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Anal Cancer Incidence and Mortality in Puerto Rico

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Abstract

Objective—Anal cancer is a rare tumor that is associated with oncogenic HPV genotypes. This study aims to compare the age-standardized rates (ASRs) of anal cancer incidence and mortality in men and women living in Puerto Rico (PR) with those of non-Hispanic whites (NHW), non-Hispanic blacks (NHB), and Hispanics (USH) living in the continental United States (US).

Methods—ASRs were calculated based on cancer data that came from the PR Cancer Central Registry and from the Surveillance, Epidemiology, and End Results (SEER) program. The age-specific relative risks (RR) and 95% Confidence Interval (95% CI) were estimated using Poisson regression models.

Results—Comparing the period of 2001 to 2004 to that of 1992 to 1996, the incidence of anal cancer increased among NHW, NHB, and PR men. In females, an increase in the incidence was observed for all racial groups except for Puerto Rican women. When evaluating findings by age groups, Puerto Rican men younger than 60 years old had a 20% higher incidence of anal cancer than did USH men of the same age strata (RR: 2.20; 95% CI = 1.48–3.29). However, Puerto Rican females had a lower incidence of anal cancer than NHW and NHB women. An increased percent change in mortality was observed only in NHW and NHB men. A decreasing trend was observed in all racial/ethnic groups except for NHW women.

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Conclusion—Our results support the notion that there are racial/ethnic differences in anal cancer incidence and mortality, with potential disparities among men and women in PR compared with USH men and women. Given the increasing incidence trends in anal cancer, particularly among PR, NHW, and NHB men, further investigation is needed to better elucidate screening practices that can aid in the prevention of anal cancer.

Keywords

Anus neoplasms; Anal Cancer; Incidence; Mortality; Puerto Rico

In recent years, increased insight into the pathogenesis of anal cancer has been gained since reports indicate that anal HPV infection with oncogenic HPV genotypes is a key causal precursor of anal intraepithelial neoplasia (AIN) and anal cancer (1). Anal cancer is similar to cervical cancer with respect to overall HPV DNA positivity, with approximately 85% of cases worldwide being associated with HPV infection. HPV-16 is the most commonly detected HPV type, representing 87% of all HPV-positive tumors. HPV-18 is the second most common type detected and is found in approximately 9% of cases (2). In the US, it is known that the annual incidence rate for anal cancer has increased for both men and women in the past 3 decades (3). The incidence of anal cancer is relatively low in the general US population, with a rate of 1.4 per 100,000 men and 1.8 per 100,000 women. Hispanics, overall, have a lower incidence of anal cancer than do non-Hispanic whites and non-Hispanic blacks (4). However, the incidence rate is higher among men who have sex with men (MSM) (5), particularly HIV+ MSM (6). Recent studies in the US and in Europe have reported that the incidence of anal cancer among HIV-positive individuals ranges from 42 to 137 cases per 100,000 person-years, a rate that is 30 to 100 times higher than that of the general population (7,8).

Receptive anal sex as well as an increasing number of receptive anal sex partners are known to be important risk factors for anal cancer (9). In Puerto Rico (PR), a population-based study reported that 64.4% of men and 57.1% of the women older than 18 years old had ever engaged in anal sex (10). This is twice the estimated rate reported by the 2002–2003 National Survey for Family Growth in the US (a US survey of men and women aged 15–44 years) (11). With regard to Puerto Rican MSM, a population-based study reported that 22.6% of MSM disclosed having had receptive anal sex with a man in the 12 months prior to the study, with more than 10% reporting having had more than 5 sex partners with whom they had engaged in receptive anal sex in their lifetime (12).

Given the current recommendation of utilizing the HPV vaccine for the prevention of HPV-associated anal intraepithelial neoplasia in certain groups, such as MSM (13,14,15), and in this time in which no national guidelines exist regarding recommendations for routine anal cancer screening (16), it is important to document the burden of anal cancer in both men and women in this Hispanic population. Therefore, in this study we will assess the age-standardized incidence and mortality rates of anal cancer in both men and women in PR and compare those rates with those of Hispanics (USH), Non-Hispanic Whites (NHW), and Non-Hispanic Blacks (NHB) in the US during the period of 1992 to 2004. Also, an

estimation of the percent change between the two extreme study periods (1992–1996 and 2001–2004) is made.

Methods

Data sources

Incident cases and deaths from anal cancer (ICD-O-3 C210-C218) for PR and US racial/ethnic groups (USH, NHW, NHB) were obtained from the PR Central Cancer Registry (PRCCR) (17) and the Surveillance, Epidemiology, and End Results Program (SEER), respectively (18). The PRCCR is part of the National Program of Cancer Registries (NPCR) administered by the Centers for Disease Control and Prevention (CDC). The PRCCR uses the coding standards of the SEER and of the North American Association of Central Cancer Registries (NAACCR); thus, the data in the PRCCR are fully comparable with SEER data. In 2003, a CDC audit concluded that 95.3% of all cancer cases diagnosed and/or treated in hospital facilities in PR were appropriately reported to the PRCCR, a result that is in keeping with what was found in the US (95%)(19). The third revision of the *International Classification of Diseases for Oncology* (ICD-O-3) was used to select all of the cases of those patients who had been diagnosed with anal cancer between 1992 and 2004 (20). Cases from 1992 to 2000, which were originally reported using ICD-O-2, were converted to ICD-O-3. Cancer mortality data for PR and for the US racial/ethnic groups were obtained, respectively, from the PRCCR (as reported by death certificates from the PR Department of Health) and from the SEER program (as reported by the National Center for Health Statistics [NCHS]) (21,22). Causes of death were coded and classified according to the tenth edition of the International Classification of Diseases (ICD-10). The study protocol was approved by the Institutional Review Board (IRB) of the University of PR Medical Sciences Campus.

Statistical Analysis

Rates—To assess the burden of anal cancer, we applied the direct method to calculate the age-standardized rates (ASR) of anal cancer incidence and mortality for the periods of 1992–1996, 1997–2000, and 2001–2004 (per 100,000 persons) for all racial/ethnic groups and using the world standard population (ASR[World]). These rates were identified as ASR (World) for both incidence and mortality (23). The change in the rates from the earliest and the latest study periods (1992–1996 and 2001–2004) was calculated as a percentage as follows:

$$\%\text{change}=\frac{\text{Rate}_{2001-2004}-\text{Rate}_{1992-1996}}{\text{Rate}_{1992-1996}}*100$$

The significant percentage of change (PC) was determined by the construction of 95% confidence intervals (CI) using the formulas from the US Census Bureau (24). If zero was not included in this interval, significant changes were declared with p-value less than 5%.

Group differences—For each racial/ethnic group, the age-specific (25) incidence and mortality rates from 2000 to 2004 were estimated (divided into three age groups [<60, 60–

70, and >70 years]). To determine relative differences among groups, the age-specific relative risks (RR) were estimated with 95% CI using the Poisson regression models (26). Then, the overall age-standardized rates were computed for each racial/ethnic group. These ASRs for incidence and mortality were estimated with 95% CI. The ratio of two standardized rates between different groups was estimated with their 95% CI to assess differences in anal cancer incidence and mortality rates between PR and NHW, USH, and NHB racial/ ethnic groups. This ratio was denoted as the standardized rate ratio (SRR) (27). Statistical analysis was performed using the statistical package STATA (version 11.0 College Station, TX).

Results

Comparison of Incidence and Mortality Rates by Gender and Ethnic/Racial Group

The incidence of anal cancer was significantly lower for Puerto Rican men than it was for Puerto Rican women (SRR: 0.60; 95% CI=0.45–0.79). A similar lower incidence rate was observed for USH men compared to USH women (SRR: 0.79; 95% CI= 0.72–0.87) (*data not shown*). For mortality, significantly lower rates of anal cancer were observed for USH men than were for USH women (SRR: 0.68; 95% CI=0.62–0.74). Also, NHW men had a 38% lower incidence rate than did NHW women (SRR: 0.62; 95% CI=0.38–0.97) (*data not shown*).

Percent Changes in Incidence and Mortality Rates by Ethnic/Racial Group (Men)

Comparing the period of 2001 to 2004 to that of 1992 to 1996, the incidence of anal cancer increased for Puerto Rican men (PC = 26.65%), NHW men (PC = 34.65%), and NHB men (PC = 33.96%). However, a significant increase between time periods was observed in NHW men only ($p<0.05$). During the same time period, a decreasing trend was observed for USH (PC = −1.49%) men. An increase in the percent change in the mortality of anal cancer was observed only in NHW (PC = 23.92%) and NHB (PC = 1.79%) men (Table 1).

Percent Changes in Incidence and Mortality by Ethnic/Racial Group (Women)

In women, an increase in the incidence of anal cancer was observed for all racial groups except Puerto Rican women (PC= −3.86%) (Table 1). Regarding mortality, a decreasing trend was observed in all racial/ethnic groups except NHW women (PC=33.84%).

Anal Cancer Incidence (2000–2004) by Ethnic/Racial Group (Men)

The age-standardized incidence (per 100,000) of anal cancer ranged from 1.29 in USH to 3.11 in NHB. Puerto Rican men had a 62% lower incidence of anal cancer than did NHW men (SRR: 0.62; 95% CI=0.48–0.77) and a 48% lower incidence than NHB men had (SRR: 0.48; 95% CI=0.36–0.64) (Table 2). The age-specific incidence increased with age in all racial/ ethnic groups. Puerto Rican men younger than 60 years old had a 37% lower incidence than did NHW men in the same age group and a 54% lower incidence than did NHB men younger than 60 years old. However, in a comparison of Puerto Rican men and USH men in the same age strata, Puerto Rican men had an incidence that was 2 times higher than the USH men had (RR: 2.20; 95% CI=1.48–3.29).

Anal Cancer Mortality (2000–2004) by Ethnic/Racial Group (Men)

The annual mortality (per 100,000) ranged from 0.11 in USH and Puerto Rican men to 0.32 in NHB men. During the period of 2000 to 2004, Puerto Rican men had a significantly lower mortality rate for anal cancer than did their NHB and NHW counterparts ($p<0.05$), with their ASR of mortality being 60% lower than that of the NHB men (SRR: 0.40; 95% CI= 0.14–0.77) (Table 2).

Age-specific mortality increased with age in all racial/ethnic groups except Puerto Rican men (Table 2). Puerto Rican men younger than 60 years old had a 76% lower risk than NHB men younger than 60 years old did; this association achieved statistical significance ($p<0.05$).

Anal Cancer Incidence (2000–2004) by Ethnic/Racial Group (Women)

Among women, the age-standardized incidence ranged from 1.70 in USH women to 2.97 in NHW. Puerto Rican women had an 18% lower incidence of anal cancer than NHW women did (SRR: 0.82; 95% CI=0.68–0.97) and a 44% higher incidence than USH women did (SRR: 1.44; 95% CI=1.11–1.87) (Table 3). The age-specific incidence increased with age among all racial/ethnic groups except Puerto Rican women. Puerto Rican women younger than 60 years had a 54% lower incidence of anal cancer than NHW women did (RR: 0.46; 95% CI=0.33–0.63). A lower incidence was also observed in the same age strata when comparing Puerto Rican women to NHB women (RR: 0.58, 95% CI=0.40–0.84). However, a two-fold increase in incidence was observed in the 60 to 69 years group comparing Puerto Rican women to USH women (RR: 2.13; 95% CI=1.34–3.39) and to NHB women (RR: 1.66; 95% CI=1.05–2.62). No other significant differences were observed in terms of anal cancer incidence by age group ($p>0.05$).

Anal Cancer Mortality (2000–2004) by Ethnic/Racial Group (Women)

Age-standardized mortality rates ranged from 0.19 in Puerto Rican women to 0.39 in NHW women. No significant differences by ethnic group or by age strata were observed in anal cancer mortality by age group ($p>0.05$) (Table 3).

Conclusion

This study shows significant disparities in trends of incidence and mortality between racial/ethnic groups. In the period of time studied, PR and USH men had lower incidence of anal cancer than PR and USH women. This has been previously reported in other studies that also explored the epidemiology of anal cancer by gender (28,29). Upon evaluating racial and ethnic differences in the incidence and mortality of anal cancer, it was found that Puerto Rican men had a lower incidence of anal cancer than did NHW and NHB men; at the same time, a higher incidence rate was observed in Puerto Rican men belonging to the younger age groups than was observed in similarly aged USH men. These two findings highlight what other epidemiological studies in PR have confirmed (30,31) regarding the assessment of potential sub-group differences within the broad Hispanic/ Latino category. Among women, an overall higher incidence was observed in Puerto Rican women than was

observed in USH women, showing, as well, important variations between the incidence rates in PR and USH women, that highlight a health disparity for PR.

In this study, although not statistically significant, an increase of 26.7% in anal cancer incidence was reported for Puerto Rican men between 1992–1996 to 2001–2004. Therefore, despite the fact that in PR anal cancer incidence and mortality are lower than in the US, our study results show that anal cancer prevention strategies are important for this population. In particular, studies have discussed the importance of developing diagnostic and therapeutic guidelines for at-risk populations for anal dysplasia/ anal cancer, such as HIV-positive men who have sex with men (32). Epidemiological studies in PR have reported a high prevalence of anal HPV infection among women who attended an OBGYN clinic in the San Juan Metropolitan Area (53.9%) (33). Thus, a substantial number of anal HPV infections and related anal carcinomas may potentially be prevented by quadrivalent HPV vaccination.

Our study has some limitations that need to be considered. Regarding the data obtained, the small number of anal cancer cases from PR may be the reason that there is a lack of statistical significance in some of the patterns observed for PR. Also, incomplete information regarding stage at diagnosis, histologic type (i.e., squamous versus melanoma versus adeno versus urethral type), grade, and the sub-site of anal cancer cases in PR limits our ability at this time to consider the impact of these variables on anal cancer trends.

In summary, although lower incidence and mortality rates were observed in PR, incidence trends seems to be increasing for men in PR. Future studies need to explore preventive strategies that might help to decrease the incidence of this malignant disease, particularly among high-risk populations in PR, including MSM and HIV-positive individuals.

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Table 1

Age-standardized incidence and mortality rates* for anal cancer in men and women both in PR and in the US (NHW, NHB, and USH)

Racial/ ethnic group	1992–1996	1997–2000	2001–2004	PC** (95% CI)
INCIDENCE				
Men				
PR	1.13	0.94	1.43	26.65 (−22.48 – 75.79)
NHW	1.72	2.10	2.32	34.65 (18.97 – 50.33)[a]
USH	1.31	1.23	1.29	−1.49 (−45.74 – 42.75)
NHB	2.32	2.36	3.11	33.96 (−5.65 – 73.58)
Women				
PR	2.27	3.00	2.19	−3.86 (−29.74 – 22.00)
NHW	2.25	2.56	2.97	31.93 (20.02 – 43.83)[a]
USH	1.45	2.11	1.70	17.37 (−22.73 – 57.49)
NHB	1.88	1.87	2.50	32.87 (−5.51 – 71.25)
MORTALITY				
Men				
PR	0.13	0.13	0.11	−19.52 (−116.59 – 77.55)
NHW	0.21	0.23	0.26	23.92 (9.83 – 38.00)[a]
USH	0.14	0.10	0.11	−20.16 (−69.87 – 29.55)
NHB	0.31	0.32	0.32	1.79 (−29.86 – 33.45)
Women				
PR	0.25	0.24	0.19	−23.85 (−93.94 – 46.24)
NHW	0.29	0.32	0.39	33.84 (22.68 – 44.99)[a]
USH	0.22	0.18	0.21	−6.73 (−47.06 – 33.61)
NHB	0.29	0.31	0.28	−3.00 (−29.26 – 23.27)

* Age-standardized to the world standard population (3 age groups: 20–59 yrs, 60–69 yrs, 70+ yrs).

** Percentage change for the periods of 1992–1996 and 2002–2004, with a 95% confidence interval.

[a] $p<0.05$

Table 2

Age-specific incidence and mortality rates for anal cancer in males, 2000–2004

	Total number of cases				Age-Specific Rate (x 100,000)				Relative Risk (RR)*		
	PR	NHW	USH	NHB	PR	NHW	USH	NHB	PR/NHW	PR/USH	PR/NHB
Incidence											
20–59 yrs	46	416	50	114	1.19	1.62	0.54	2.56	0.73 (0.54–0.99)	2.20 (1.48–3.29)	0.46 (0.33–0.65)
60–69 yrs	19	149	17	16	3.34	4.37	3.16	3.87	0.76 (0.47–1.23)	1.06 (0.55–2.04)	0.86 (0.44–1.68)
70+ yrs	17	259	23	27	3.25	6.89	5.55	8.11	0.47 (0.29–0.77)	0.59 (0.31–1.10)	0.40 (0.22–0.73)
Overall	82	824	90	157	1.43†	2.32†	1.29†	3.11†	0.62 (0.48–0.77)‡	1.03 (0.73–1.48)‡	0.48 (0.36–0.64)‡
Mortality											
20–59 yrs	_a	335	29	79	0.05	0.15	0.07	0.22	0.34 (0.08–1.36)	0.79 (0.19–3.29)	0.24 (0.06–0.98)
60–69 yrs	_a	190	9	25	0.53	0.59	0.33	0.71	0.89 (0.28–2.78)	1.59 (0.43–5.86)	0.74 (0.22–2.46)
70+ yrs	_a	298	8	28	0.38	0.85	0.38	0.97	0.45 (0.11–1.80)	1.00 (0.21–4.71)	0.40 (0.09–1.66)
Overall	7	823	46	132	0.11†	0.26†	0.11†	0.32†	0.49 (0.18–0.92)‡	1.07 (0.38–2.27)‡	0.40 (0.14–0.77)‡

*Relative risk (RR), with a 95% confidence interval.

†Age-standardized rates (ASR) (standardized to the world standard population).

‡SRR: The ratio of two age-standardized rates (using the world standard population), with a 95% CI.

aCounts less than six (< 6) are not presented to avoid potential identification.

Table 3

Age-specific incidence and mortality rates for anal cancer in females, 2000–2004

	Total number of cases				Age-Specific Rate (x 100,000)				Relative Risk (RR)*		
	PR	NHW	USH	NHB	PR	NHW	USH	NHB	PR/NHW	PR/USH	PR/NHB
Incidence											
20–59 yrs	40	512	59	82	0.94	2.03	0.70	1.62	0.46 (0.33–0.63)	1.34 (0.90–2.00)	0.58 (0.40–0.84)
60–69 yrs	57	242	26	27	8.51	6.58	4.00	5.14	1.29 (0.97–1.73)	2.13 (1.34–3.39)	1.66 (1.05–2.62)
70+ yrs	55	461	40	40	7.85	8.12	6.38	7.02	0.97 (0.73–1.28)	1.23 (0.82–1.85)	1.12 (0.74–1.68)
Overall	152	1,215	125	149	2.19†	2.97†	1.70†	2.50†	0.82 (0.68–0.97)‡	1.44 (1.11–1.87)‡	1.00 (0.79–1.27)‡
Mortality											
20–59 yrs	_a	483	17	57	0.05	0.22	0.04	0.14	0.21 (0.05–0.85)	1.09 (0.25–4.71)	0.34 (0.08–1.38)
60–69 yrs	_a	261	12	22	0.15	0.74	0.38	0.48	0.20 (0.03–1.43)	0.40 (0.05–3.06)	0.31 (0.04–2.31)
70+ yrs	7	703	29	55	1.00	1.33	0.95	1.08	0.75 (0.36–1.58)	1.05 (0.46–2.40)	0.93 (0.42–2.04)
Overall	10	1447	58	134	0.19†	0.39†	0.21†	0.28†	0.49 (0.23–0.83)‡	0.96 (0.43–1.76)‡	0.67 (0.31–1.18)‡

*Relative risk (RR), with a 95% confidence interval.

†Age-standardized rates (ASR) (standardized to the world standard population).

‡SRR: The ratio of two age-standardized rates with a 95% CI.

aCounts less than six (< 6) are not presented to avoid potential identification.

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