Incidence of Oral Cavity and Pharyngeal Cancers by Anatomical Sites in Population-based Registries in Puerto Rico and the United States of America

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Objective: Puerto Rico's (PR) epidemiological data on each oral cavity and pharynx cancer (OCPC) site is yet largely unexplored. Our aim was to compare OCPC incidence in PR, by anatomical site, with that of non-Hispanic whites (NHW), non-Hispanic blacks (NHB), and Hispanic (USH) individuals in the USA.

Methods: Data from the Surveillance Epidemiology and End Results program and the PR Central Cancer Registry were collected and analyzed. Age-standardized rates, percent changes, and standardized rate ratios were estimated with 95% confidence intervals.

Results: Although declining incidence rates were observed for most anatomical sites in most racial/ethnic groups and in both sexes, the incidence of oropharynx cancers slightly increased for cancers in the oropharynx among PR women, both in the base of tongue and soft palate/other oropharynx (p>0.05). The incidence of soft palate/other oropharynx cancers in PR men was about 2.8 times higher than in USH men (p<0.05) and about 1.4 times higher than in NHW men but 21% lower than in NHB men (p>0.05). Significant interactions terms formed with racial/ethnic group and age were shown in various sites. The largest differences between sexes were consistently noted in PR.

Conclusion: Further research in PR should assess the effect of the HPV infection, as well as of other risk factors, in OCPC incidence by anatomical site in younger populations. These data could explain more precisely the reasons for the differences observed in this study, particularly among sexes in PR. [P R Health Sci J 2013;4: 175-181]

Key words: Oral cavity and pharyngeal cancer, SEER, Puerto Rico, Incidence, Trends

ral cavity and pharyngeal cancer (OCPC), as a group, is the sixth most common cancer in the world (1). Worldwide, the annual estimated incidence is approximately 275,000 for oral cavity cancers and 130,300 for pharyngeal cancers, excluding those of the nasopharynx (2). However, OCPC incidence rates vary up to 20-fold according to geographic location (1). Among all Caribbean islands, for example, Puerto Rico (PR) has the highest reported ageadjusted (World standard) OCPC incidence (8 per 100,000 inhabitants; excluding nasopharynx) even slightly higher than in the United States of America (USA) (7.2 per 100,000 inhabitants; excluding nasopharynx) (3).

According to the PR Central Cancer Registry (PRCCR), OCPC is the fourth and twelfth most common cancers among Puerto Rican men and women, respectively; approximately 357 cases (273 men and 84 women) are diagnosed each year (4). From 1992 to 2002, the OCPC incidence among Puerto Rican women increased by 5.3% each year whereas among Puerto Rican men remained constant (p > 0.05) (5). In the USA, on the other hand, the OCPC incidence in women decreased by

approximately 1% per year from 1992 to 2008, and the OCPC incidence in men decreased by approximately 1.4% per year from 1992 to 2006, although some differences have been observed according to race, sex, and anatomical site (6).

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Various known risk factors such as alcohol use, tobacco use, human papillomavirus (HPV) exposure, poor nutrition, and poor oral hygiene may influence the trends of OCPC incidence in PR and the USA. In fact, some of these factors (e.g., HPV exposure and tobacco use) have been more closely associated with OCPC incidence at certain anatomical sites (7, 8). Hence, determining the incidence of OCPC in PR by anatomical site and comparing it with that in non-Hispanic white (NHW), non-Hispanic black (NHB), and Hispanic (USH) Americans may help to determine where to focus our cancer prevention and control efforts to reduce the OCPC burden in PR. Thus, our aim was to assess the age-standardized OCPC incidence by anatomical site in PR and contrast these statistics with national data for USH, NHW, and NHB groups in the USA as reported by the Surveillance, Epidemiology, and End Results (SEER) program from 1992 to 2009.

Materials and methods

Data sources

Data from the SEER program and the PRCCR were collected and analyzed as previously described in various studies (5, 9, 10). The PRCCR, part of the National Program of Cancer Registries, is administered by the Centers for Disease Control and Prevention (CDC) and uses the coding standards of the SEER program and the North American Association of Central Cancer Registries. Therefore, PRCCR data are fully comparable with SEER data. According to a CDC audit, in 2003, 95.3% of all cancer cases diagnosed or treated in hospital facilities in Puerto Rico were appropriately reported to the PRCCR, which is comparable to the proportion in the USA (95%) (11).

The criteria specified in the third revision of the International Classification of Diseases for Oncology (ICD-O-3) were used to select cases of OCPC from 2001 and later for this analysis (12). Cases from 1992-2000 were initially reported using ICD-O-2 and later converted to ICD-O-3 by the SEER program (13). This study was approved by the University of Puerto Rico Medical Sciences Campus Institutional Review Board.

Study population

Individuals older than 39 years and diagnosed with OCPC at three different primary sites: 1) oral cavity [oral tongue (C020-C023), floor of mouth (C040-C049), and gingivobuccal (C030-C039,C050, and C060-C069)], 2) oropharynx [base of tongue (C019 & C024), tonsil (C090-C099), and soft palate/other oropharynx (C051-C052, C100-C109)], and 3) hypopharynx (C129, C130-C139) were included in the analyses. Cases of lip, salivary gland, and nasopharynx cancer were not included given their different epidemiologic characteristics (7). Moreover, patients with cancers in other ill-defined sites in the lip, oral cavity, and pharynx were excluded from this study because the number of these cases diagnosed in PR during the study period

was rather small (1992-2009; 77 in women and 347 in men). This study did not account for ethnic differences within the USH population.

Statistical analysis

Using the world standard population as a reference, we applied the direct method to compute the age-standardized rates [ASR (World)] for each OCPC anatomical site during 1992-2009 (14). The change in the ASR (World) for each OCPC anatomical sites from the earliest and the latest study period (1992-1998 and 2003-2009) was calculated as a percent change (PC) as follows:

$$PC = \frac{Rate_{2003-2009} - Rate_{1992-1998}}{Rate_{1992-1998}} * 100$$

A Bonferroni test adjusted for multiple comparisons was performed using 99.4% confidence for eight comparisons (two sex categories and four racial/ethnic groups), for each site, in order to assess a significant change of the PCs. As a consequence, the overall significant type I error was approximately 5%. The confidence intervals (CIs) were calculated with the formulas recommended by the U.S. Census Bureau (15). Significant changes were declared with p<0.05 for each anatomical site if 0 was not included in the interval.

We also assessed racial/ethnic group differences in OCPC incidence by anatomical sites, during 2005-2009, by estimating

$$the\ ratio\ of\ two\ standardized\ rates \\ \boxed{\frac{ASR\ (world)_i}{ASR\ (world)_j}} between\ sexes$$

(i = men and j = women) and any two groups (i = PR and j = other racial/ethnic group) with 95% CIs (16). This ratio is referred to as the standardized rate ratio (SRR). The Poisson regression model was used to formally assess the interaction terms between the predictors (sex and racial/ethnic groups) and age in order to determine if age-specific rates were different. The statistical analysis was performed using Stata/SE statistical software version 11.0 (Stata Corp., L.P., College Station, TX).

Results

Age standardized rates (world)

The incidence of each OCPC anatomical site during 1992-2009 is shown in Table 1. Although declining incidence rates were observed for most anatomical sites in most racial/ethnic groups and in both sexes, the incidence of oropharynx cancers, mainly base of tongue (PC = 62.3) and tonsil (PC = 64.3), significantly increased in NHW men from 1992-1998 to 2003-2009 (p<0.05; Table 2). PR also showed a slight increase for cancers in the oropharynx among women, both in the base of tongue and soft palate/other oropharynx (p>0.05; Table 2). Among women, PR showed the larger increase for cases of oral tongue cancers (PC = 40.5; p>0.05) and the only group

with increasing trends of floor of mouth cancers (PC=9.2; p>0.05). Hispanic men, both Puerto Ricans (PC=18.7) and USH (PC = 7.8), were the only groups with increasing trends of gingivobuccal cancers (p>0.05). Cancers from all OCPC sites diminished among NHB (Table 2). Hypopharynx cancers declined in all racial/ethnic groups (Table 2).

Standardized rates ratios

During 2005-2009, the incidence of OCPC at any anatomical site was consistently lower in Puerto Rican women than in any other group (Table 3). Among men, however, the OCPC incidence in PR varied compared to that among USH and NHW. For example, the incidence of soft palate/other oropharynx cancers in Puerto Rican men was about 2.8 (95%CI = 2.08, 3.91) times higher than in USH men and about 1.4 (95%CI = 1.20, 1.71) times higher than in NHW men but 21% (SRR: 0.79; 95%CI = 0.62, 1.00) lower than in NHB men. Accordingly, the

Table 1. Age-standardized rates (incidence per 100,000 individuals) for oral cavity and pharynx cancer by anatomical sites, sex, and racial/ethnic group, 1992-2009.

Anatomical sites		PR	ASR (wo		rld) NHW		NHB	
	Men	Women	Men	Women	Men	Women	Men	Women
Oral cavity	4.5	1.3	4.9	2.8	8.5	4.9	9.2	3.8
Oral tongue	0.9	0.3	1.5	1.1	2.8	1.6	2.2	0.8
Floor of mouth	1.7	0.2	1.7	0.4	2.7	1.1	3.9	1.1
Gingivobuccal	1.8	0.7	1.8	1.3	3.0	2.2	3.2	1.9
Oropharynx	7.5	1.1	7.1	1.7	14.0	3.5	18.6	4.4
Base of tongue	2.2	0.4	2.4	0.6	5.7	1.3	6.2	1.5
Tonsil	2.8	0.5	3.3	0.7	6.1	1.4	7.5	1.7
Soft palate/								
Other Oropharynx	2.5	0.2	1.3	0.4	2.1	0.8	4.9	1.3
Hypopharynx	2.4	0.2	2.4	0.3	2.8	0.7	6.0	1.2

ASR = Age-standardized rates; PR = Puerto Rico; USH = Hispanics in the U.S.; NHW = non-Hispanic whites; NHB = non-Hispanics blacks

Table 2. Percent change (1992-1998 to 2003-2009) for oral cavity and pharynx cancer by anatomical site, sex, and racial/ethnic group.

	Percent change							
Anatomical site	PR		USH		NHW		NHB	
	Men	Women	Men	Women	Men	Women	Men	Women
Oral cavity	-5.2	5.2	-21.5*	-8.4	-18.9*	-18.0*	-44.4*	-22.3*
Oral tongue	1.0	40.5	-13.4	37.3	-0.8	7.4	-20.3	-11.4
Floor of mouth	-27.5*	9.2	-48.0*	-41.7*	-38.8*	-45.8*	-60.3*	-46.0*
Gingivobuccal	18.2	-7.5	7.8	-20.2	-13.0*	-17.5*	-35.4*	-8.8
Oropharynx	-3.9	2.0	-5.2	-14.2	47.6*	-5.9	-20.9*	-14.7
Base of tongue	-13.5	18.2	-1.0	-16.3	61.9*	-0.8	-15.1	-5.6
Tonsil	-2.1	-12.9	4.3	-7.1	65.3*	-0.5	-13.5	-26.4
Soft palate/								
Other oropharynx	3.8	10.8	-30.5*	-24.8	-15.3*	-21.1*	-37.4*	-6.4
Hypopharynx	-25.5*	-71.2*	-24.4*	-42.3	-35.2*	-37.8*	-40.8*	-46.2*

PR = Puerto Rico; USH = Hispanics in the U.S.; NHW = non-Hispanic whites; NHB = non-Hispanics blacks; *P < 0.05

incidence of cancer in oropharyngeal sites in men was slightly higher in PR than in USH (p>0.05). Likewise, men in PR had about 28% (SRR: 1.28; 95%CI = 0.91, 1.82) higher incidence of floor of mouth cancer as compared to USH men. All OCPC sites showed lower SRR in PR than NHB (Table 3).

Despite these findings, significant interactions terms formed with racial/ethnic group and age were shown in various sites (p<0.05). For example, among men the oral cavity and oropharynx sites showed higher cancer incidence among those individuals between 40-49 years old and 50-59 years old in PR as compared to USH [data not shown]. The incidence of cancers of the soft palate/other oropharynx among individuals older than 70 years of age was about 25% lower in PR than in USH and NHW (p>0.05; data not shown) whereas among younger individuals (40-69 years of age) the relative risks (RR) ranged from 1.39 to 5.21 (p<0.05; data not shown). Younger women (40-49 years old) in PR showed higher risks of oropharynx

cancer than USH women of the same age group (RR: 2.39; 95%CI = 1.12, 5.07) [data not shown]. Likewise, the incidence of soft palate/other oropharynx cancers among women in PR between 40-49 years old (RR: 8.86; 95%CI = 0.99, 79.28) and 50-59 years old (RR: 1.03; 95%CI = 0.28, 3.85) was higher than in USH women. Most of the sites showed an inverse dose-response relationship among those racial/ethnic groups' comparisons with significant interactions terms in the Poisson model [data not shown].

In all racial/ethnic groups and at all anatomical sites, the incidence of OCPC was higher in men than in women; this excess was not significant (p>0.05) neither for oral tongue cancer in USH nor for gingivobuccal cancer in NHB (Table 4). The largest differences in OCPC incidence between sexes were consistently noted in Puerto Rican individuals except for base of tongue cancers (Table 4); it was manly observed for cancer of the hypopharynx (SRR: 29.6; 95% CI = 14.1, 86.3). For each racial/ethnic group, various sites showed significant interaction terms formed with sex and age (p<0.05). Those individuals between 60-69 years old in PR and 50-59 years old in NHW showed higher RR in men than in women [data not shown]. Also, the incidence floor of mouth cancer among USH men was much higher than in USH women for those between 60-69 years old (RR: 11.1; 95%CI = 2.6, 47.6) [data not shown]. NHB had the highest difference between sexes for tonsil cancer among individuals that were ≥ 70 years of age (p<0.05; data not shown).

Table 3. Standardized rate ratio for oral cavity and pharynx cancer by anatomical sites and sex, 2005-2009

Anatomical site	SRR PR vs. USH (95%CI)		SRR PR vs. NF	IW (95%CI)	SRR PR vs. NHB (95%CI)	
	Men	Women	Men	Women	Men	Women
Oral cavity	0.92† (0.77, 1.11)	0.49* (0.38, 0.64)	0.55*† (0.47, 0.63)	0.31*† (0.24, 0.38)	0.66*† (0.55, 0.79)	0.42* (0.32, 0.55)
Oral tongue	0.71† (0.49, 1.02)	0.33*† (0.20, 0.53)	0.33*† (0.25, 0.44)	0.24* (0.15, 0.36)	0.52* (0.36, 0.76)	0.50* (0.28, 0.84)
Floor of mouth	1.28 (0.91, 1.82)	0.58 (0.28, 1.14)	0.70*† (0.55, 0.88)	0.25* (0.13, 0.43)	0.64* (0.47, 0.89)	0.30* (0.15, 0.56)
Gingivobuccal	0.86† (0.65, 1.14)	0.64* (0.44, 0.91)	0.63*† (0.51, 0.77)	0.38* (0.28, 0.50)	0.78 (0.58, 1.04)	0.43* (0.30, 0.61)
Oropharynx	1.08† (0.94, 1.24)	0.71*† (0.51, 0.98)	0.44*† (0.40, 0.49)	0.35*† (0.26, 0.45)	0.45*† (0.40, 0.52)	0.28*† (0.21, 0.38)
Base of tongue	0.82† (0.63, 1.05)	0.80 (0.46, 1.35)	0.28* (0.23, 0.34)	0.34*† (0.21, 0.50)	0.35* (0.27, 0.43)	0.32*† (0.19, 0.50)
Tonsil	0.77*† (0.62, 0.96)	0.57*† (0.33, 0.93)	0.35* (0.29, 0.41)	0.32*† (0.19, 0.48)	0.38*† (0.31, 0.46)	0.28* (0.16, 0.45)
Soft palate/						
Other orpharynx	2.82*† (2.08, 3.91)	0.89† (0.45, 1.71)	1.44*† (1.20, 1.71)	0.42* (0.24, 0.67)	0.79† (0.62, 1.00)	0.25* (0.14, 0.42)
Hypopharynx	1.00† (0.77, 1.31)	0.32* (0.10, 0.84)	0.90† (0.74, 1.09)	0.12* (0.04, 0.24)	0.42* (0.33, 0.53)	0.10* (0.03, 0.22)

SRR = Standardized rate ratio; PR = Puerto Rico; USH = Hispanics in the U.S.; NHW = non-Hispanic whites; NHB = non-Hispanics blacks; CI = Confidence Interval; *P < 0.05; †Interaction between age and racial/ethnic group was found (P < 0.05).

Table 4. Standardized rate ratios for oral cavity and pharynx cancer by anatomical sites and racial/ethnic group, 2005-2009.

Anatomical site	SRR men vs. women (95%CI)							
	PR	USH	NHW	NHB				
Oral cavity	3.06*† (2.38, 3.98)	1.63* (1.34, 2.00)	1.71*† (1.59, 1.83)	1.95* (1.58, 2.27)				
Oral tongue	2.19* (1.34, 3.75)	1.04 (0.74, 1.45)	1.59* (1.42, 1.78)	2.08* (1.39, 2.78)				
Floor of mouth	7.26* (4.15, 14.27)	3.27*† (2.05, 5.45)	2.62*† (2.26, 3.05)	3.35* (2.25, 4.25)				
Gingivobuccal	2.40*† (1.72, 3.41)	1.77* (1.32, 2.40)	1.44*† (1.30, 1.60)	1.33 (0.98, 1.74)				
Oropharynx	6.30*† (4.84, 8.44)	4.16* (3.35, 5.22)	4.93*† (4.60, 5.28)	3.94* (3.36, 4.31)				
Base of tongue	4.48* (2.92, 7.32)	4.37* (3.04, 6.51)	5.36* (4.82, 5.98)	4.11* (3.14, 4.75)				
Tonsil	6.31* (4.09, 10.50)	4.62* (3.39, 6.46)	5.78*† (5.20, 6.45)	4.69*† (3.62, 5.35)				
Soft palate/								
Other oropharynx	8.96*† (5.58, 15.96)	2.83* (1.73, 4.86)	2.61*† (2.24, 3.06)	2.85* (2.10, 3.45)				
Hypopharynx	29.61* (14.09, 86.27)	9.57* (5.58, 18.43)	3.81* (3.24, 4.52)	6.93* (4.84, 8.10)				

SRR = Standardized rate ratio; PR = Puerto Rico; USH = Hispanics in the U.S.; NHW = non-Hispanic whites; NHB = non-Hispanics blacks; CI = Confidence Interval; *P < 0.05; †Interaction between age and sex was found (P < 0.05).

Discussion

The results of this study indicate that the incidence of OCPC by anatomical site in PR differs from that in other racial/ethnic groups in the continental USA. Differences in OCPC incidence between PR and continental USA by anatomical site could be the result of differences in the prevalence of OCPC risk factors in these populations, including smoking, alcohol drinking, poor oral hygiene, poor dietary habits, HPV infection, and risky sexual behaviors. Furthermore, we cannot discount genetic predisposition as a relevant factor; for example, a study conducted in PR (17) indicated that in persons with the GSTT1-present genotype, the risk of oral cancer increased as cigarette use increased. However, to our knowledge, no studies have shown that the frequency of genetic polymorphisms associated with oral cancers is different in Puerto Rican and American individuals.

In addition, the lower incidence of certain OCPC (i.e. soft palate/other oropharynx and floor of mouth) in USH men than in Puerto Rican men could be the result of what is known as the "healthy migrant effect," which suggests that people who

migrate are healthier than those who remain in their countries of origin (18). The fact that USH individuals may possess better health-enhancing behavioral profiles (18) may influence the incidence rates in this USA population. Nonetheless, given that in our study, we only observed such patterns among men; further research is warranted to determine whether this hypothesis in fact applies only to men and to elucidate the reasons for this sexbased disparity between Puerto Rican and USH individuals.

Despite the differences found, for all racial/ethnic groups the most common cancer was the tonsils followed by the soft palate/other oropharynx among men in PR and the base of tongue among men in the continental USA. On the other hand, in all racial/ethnic groups, women mainly had cancers in the gingivobuccal subsite followed by the tonsils in Puerto Rican and NHB women and the oral tongue in USH and NHW women. An increase in the incidence of cancers in the tonsils and oral tongue was previously observed in NHW individuals from 1975-1982 to 1992-1998 (19) and, as seen in our study, the incidence of these cancers continues increasing in this group among men and women, respectively. Also, other researchers have found that the incidence of oral tongue, base of the tongue and tonsil squamous cell carcinomas has increased over time (20). Squamous cell carcinoma of the tonsil and the base of tongue has previously been associated with HPV (21-23). OCPC of the oropharynx has also been related to HPV, and our findings suggest the incidence of oropharyngeal cancers is slightly increasing among women older than 39 years old in PR but not in the continental USA. However, Puerto Rican women presented lower risks of oropharyngeal cancers than any other racial/ethnic group in the

continental USA; only women between 40-49 years old in PR showed higher risks (RR: 2.39; 95%CI = 1.12-5.07) than USH women within the same age group. Higher risks were also found for oropharyngeal cancers among men in PR when compared to USH men between the 40-49 and 50-59 age groups. Soft palate/other oropharynx cancers as well showed higher risks in younger groups when comparing PR to NHW and USH. These findings could suggest not only differences in HPV infection but also in sexual behaviors between the groups, because various studies have found that an increasing number of lifetime sex partners is associated with an increasing risk of oropharyngeal cancer; the risk of oropharyngeal cancer is increased by 34-fold in individuals with more than 9 lifetime sex partners (24).

Population-based data on oral HPV infection are not available for PR, so we cannot make a direct comparison with the data of the USA, based on the National Health and Nutrition Examination Survey (NHANES) (25). Nonetheless, a population-based study performed in PR during 2005-2008 suggested that oral sex practices and higher numbers of sexual partners could be more prevalent in PR than in Mexican Americans in the USA (26). Hence, monitoring the impact of HPV vaccines (27) on the trends in oropharyngeal cancer incidence in PR and the continental USA may be of interest. However, given the low uptake of the vaccine, (28, 29) the impact of vaccination on disease trends may be delayed.

The decline in the incidence of cancers of the hypopharynx, floor of the mouth, and gingivobuccal in the mouth from 1992-1998 to 2003-2009 is consistent with the declines in smoking and alcohol consumption, which are the major risk factors for OCPC (30). According to the Behavioral Risk Factor Surveillance System survey, from 1997 to 2010, tobacco consumption declined in PR (14.4% to 11.9%) and in the USA (23.2% to 17.3%) (31). Moreover, a small fluctuation in the prevalence of heavy alcohol drinking was observed in Puerto Rico (3.8% to 3.0%) and the USA (5.1% to 5.0%) from 2001 to 2010 (31). Nonetheless, caution must be taken when considering these prevalence estimations as a possible justification for declining trends in the incidence of cancer at these sites, since there could be a delay of several years between exposure and the development of these cancers. These lifestyles (smoking and alcohol drinking) could partly explain the observed sex-based differences in OCPC incidence, as the risk of OCPC that is attributed to these factors is about 76% (95% CI = 65-87%) for men and 52% (95% CI = 28-75%) for women (32). However, we cannot discount the existence of other differences between men and women regarding the prevalence of other factors that may influence disease trends, such as HPV infection, sexual behaviors, and preventive care use, that may have also influenced our results.

The preventive care use, specifically dental checkups, is lower in men than in women in the USA (33) so it could potentially explain sex-based differences in OCPC incidence

at different anatomical sites. During the early 1990s, Marshall and colleagues (34) found that poor oral hygiene also increases the risk of OCPC but to a lesser degree than do smoking and alcohol drinking. Poor oral hygiene can result in periodontitis, which has been related to oral premalignant lesions and OCPC. According to Lissowska et al., (35) the attributable risk of OCPC for low frequency of tooth brushing and dental checkups is about 56% and 47%, respectively. This chronic inflammatory disease (i.e., periodontitis) could affect tissues at distant sites through periodontal bacteria, via saliva and the bloodstream, and cause tissue injury through inflammatory reactions (36-38). Furthermore, an oral inflammatory disease may lead to enhanced penetration of other carcinogens (e.g., tobacco, alcohol, and dietary metabolites) (39) as well as the acquisition and persistence of oral HPV infection (40).

According to NHANES, during 2009-2010 the prevalence of oral infection with any of 37 HPV DNA types evaluated was significantly higher among men than women (10.1% vs. 3.6%; p < 0.05) (25), and this disparity may be related to the number of sexual partners. In fact, Ortiz and colleagues (26) reported that the prevalence of multiple sexual partners (\geq 7 lifetime partners) is higher in men than in women in PR (47.9% and 13.2%, respectively). Thus, this pattern may contribute to explain the largest sex-based differences in OCPC incidence among Puerto Ricans, particularly for anatomical sites related to HPV infection.

To our knowledge, this is the first study to describe OCPC incidence by anatomical site in PR and compare it with that of other racial/ethnic groups in the USA. Nonetheless, some limitations of this study should be acknowledged. First, we were unable to collect information regarding risk factors for OCPC for any of the racial/ethnic groups. Nevertheless, our findings suggest different behavior patterns in PR that could be affecting our OCPC incidence rates in each site. Second, our results may have been influenced by poor accuracy in the classification of Hispanic cancer cases in the SEER 13 program. However, this bias can be reduced by combining surname and medical record information (41). Because this method is used by the SEER 13 program when classifying persons as USH individuals (42), we do not expect our conclusions to be affected. Last, reduced cancer reporting by the Department of Veterans Affairs hospitals impacted the most recent USA and Puerto Rican cancer surveillance data (2005-present) (43). Even though incidence rates after 2004 may be underestimated, differences between Puerto Ricans and the other racial/ethnic groups in the USA are expected to remain the same, as both groups were affected by underreporting.

Conclusion and recommendations

The incidence of each OCPC anatomical site in PR differed from that in NHW, NHB, and USH in the USA. Our study showed that younger individuals in PR had higher risks of oropharyngeal cancers, particularly in the soft palate/other oropharynx, than USH (both sexes) and NHW (only women) of the same age group. Therefore, further research in PR should assess the effect of the HPV infection, as well as of other risk factors, in OCPC incidence by anatomical site in younger populations. Another important finding was the risks differences between sexes, particularly in PR which showed the most extreme ratios. Thus, future research should also consider assessing the interaction between sex and different risk factors for each OCPC sites. These data could explain more precisely the reasons for the differences observed in this study and could provide relevant data that would help to identify future recommendations aimed at reducing the burden of OCPC in PR.

Resumen

Objetivo: Aún existe desconocimiento de la epidemiología del cáncer en distintas localizaciones anatómicas de la cavidad oral y orofaringe en Puerto Rico (PR). Nuestro objetivo fue comparar la incidencia de cáncer de cavidad oral y orofaringe en PR, por localización anatómica, contra la población blanca no hispana, afroamericana e hispana en los Estados Unidos de América (EE.UU.). Métodos: Datos del programa "Surveillance Epidemiology and End Results" y del Registro Central de Cáncer de PR fueron recopilados y analizados. Tasas estandarizadas por edad, cambios porcentuales, y la razón de las tasas estandarizadas fueron estimadas con intervalos de confianza al 95%. Resultados: A pesar que se observó una disminución en la incidencia de cáncer de cavidad oral y orofaringe en la mayoría de los grupos raciales/étnicos y en ambos sexos, las mujeres en PR mostraron un aumento de cáncer de orofaringe, en base de lengua y paladar blando/otros orofaringe (p>0.05). En hombres, la incidencia de cánceres en el paladar blando/otros orofaringe en PR fue alrededor de 2.8 veces mayor (p<0.05) que en Hispanos en EE.UU. y alrededor de 1.4 veces mayor que en blancos no-Hispanos en EE.UU. pero 21% menor que en afroamericanos en EE.UU. (p>0.05). Términos de interacción fueron observados (p<0.05). La mayor diferencia entre sexo se observó consistentemente en PR. Conclusión: Investigaciones futuras en PR deben evaluar los efectos de la infección por VPH y de otros factores en la incidencia de cáncer de cavidad oral y orofaringe por localización anatómica en jóvenes. Estos datos podrían explicar con mayor precisión las diferencias observadas.

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References

- Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncol 2009;45:309-16.
- Parkin M, Bray F, Ferlay J, Pisani P. Global Cancer Statistics, 2002. CA Cancer J Clin 2005;55:74-108.
- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. GLOBO-CAN 2008: Estimated cancer Incidence, Mortality, Prevalence and Disability-adjusted life years (DALYs) Worldwide in 2008 [internet]. International Agency for Research on Cancer, World Health Organization; c2010 [updated 2012 Oct; cited 2011 July 7]. Available from: Url: http:// globocan.iarc.fr.
- Departamento de Salud: Gobierno de Puerto Rico [Puerto Rico Department of Health] [internet]. San Juan: Puerto Rico Central Cancer Registry; c2007. Cancer of the Oral Cavity and Pharynx Stat Fact Sheet; 2008 Sep. Available from: Url: http://www.salud.gov.pr/RCancer/Reports/Pages/default.aspx.
- Suárez E, Calo WA, Hernández EY, Díaz EC, Figueroa NR, Ortiz AP. Agestandardized incidence and mortality rates of oral and pharyngeal cancer in Puerto Rico and among Non-Hispanics Whites, Non-Hispanic Blacks, and Hispanics in the USA. BMC Cancer 2009;9:129.
- Surveillance Epidemiology and End Results (SEER) [internet]. Bethesda (MD): National Cancer Institute. SEER Cancer Statistics Review, 1975-2008; 2011. Available from: Url: http://seer.cancer.gov/csr/1975 2008/.
- Mayne ST, Morse DE, Winn DM. Cancers of the oral cavity and pharynx. In: Schottenfeld D, Fraumeni JF (eds). Cancer Epidemiology and Prevention. New York, NY: Oxford University Press; 2006:674-696.
- Dhar PK, Rao TR, Sreekumaran Nair N, et al. Identification of risk factors for specific subsites within the oral and oropharyngeal region--a study of 647 cancer patients. Indian J Cancer 2000;37:114-22.
- Soto-Salgado M, Suárez E, Calo W, Cruz-Correa M, Figueroa-Vallés NR, Ortiz AP. Incidence and mortality rates for colorectal cancer in Puerto Rico and among Hispanics, non-Hispanics whites, and non-Hispanics blacks in the United States, 1998-2002. Cancer 2009;115:5126-7.
- González L, Magno P, Ortiz AP, et al. Esophageal cancer incidence by histological type and overall: Puerto Rico versus the United States SEER population, 1992-2005. Cancer Epidemiol 2013;37:5-10. doi: 10.1016/j. canep.2012.09.002. Epub 2012 Oct 11.
- National Program of Cancer Registries: Technical Assistance and Audit Puerto Rico Central Cancer Registry 2000, Case Completeness and Data Quality Audit. Atlanta, Georgia: Centers for Disease and Control and Prevention; 2003.
- 12. Fritz G, Percy C, Jack A, Sobin LH, Parkin MD. International Classification of Diseases for Oncology. 3rd ed. Geneva: World Health Organization; 2000. 240 p.
- Surveillance Epidemiology and End Results [Internet]: Bethesda: National Cancer Institute; [cited 2012 Feb 1]. SEER Behavior Recode for Analysis. Available from: Url: http://seer.cancer.gov/behavrecode/.
- Waller LA, Gotway CA. Applied spatial statistics for public health data. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2004.
- United States Census Bureau. Percent Changes [Internet]. Washington D.C.: U.S. Census Bureau; [cited 2012 Dec 5]. 4 p. Available from: Url: http://www.census.gov/acs/www/Downloads/data_documentation/ Accuracy/PercChg. pdf.
- Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Res 2006;15:547–69.
- 17. Xie H, Hou L, Shields PG, et al. Metabolic polymorphisms, smoking, and oral cancer in Puerto Rico. Oncol Res 2004;14:315-320.

- Singh GK, Miller BA. Health, life expectancy, and mortality patterns among immigrant populations in the United States. Can J Public Health 2004;95:114-21.
- 19. Canto MT, Devesa SS. Oral cavity and pharynx cancer incidence rates in the United States, 1975-1998. Oral Oncol 2002;38:610-617.
- Shiboski CH, Schmidt BL, Jordan RC. Tongue and tonsil carcinoma: increasing trends in the U.S. population ages 10-44 years. Cancer 2005; 103:1843-1849.
- Gillison ML, Koch WM, Capone, et al. Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. J Natl Cancer Inst 2000;92:709-720.
- D'Souza G, Kreimer AR, Viscidi R, et al. Case-control study of human papillomavirus and oropharyngeal cancer. N Engl J Med 2007;356:1944-1956.
- Venuti A, Badaracco G, Rizzo C, Mafera B, Rahimi S, Vigili M. Presence of HPV in head and neck tumours: high prevalence in tonsillar localization. J Exp Clin Cancer Res 2004;23:561-566.
- Dahlstrom KR, Li G, Tortolero-Luna G, Wei Q, Sturgis EM. Differences in history of sexual behavior between patients with oropharyngeal squamous cell carcinoma and patients with squamous cell carcinoma at other head and neck sites. Head Neck 2011;33:847-55. doi: 10.1002/hed.21550.
- Gillison ML, Broutian T, Pickard RK, et al. Prevalence of oral HPV infection in the United States, 2009-2010. JAMA 2012;307:693-703.
- Ortiz AP, Soto-Salgado M, Suárez E, del Carmen Santos-Ortiz M, Tortolero-Luna G, Pérez CM. Sexual behaviors among adults in Puerto Rico: a population-based study. J Sex Med 2011;8:2439-49.
- Gillison ML, Chaturvedi AK, Lowy DR. HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. Cancer 2008;113(10suppl):3036-3046.
- Stupiansky NW, Alexander AB, Zimet GD. Human papillomavirus vaccines and men: what are the obstacles and challenges? Curr Opin Infect Dis 2012;25:86-91.
- Cassidy B, Schlenk EA. Uptake of the human papillomavirus vaccine: a review of the literature and report of a quality assurance project. J Pediatr Health Care doi:10.1016/j.pedhc.2010.06.015
- Brown LM, Check DP, Devesa SS. Oropharyngeal cancer incidence trends: diminishing racial disparities. Cancer Causes Control 2011;22:753-63.
- Behavioral Risk Factor Surveillance System Survey (BRFSS) [internet]:
 Atlanta: Center for Disease Control and Prevention; 2011 [cited 2011

- June 30]. Prevalence and Trends Data; [about 1 screen]. Available from: Url: http://apps.nccd.cdc.Gov/BRFSS/.
- 32. Hayes RB, Bravo-Otero E, Kleinman DV, et al. Tobacco and alcohol use and oral cancer in Puerto Rico. Cancer Causes Control 1999;10:27-33.
- Vaidya V, Partha G, Karmakar M. Gender differences in utilization of preventive care services in the United States. J Womens Health (Larchmt) 2012;21:140-5.
- Marshall JR, Graham S, Haughey BP, et al. Smoking, alcohol, dentition and diet in the epidemiology of oral cancer. Eur J Cancer B Oral Oncol 1992;28B:9-15.
- Lissowska J, Pilarska A, Pilarski P, et al. Smoking, alcohol, diet, dentition and sexual practices in the epidemiology of oral cancer in Poland. Eur J Cancer Prev 2003;12:25-33.
- Scannapieco FA, Wang B, Shiau HJ. Oral bacteria and respiratory infection: effects on respiratory pathogen adhesion and epithelial cell proinflammatory cytokine production. Ann Periodontol 2001;6:78-86.
- Haraszthy VI, Zambon JJ, Trevisan M, Zeid M, Genco RJ. Identification of periodontal pathogens in atheromatous plaques. J Periodontol 2000;71:1554-60.
- 38. Iacopino AM. Periodontitis and diabetes interrelationships: role of inflammation. Ann Periodontol 2001;6:125-37.
- Pöllänen MT, Salonen JI, Uitto VJ. Structure and function of the toothepithelial interface in health and disease. Periodontol 2000 2003;31:12-31.
- Tezal M. Interaction between Chronic Inflammation and Oral HPV Infection in the Etiology of Head and Neck Cancers. Int J Otolaryngol 2012;2012:575242. doi:10.1155/2012/575242.
- Stewart SL, Swallen KC, Glaser SL, Horn-Ross PL, West DW. Comparison of methods for classifying Hispanic ethnicity in a population-based cancer registry. Am J Epidemiol 1999;149:1063-1071.
- NAACR Uniform Data Standard committee. Subcommittee on methodological problems in measuring cancer in Hispanics: Final Report of Atlanta Symposium [internet]. Atlanta: NAACR; 1996 [cited 2011 Aug 4].
 p. Available from: Url: http://www.naacr.org/LinkClick.aspx?fileticket=pzDOtUUz9k0%3D &tabid=95&mid=477.
- Surveillance Epidemiology and End Results (SEER) [internet]. Veterans Affairs Adjustment, CSR 1975-2009: Bethesda: National Cancer Institute; [cited 2010 Oct 20]. 17 p. Available from: Url: http://seer.cancer. gov/csr/1975_2009_pops09/results_merged/sect_33_VA_adjustment.pdf