: a systematic review. Am J Obstet Gynecol 2015;213:278-309.

2. Benson LS, Martins SL, Whitaker AK. Correlates of heterosexual anal intercourse among women in the 2006–2010 survey of family growth. J Sex Med 2015;12:1746-52.

3. Javanbakht M, Guerry S, Gorbach PM, et al. Prevalence and correlates of heterosexual anal intercourse among clients attending public sexually transmitted disease clinics in Los Angeles County. Sex Transm Dis 2010;37:369-76.

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REPLY

We appreciate the comments by Vidulich et al concerning the role of heterosexual anal intercourse (HAI) in anal human papillomavirus (HPV) acquisition. We agree that HAI is likely underreported, and that condoms are strongly recommended for prevention of sexually transmitted infection transmission for both women and men engaging in anal receptive intercourse.

There were 2 studies in our review that specifically addressed anal HPV in the context of HAI. Goodman et al,[1] evaluating a cohort of healthy adult women in Hawaii, found that: (1) 29% of women reported ever having HAI; and (2) the risk of an incident anal HPV infection among women with a preceding concordant cervical HPV infection was 20.5 (95% confidence interval [CI], 16.3–25.7) whereas the risk of a cervical HPV infection after an anal HPV infection with a concordant genotype was 8.8 (95% CI, 6.4–12.2). Moreover, in the absence of a self-reported history of anal sex, they found that the risk of acquiring concordant anal HPV genotypes was higher after documented infection of those ge-

TEMPO PER UN'ATTENZIONE SISTEMATICA?

Cancer - screening methods (i)

Problem	Patients	Procedure	Evidence of benefit	Screening interval	Additional comments
Anal cancer	Homosexual men	Digital rectal exam ± Papanicolau test	Unknown advocated by some experts	1-3 years	If Pap test abnormal, anoscopy
Breast cancer	Women 50-70 yrs	Mammography	↓ Breast cancer mortality	1-3 years	
Cervical cancer	Sexually active women	Papanicolau test	↓ Cervical cancer mortality	1-3 years	Target age group should include at least the age range 30 to 59 years. Longer screening interval if prior screening tests repeatedly negative
Colorectal cancer	Persons 50-75 yrs	Faecal Occult Blood test	↓ Colorectal cancer mortality	1-3 years	Benefit is marginal
Hepatocellular carcinoma	Persons with cirrhosis	Ultrasound and alphafoetoprotein	Diagnosis earlier allowing for improved ability for surgical eradication	Every 6 months	
Prostate cancer	Men > 50 yrs	Digital rectal exam ± prostate specific antigen (PSA)	Use of PSA is controversial	1-3 years	**Pros:** ↑ early diagnosis **Cons:** Overtreatment, no ↓ cancer-related mortality

EACS Guidelines

DOCUMENTO PROVVISORIO PER LA DISCUSSIONE - DA NON DIVULGARE
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- **A HIV/AIDS ITALIAN EXPERT PANEL LG HIV 2016**
- **A MEMBRI SEZIONI L E M DEL COMITATO TECNICO SANITARIO MINISTERO DELLA SALUTE**

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Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1

Giorno, mese, 2016

TUMORE	POPOLAZIONE	PROCEDURE SCREENING	TEMPISTICHE SCREENING	RACCOMANDAZIONE (FORZA/EVIDENZA)	RIFERIMENTI BIBLIOGRAFICI
Mammella	Donne 50-70 aa(E) Donne>40 aa (A)	Mammografia	1-2 aa (E) Annuale (A)	[AI]	[39,40]
Prostata	Uomini≥50 aa	Esame rettale + PSA test	Annuale	[AI]	[39,40]
Colon-retto	Tutti, 50-75 aa (E) ≥ 50 aa (A)	° Ricerca sangue occulto feci °°rettosigmoidoscopia § rettocolonscopia	° annuale °° ogni 5 aa § ogni 10 aa	[AI]	[39,40]
E: Linee guida Europee; A: Linee guida Americane					

TUMORE	POPOLAZIONE	PROCEDURE SCREENING	TEMPISTICA SCREENING	RACCOMANDAZIONE (FORZA/EVIDENZA)	RIFERIMENTI BIBLIOGRAFICI
Cervice uterina	Donne sessualmente attive ≥20 aa (E) ≥ 18 aa (A)	-PAP test convenzionale - PAP test su base liquida - Colposcopia	Annuale se 2 esami consecu-tivi neg Se Pap test patologico	[AI]	[39-42]
Ano	-MSM; -Tutti con storia di condilomi ano- genitali; -Donne con istologia genitale patologica ∞∞∞∞∞∞∞ MSM*	-PAP test convenzionale - PAP test su base liquida Anoscopia ad alta risoluzione	*Annuale, se 2 esami consecutivi neg Se Pap test patologico	[AIII [AII]	[41-46] [45,46]
Fegato	-HCV coinfetti con cirrosi; -Tutti HBV/HCV resistenti agli antivirali	Ecografia addome +/- α-fetoproteina	Ogni 6-12 mesi	[AI]	[41,42,47-51]
Polmone	-Fumatori ≥ 30 pacchetti s./anno; -se ex-fumatori entro 15 anni dalla cessazione	TAC spirale a basso dosaggio	Annuale	[AI]	[41,42,52,53]

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2016, VOL. 12, NO. 6, 1542–1550
http://dx.doi.org/10.1080/21645515.2015.1115935

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RESEARCH PAPER

Perceptions of Human Papillomavirus (HPV) infection and acceptability of HPV vaccine among men attending a sexual health clinic differ according to sexual orientation

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ABSTRACT

Our aim was to gain a better understanding of the knowledge about Human Papillomavirus (HPV) infection and attitudes toward the HPV vaccine among men at risk for sexually transmitted infections (STI). A self-administered questionnaire was completed by attendees of the largest STI Center in Rome, Italy, from April to June 2013. Determinants of vaccine acceptability were investigated using a Structured Equation Model.

A total of 423 males participated in the survey: 296 (70.0%) men who have sex with men (MSM) and 127 (30.0%) men who have sex with women (MSW). Only one half of the participants knew that HPV is the cause of genital warts (56.9% of MSM vs. 49.5% of MSW, p=0.28). Even less were aware that HPV causes cancer in men (37.2% vs. 27.3%, p=0.08). MSW were more likely to indicate HPV as a cause of cervical cancer (80.8% vs. 69.3%, p=0.03) and to have heard about the vaccine (58.3 vs. 43.6%, p=0.01). Moreover, 72.1% of MSM and 70.3% of MSW were willing to be vaccinated. A rise of one-unit in the HPV awareness score increased the OR of vaccine acceptability among MSM by 25% (OR 1.25, 95%CI: 1.05–1.49; p=0.013). Differently, only attitudes had a relevant effect on willingness to be vaccinated among MSW (OR 3.32, 95%CI: 1.53–7.17; p=0.002).

Efforts should be made to maximize awareness of HPV, especially as a causative agent of genital warts and male cancers, and to reinforce positive attitudes toward vaccination among men visiting STI centers.

conclusioni

- La condilomatosi anale è in aumento al pari del carcinoma anorettale, come conseguenza della promiscuità in entrambi i sessi
- Il recupero immunitario modula nell'espressione ma non riduce sostanzialmente la prevalenza della condilomatosi e l'alto rischio di progressione a tumore associato ai ceppi HR
- La vaccinazione dei soggetti a rischio potrà avere un ruolo protettivo se sistematicamente implementata nel tempo