EPIDEMIOLOGY

Descriptive Epidemiology of Head and Neck Squamous Cell Carcinoma in Puerto Ricans

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ABSTRACT. This study comprised 134 patients who had developed head and neck squamous carcinoma (HNSCC), and attended the cancer clinics of the Otolaryngology Department at the Isaac González Martínez Oncologic Hospital between August 1993 and November 1995. In-person interviews, and medical record review of the HNSCC patients provided data on demography, family history of cancer, history of a second primary cancer, history of environmental, tobacco and ethanol exposure, and current disease status. The average age at the time of diagnosis was 62.3 (range 18 - 94), and eighty percent of the subjects were male. Most (59%) of the patients had moderately differentiated tumors and 14% had a recurrence of the carcinoma. The most frequent primary site in males was the laryngeal area, and the oral cavity in females. Exposure to alcohol and smoking were identified as predisposing factors in 95% of the patients. *Key Words: Squamous cell carcinoma, Epidemiology, Head and neck carcinoma, Puerto Rico.*

Head and neck squamous carcinoma (HNSCC) account for 5% of all malignant neoplasms in the United States and Europe (1-3). In 1993 there were 42,400 new cases of HNSCC in the United States and 11,500 deaths (3). Each year in the U.S. there are approximately 21 new cases of cancer of the oral cavity, pharynx and larynx per 100,000 males and seven new cases per 100,000 females (2, 4). The incidence in Puerto Rico is 26.4 new cases per 100,000 males, and five new cases per 100,000 females (4, 5). Approximately 410 cases of pharyngeal and oral cancer are expected by the year 2000 (4, 5). Of those patients diagnosed, 32% eventually die of these diseases (2). Squamous cell carcinoma accounts for 90% of the malignancies arising in the head and neck region (6, 7), and over the past few decades the incidence has been steadily increasing (7).

Many predisposing factors are suspected to be involved in the development of HNSCC. The risks of developing a certain cancer are determined by individual differences in susceptibility in combination with external factors. Whereas racial and ethnic differences in cancer incidence and mortality rates in the United States are well documented, these differences have not been completely characterized (3, 8- 11). In the United States, cancer occurs more frequently in blacks than in whites, and is less common among Hispanics and Native Americans. Reasons for these racial differences are unclear although dietary, hormonal, and environmental determinants have been suggested (8- 11). Furthermore, several epidemiologic studies have shown a direct association between the use of alcohol and smoking with development of HNSCC (12-15). Tobacco and alcohol are believed to be the two important causes of HNSCC with the weight of evidence suggesting a synergistic effect (15). Moreover, alcohol is considered a cocarcinogen (14) although some studies suggest that it is also an independent factor (15, 16). Occasionally, nonsmokers and non drinking patients develop cancer of the head and neck suggesting that in addition to tobacco and alcohol, other environmental, immunologic, or genetic factors participate in the development of HNSCC (16). Occupational groups have been reported at excess risk for developing certain cancers. In that respect there are several environmental or occupational carcinogens described to cause HNSCC (17, 18). Most likely the etiology of HNSCC is multifactorial with a large amount

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of interaction between the carcinogenic effects of different factors. The purpose of this study is to describe a population of patients with a diagnosis of HNSCC in order to asses its clinical, social, and individual characteristics.

Subjects and Methods

Study population. The study population consisted of Puerto Rican adults with a confirmed diagnosis of HNSCC, (International Classification of Disease [ICD]), and treated between August 1993 and June 1995 in the cancer clinics of the Otolaryngology Department at the Isaac González Martínez Oncologic Hospital. Patients without a histopathological diagnosis of HNSCC, and nonresidents were excluded. The Oncologic Hospital is an 80-bed semi-private hospital located at the Puerto Rico Medical Center that treats approximately 15.6% of the island registered cancers (5). Sources of data included hospital records and a structured questionnaire. In-person interviews were conducted by the Otolaryngology-Head and Neck Surgery (OTO-HNS) research fellow at the outpatient cancer clinics of the Oncologic Hospital. A written informed consent to participate in the study was obtained at the moment of the interview; if the subject could not talk, the next-of-kin was interviewed. Questionnaires were designed to collect detailed information on sociodemographic characteristics, lifestyles, family history of cancer, concurrent diseases, and employment history. Note was also made of poor oral hygiene or the presence of a dental prosthesis. With respect to the job description, questions were asked regarding the exposure to potential carcinogens such as exposure to ionizing radiation, or to inhaled irritants. The reliability of the questionnaire was tested by reinterviewing control subjects after 6-12 months (19).

Alcohol and tobacco use were analyzed as to quantity, quality and frequency of use. Alcohol drinkers were defined as those who reported consuming at least one drink of beer, wine or hard liquor per month for at least for six months. Consumption of alcohol was estimated based on one drink equivalency to 12 ounces of beer, 4 ounces of wine and 1.5 ounces of hard liquor. Tobacco smokers were defined as those who reported smoking at least one cigarette per day or one cigar or pipe per week during at least six months. Questions were asked on the number of years and amount smoked. The subject was considered to be ex-smoker if he had stopped smoking two years or more prior to the study.

Initial descriptive analysis of the data was done with the statistical programs SPSS-X, and EPI-INFO. Univariate and multivariate analysis was performed to evaluate tumor recurrence, and to relate reported exposures in groups of individual to disease occurrence. Association of suspected factors and gender on HNSCC risk were evaluated by Chi square.

Results

Table 1 summarizes the distribution of demographic and other characteristics of the 134 interviewed patients who had developed HNSCC. There was a male predominance

Table 1. Demographics and Other Characteristics of Patients with Head and Neck Squamous Carcinoma

Characteristic	Total (%)
Number of subjects	134
Sex	
Female	26 (19.4%)
Male	108 (80.6%)
Age at HSSC diagnosis (yrs)	
< 50	16 (11.9%)
50-59	39 (29.1%)
60-69	41 (30.6%)
>70	38 (28.3%)
Tumor site	
Oral cavity	36 (26.9%)
Oropharynx	33 (24.6%)
Larynx	48 (35.8%)
Hypopharynx	6 (4.5%)
Nasopharynx	6 (4.5%)
Others	5 (4.4%)
Primary tumor status (T)*	
T1	28 (21.1%)
T2	39 (29.3%)
T3	28 (21.1%)
T4	38 (28.6%)
Grade	
Well differentiated	22 (16.4%)
Moderately differentiated	80 (59.7%)
Poorly differentiated	19 (14.2%)
Unknown	13 (9.7%)
Occupational category †	
Farming, fishing	21 (19.8%)
Administrative, professional	3 (2.3%)
Manufacture	34 (26.0%)
Technical, clerical, sales	13 (9.9%)
Crafts, repair	5 (3.8%)
Service occupations	9 (6.8%)
Other	16 (12.2%)

*One missing observation.
†The occupatoinal category includes a broad range of job types.

The mean age at the time of diagnosis was 62.3 years. For males the mean age was 62.0 (SD = ± 12.8) with a minimum age at time of diagnosis of 18 and a maximum of 94 years. The mean age for females was 63.6 years (SD = ± 9.5) with a minimum age at 41 and a maximum at 81 years.

Distribution of the carcinoma by primary tumor site showed a predominance of squamous cell carcinomas (SCC) of the larynx (35.8%), followed by SCC of the oral cavity (26.9%) and the oropharynx (24.6%). The predominant lesions in the oral cavity were found on the floor of mouth (52.8%) or involving the tongue (33%). In the oropharynx, lesions of the tonsillar area were the most remarkable (51.5%). The most common hypopharyngeal tumors were located at the pyriform sinus (67%)and tumors of the vocal cords (87%) were the most common of the laryngeal tumors. Interestingly, in women predominate malignancies of the oral cavity (34.6%) in contrast to men in whom tumors in the larynx remain preponderant (39.8%). In women, lesions at the larynx are much lower with 19.2% of the total. The distribution by grade shows that most frequent tumors were moderately differentiated squamous cell carcinomas (SCC) in 80 patients (59.7%) and the least frequent were poorly differentiated SCC in 19 patients (14.2%).

Twenty-three patients (17.2%) had a recurrence; five of them were female and 18 were male. The mean age of the patients when the recurrence was diagnosed, was 63 years. In general, the time between diagnosis and the recurrence of the disease was shorter for males (4.6 years) as compared to the females (6.7 years). Sites of the recurrence (n =23) were located in the oral cavity (47%), oropharynx (21.7%), the larynx (26.1%) and nasopharynx (4.3%). Recurrence in the oral cavity was more common at the tongue (37%). Meanwhile, the most prominent lesion of the larynx involved the vocal cords (100%). Most of the recurrences were classified as moderately differentiated SCC (76.9%), followed by well-differentiated SCC (15.4%).

One hundred and fifteen patients (85. 8%) were documented smokers (Table 2), 97 (84.3%) were male and 18 (15.7%) females. Non smokers represented 14.2% of the population; of these, 30.8% were females and 10.2% were males. On this category, the ratio of smokers to nonsmokers was significantly higher (p-value = 0.00691) in males as compared with females. Among the smokers, 84% smoked cigarettes, 5% smoked cigars and the rest were mixed smokers (ie. cigarettes, cigars, and pipes). About half of those interviewed smoked between 1 and 2 packs per day (59.1%). When the different tobacco products were normalized to the equivalent of one pack of cigarettes, 50% of the patients smoked between 1 and 2 packs per day. The majority of the smokers had used tobacco for more than 20 years (86.1 %), while 11.3% had smoked between 10-20 years. Seventy five percent of the smokers that had suffered a recurrence had smoked more than 2 packs/day for 20 or more years. Half of them stopped smoking when HNSCC was diagnosed.

Table 2. Smoking Characteristics of HNSC Patients*

	Total	Male	Female
Exposure			
Ever smoked	115 (85.8%)	97 (89.8%)	18 (69.2%)
Never smoked	19 (14.2%)	11 (10.2%)	8 (30.8%))
Type			
Cigarette smoker	97 (84.3%)		
Cigars or pipes only	9 (8.0%)		
All	9 (8.0%)		
Intensity (cigarettes/day)			
1-19	21 (18.3%)	16 (14.8%)	5 (19.2%)
20-40	67 (50..1%)	57 (57.8%)	10 (38.5%)
> 41	17 (12.7%)	14 (13.9%)	2 (7.7%)
Years of smoking			
< 10	3 (2.6%)	1 (1.0%)	2 (11.1%)
10-20	13 (11.3%)	9 (69.3%)	4 (22.2%)
> 20	99 (86.1%)	87 (89.7%)	12 (66.7%)
Cigarette smoking status			
Currently smoking	29 (21.6%)	27 (25.0%)	2 (7.7%)
Quit at or after diagnosis	88 (65.7%)	72 (66.7%)	16 (61.5%)

* 1 cigar =5 cigarettes 1 pipe =2.5 cigarettes

Table 3 depicts the characteristics of patients that were alcohol consumers; one hundred and nine (81.3%) patients were consumers of alcohol. While half of the females drank alcohol, 88.9% of the men were drinkers and the majority (58.7%) used alcohol on a daily basis until intoxication. Half the drinkers reported having abandoned drinking before being diagnosed with HNSCC. Alcohol users in our study had concomitant use of tobacco in 93.6% of the cases. We standardized alcohol consumption to ounces of alcohol consumed weekly. The group consumed a mean of 32.9 ounces of alcohol (0.11oz. n 252 oz.) during the week. Men consumed a significantly (p< 0.01) higher quantity of alcohol (34.8

Table 3. Drinking Characteristics of HNSC Patients*

Characteristic	Total	Male	Female
Never drank	25 (18.7%)	12 (11.1%)	13 (50.0%)
Ever drank	109 (81.3%)	96 (88.9%)	13 (50.0%)
Intensity (drinks/day)			
1-11	43 (36.4%)		
12-25	7 (5.7%)		
> 26	44 (37.4%)		
Quit at or before diagnosis	55 (50.5%)	50 (52.1%)	5 (38.5%)

*One drink = 12 oz of beer = 4 oz wine = 1.5 hard liquor

(0.11oz. n 252 oz.) during the week. Men consumed a significantly ($p< 0.01$) higher quantity of alcohol (34.8 oz.) than women (19.2 oz.). Of the different treatment modalities, 119 patients (89%) received radiotherapy, and three (8%) also received chemotherapy. All patients with a recurrence were irradiated and 13% were treated with antineoplastic drugs. Average time between completion of radiotherapy and recurrence was 4.1 years and 1.5 years for those who received chemotherapy.

When evaluated as to family history of carcinomas, 55% of our sample had at least one first degree relative with cancer. The most frequent were carcinomas of the colon, breast, and SCC of the larynx. Only seven patients (5%) had history of a second cancer, those were: one adenomatous colorectal polyp, three skin neoplasms (one of them a basal cell carcinoma in the face), two prostate carcinomas and a metastatic testicular carcinoma. All of the patients with a history of a second carcinoma were drinkers and nearly all (83%) had been tobacco smokers.

The association of head and neck cancer with the patient's occupation was also studied. Occupations were stratified into seven occupational categories and subsequently stratified into two risk categories: those that represent a higher risk of developing HNSCC and those that did not (18). The most frequent occupations among the cancer patients were farming (19.8%) and manufacture (26%). Among the most common irritants that they were exposed were cement dust (13.8%), herbicides (11.3%) and insecticides (10%). Occupational risks were assessed in relation to gender and were found statistically significant ($p= 0.00000$). Men in this study had 11.5 more opportunities of having worked in jobs classified as high risk than women.

Discussion

The incidence of SCC of the oral cavity, pharynx and larynx in Puerto Rican men is higher than in white males in the United States (5). In this study we describe the characteristics of a group of patients with HNSCC at the Isaac Gonzalez Martínez Oncologic Hospital. Our findings confirm the high prevalence of tobacco and alcohol exposure among patients with HNSCC whereas 85.8% of them were smokers and 81.3% consumed alcohol. Otherwise, since so few patients in our study abstained from smoking or drinking it was not possible to assess the roles of smoking or drinking independent from each other. Alcohol consumption was significantly associated to men (89.8% vs. 69.2%). The lower rates of women drinkers may be expected because in Puerto Rico there are fewer women drinkers older than 50 years(20).

There is increasing evidence that links exposure to asbestos, wood dust and nickel exposure in smelting, to an increased incidence of laryngeal and oral cancer (21, 22, 23). Most of the patients in this study worked in jobs associated to farming (19.8%), and manufacture (26%). In the category of manufacture, 13 (38%) patients out of 34 were construction workers that could have been exposed to asbestos besides wood dust. Analysis of occupational exposure risks was difficult to establish because of lack of information. For example, the individuals who had worked in construction might have been exposed to asbestos without ever knowing of such exposure. We also observed that seven patients had a second cancer including one adenomatous colorectal polyp and two prostate cancers. These findings are very important, since neoplasias such as prostate carcinoma and adenocarcinoma of the colon are associated with tobacco use and alcohol consumption (24, 25, 26).

In conclusion, our findings document the high incidence of cigarette smoking and alcohol consumption in patients with HNSCC. Furthermore, recent evidence in our laboratory linking HNSCC with human papilloma virus, *c-myc* amplification and *ras* mutations suggest that host genetics need to be studied in concert with epidemiological data. Our data underscores the importance of a larger population-based case control study. This study will provide a wider range of information to explore fully the roles of tobacco, alcohol and host genetics in HNSCC in Puerto Ricans.

Resumen

Se llevó a cabo un estudio con 134 pacientes diagnosticados con carcinoma epidermoide de cabeza y cuello entre agosto de 1993 y noviembre de 1995 que fueron atendidos en las clínicas del Departamento de Otorrinolaringología del Hospital Oncológico Isacc González Martínez. La información sobre los pacientes se obtuvo a través de entrevistas con los propios pacientes y la revisión de sus expedientes clínicos. Los datos de los pacientes se evaluaron según perfil demográfico; historial familiar de cáncer; antecedentes de segundos cánceres primarios; historial de exposición a agentes carcinógenos, al tabaco y a las bebidas alcohólicas; además del estado de salud del paciente. La edad media al momento del diagnóstico del cáncer fue de 62.3 años (rango 18 a 94 años). El 80% de los individuos eran varones y la mayoría, 59%, de los pacientes presentaban tumores moderadamente diferenciandos mientras que el 14% sufría recurrencias del carcinoma. En los hombres el área más afectada fue la laringe, mientras que en las mujeres fue la cavidad oral. El alcohol y el tabaco fueron identificados

como factores predisponentes en 95% de los casos.

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