Anal Cancer Trends in Puerto Rico from 1985 to 2005: The Potential Impact of the AIDS Epidemic

Ana Patricia Ortiz, PhD, MPH,^{1,3} Karen J. Ortiz-Ortiz, MA, MPH,^{1–3} Maricarmen Traverso-Ortiz, MPH, CGG,^{1–3}
Moraima Y. Ríos, MS,^{1,3} Vivian Colón-López, PhD, MPH,^{1,3,4} and Joel M. Palefsky, MD⁵

Dear Editor:

Anogenital carcinomas are an uncommon malignancy in Puerto Rico (PR), but its incidence is increasing. In the United States (US), incidence rates of anal squamous cell carcinoma (SCC) from 2004 to 2008 were higher for females (1.8 per 100,000) than for men (1.2 per 100,000).¹ As in the US, in PR, age-standardized (US 2000 population) incidence rates are also higher for women than for men (1.55 vs. 1.04 per 100,000). Approximately 84% of anal carcinomas are caused by human papilloma virus (HPV), mostly by oncogenic HPV types 16 and 18.² Other anal cancer risk factors include history of multiple sexual partners, being a man having sex with men (MSM), receptive anal intercourse, a history of anogenital warts, other anogenital cancers (in women) or sexually transmitted infections (such as HIV), immunosuppression, and current smoking.^{3–5}

A study in the US showed that the progressive increase in male anal cancer rates between 1980–2005 was strongly influenced by the effect of HIV-infected cancer cases, although HIV had little impact on trends among women.⁶ PR is among the top ten US States and territories with the highest cumulative number of AIDS cases.⁷ Meanwhile, since 2009, cancer is the leading death cause among the Hispanic/Latinos in US.⁸ Given the limited amount of data for PR on the burden of the HIV epidemic on anal cancer occurrence, we aimed to describe the proportion of anal cancer cases in PR among persons (15+ years) living with AIDS (PWA) and the impact of PWA status on anal cancer incidence trends from 1985 to 2005, by sex and age.

The PR Central Cancer Registry (PRCCR) and the PR AIDS Surveillance Program databases, both CDC-funded population-based registries, were linked using a probabilistic linkage algorithm with Link Plus v.2.0 software (Release 2.0, CDC, Atlanta, GA). Anal cancers were limited to those invasive primary cancers diagnosed between 1985–2005, and 3 months after an AIDS diagnosis (to establish a risk measure). Anal cancers were defined using the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3), topography codes C210-212, 218 (Anus, Anal Canal, and

Anorectum), and excluding hematologic malignancies and Kaposi sarcoma.⁹ The number of anal cancer cases in the general population, and by PWA status, was summed in categories defined by age (15–19, 20–49, 50–69, and ≥70 years), sex, and histologic subtype [squamous cell carcinoma (SCC), adenocarcinoma, cloacogenic/basaloid, carcinoma NOS, other]. We estimated the following general population incidence rates stratified by age and sex, overall, and excluding PWA. Incidence rates were standardized to the 2000 U.S. population and were calculated per 100,000 persons. Temporal trends were estimated in a log-linear model using Joinpoint (version 4.0.1).¹⁰ Annual percent change was defined as $100 * [\exp(\beta) - 1]$, where β is the slope of the trend provided by Joinpoint.¹⁰ STATA System release 11.0 (STATA Corp, College Station, Texas) was used for the statistical analysis. The study was approved by the Institutional Review Board of the University of PR Medical Sciences Campus.

From 1985 through 2005, a total of 736 cases of anal cancer were diagnosed in PR. Of those, the most common histologic type was SCC (54.2%), followed by cloacogenic/basaloid tumors (20.1%). Most cases (46.88%) occurred among adults aged 50–69 years and a higher proportion of anal cancer cases were females (70.8%). Nonetheless, the proportion of anal cancer cases being PWA was higher among males ($n=22$, 11.4%) than in females ($n=4$, 0.77%), and was also higher in the 20–49 year age group ($n=20$, 20.2%) than in the 50–69 year age-group ($n=6$, 1.77%) (Table 1). All anal cancer cases among male PWA were in the 20–49 and 50–69 age groups, representing 37% (17/46) and 4.8% (5/105), respectively, of all anal cancer cases in those age groups. In women, the same pattern was observed, with 5.7% (3/53) and 0.4% ($n=1/240$) of anal cancer cases in those age groups being women PWA (data not shown). Regarding anal cancer incidence trends, in men, incidence increased significantly ($p<0.05$) with an APC of 3.23 when PWA cases were considered, whereas the increase was reduced to 2.01 when these were excluded ($p>0.05$). In women, anal cancer incidence increased with an APC of 0.97 when PWA cases were considered; whereas the increase was

¹University of Puerto Rico Comprehensive Cancer Center, San Juan, Puerto Rico.

²Puerto Rico Central Cancer Registry, San Juan, Puerto Rico.

³Graduate School of Public Health, Medical Sciences Campus, University of Puerto Rico (UPR), San Juan, Puerto Rico.

⁴Cancer Control and Population Sciences Program, University of Puerto Rico Comprehensive Cancer Center, San Juan, Puerto Rico.

⁵Division of Infectious Diseases, School of Medicine, University of California, San Francisco, California.

TABLE 1. CHARACTERISTICS AND PROPORTION OF ANAL CANCER CASES IN THE GENERAL POPULATION OF PUERTO RICO (1985–2005), BY PEOPLE WITH AIDS (PWA) STATUS^a

Characteristics	Anal cancer					
	Non-PWA		PWA		All cases	
	No. of cancers	(%)	No. of cancers	(%)	Total	(%)
Total	710	100.00	26	100.00	736	100
Sex						
Male	193	27.20	22	84.60	215	29.21
Female	517	72.80	4	15.40	521	70.79
Age at cancer diagnosis						
15–20	1	0.10	–	–	1	0.14
20–49	79	11.10	20	76.90	99	13.45
50–69	339	47.80	6	23.10	345	46.88
> 70	291	41.00	–	–	291	39.54
Histologic subtype						
SCC	376	53.00	23	88.50	399	54.21
Adenocarcinoma	117	16.50	1	3.90	118	16.03
Cloacogenic or basaloid	148	20.90	0	0.00	148	20.11
Carcinoma, NOS	10	1.40	1	3.90	11	1.49
Other	59	8.30	1	3.90	60	8.15

^aProportions of anal cancer cases with PWA status were estimated by dividing the number of PWA anal cancer cases by the total number of anal cancer cases. –, no cases reported.

only of 0.85 when these were excluded. Nonetheless, none of the increases in women were statistically significant ($p > 0.05$) (Fig. 1). Meanwhile, among women younger than 50 years, anal cancer incidence increased significantly ($p < 0.05$) with an APC of 2.5 when PWA cases were considered, while the increase was 2.0 when these cases were excluded ($p > 0.05$). On the other hand, in women aged 50 years or older the increase was not statistically significant either when PWA cases were considered or not. In the case of men, the APCs could not be calculated because of small numbers (data not shown).

Our findings indicate that from 1985 and 2005, increasing trends of anal cancer in men in PR were influenced by the

HIV/AIDS epidemic. In women, this pattern was only significant among younger women (< 50 years). Our results are similar with the US trends,⁶ where the HIV epidemic seems to be a stronger predictor of anal cancer occurrence in men than in women. Literature suggests that primary prevention with HPV vaccination^{11,12} and possibly secondary prevention with anal cytology and high-resolution anoscopy, followed by treatment of anal high-grade squamous intraepithelial lesions, can help in the prevention of anal cancer.⁹

Our study is limited in statistical power, given the low incidence of PWA/anal cancer cases. In addition, our results are dependent on not having biases and secular trends in the

FIG. 1. Age-adjusted incidence rates of anal cancer in Puerto Rico, 1985–2005. Adjusted to the US population; $p < 0.05$.

AIDS ascertainment of anal cancer cases; we expect this possibility to be low, given the matching performed of the HIV/AIDS and Cancer Registry databases. Despite these limitations, our results support the need for primary and secondary preventive efforts among PWA, to minimize anal cancer risk in these groups. Future research should assess other factors associated to anal cancer occurrence in this population, particularly among women, as HIV/AIDS does not seem to be a strong predictor of anal cancer occurrence among them. Given that data for this analysis was only available until 2005, future research should contrast our results with trends after this study period, when more potent ART regimens were standard. The effectiveness of anal Pap testing in the prevention of anal malignancies should be assessed. Also, methods to enhance prevention and early detection of anal cancer by using simple screening and molecular methods should be further explored and developed.^{13,14}

Acknowledgments

This work was supported by the National Cancer Institute (5U54CA096297-09S1 and 5U54CA096297-10S1); the UPR/MDACC Partnership for Excellence in Cancer Research, supplement entitled Community-Engaged Research on HIV/AIDS Related Cancers among Diverse Racial/Ethnic and Underserved Populations, NCI, NIH (3U54CA096297-08S1); the UPR/MDACC Partnership for Excellence in Cancer Research, NCI, NIH (U54CA96297 and U54CA96300); the CDC/National Program Cancer Registries (5U58-DP 003863-02); and the CDC-HIV/AIDS Surveillance (105U62PS000996).

Author Disclosure Statement

No competing financial interests exist.

References

- Centers for Disease Control and Prevention. Human papillomavirus-associated cancers—United States, 2004–2008. *Morb Mortal Wkly Rep* 2012;61:258–261.
- DeVuyst H, Clifford GM, Nascimento MC, Madeleine MM, Franceschi S. Prevalence and type distribution of human papillomavirus in carcinoma and intraepithelial neoplasia of the vulva, vagina and anus: A meta-analysis. *Int J Cancer* 2009;124:1626.
- Djenaba A, Jaqueline W, Xiaocheng Wu, et al. Understanding the burden of human papillomavirus-associated anal cancers in the USA. *Am Cancer Soc* 2008; DOI: 10.1002/cncr.23744.
- Coutlée F, de Pokomandy A, Franco EL. Epidemiology, natural history and risk factors for anal intraepithelial neoplasia. *Sex Health* 2012;9:547.
- Grulich AE, Poynten IM, Machalek DA, Jin F, Templeton DJ, Hillman RJ. The epidemiology of anal cancer. *Sex Health* 2012;9:504.
- Shiels MS, Pfeiffer RM, Chaturvedi AK, et al. *Impact of the HIV Epidemic on the Incidence Rates of Anal Cancer in the United States*. Oxford University, New York. 2012. DOI: 10.1093/jnci/djs371.
- Centers for Disease Control and Prevention. HIV Surveillance Report, 2011; vol. 23. <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/>. Published February 2013. July 2013.
- Siegel R, Naishadham D, Jemal DA. Cancer Statistics for Hispanics/Latinos, 2012. *Cancer J Clin* 2013;283.
- World Health Organization. *International Classification of Diseases for Oncology*, 3rd ed. Geneva: World Health Organization, 2000.
- Statistical Research and Applications Branch NCI. Joint-point Regression Program, Version 4.0.1. 2013.
- Joseph D, Jaqueline M, Wu X, et al. Understanding the burden of human papillomavirus associated anal cancer in the US. *Am Cancer Society Cancer Supplement* 2008; 2892–2900.
- Chiao E, Giordano T, Palefsky J, Tyring S, Serag H. Screening HIV-infected individuals for anal cancer precursor lesions: A systematic review. *Clin Inf Dis* 2006;223–233.
- Bosch F, Broker T, Forman D, et al. Comprehensive control of human papillomavirus infections and related diseases. *Vaccine* 2013;31:H1–H31.
- Phanuphak N, Teeratakulpisarn N, Keelawat S, et al. Use of human papillomavirus DNA, E6/E7 mRNA, and p16 immunocytochemistry to detect and predict anal high-grade squamous intraepithelial lesions in HIV-positive and HIV-negative men who have sex with men. *PLoS One* 2013;8.

Address correspondence to:

Ana Patricia Ortiz, PhD

University of Puerto Rico Comprehensive Cancer Center

PMB 711 89 De Diego Avenue,

Suite 105 San Juan 00927-6346

Puerto Rico

E-mail: ana.ortiz7@upr.edu