

ORIGINAL

Head and neck squamous cell carcinoma: decline in clinical stage at the time of diagnosis in a reference hospital in southern Brazil

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ABSTRACT

Objective: Developing countries have a high incidence of head and neck squamous cell carcinoma (HNSCC). Risk factors are smoking and alcohol consumption; socioeconomic status and oral health may be associated with etiology. The aim of this study was to evaluate the sociodemographic profile and oral health of patients with primary HNSCC, as well as the clinical and histopathological characteristics of the tumor. **Material and Methods:** We evaluated 78 patients; data about sex, age, skin color, schooling, oral hygiene, smoking, alcohol consumption and socioeconomic status were collected using a structured questionnaire. An intraoral examination provided data about caries, missing teeth and dental prosthesis. Hospital records were reviewed to collect clinical tumor information. **Results:** Mean age was 57.6 years; most participants were male, white, former or current smokers and moderate or high consumption of alcoholic beverages with low socioeconomic and educational levels. The majority of patients were disease-free at 2 year-follow up. Classification showed 60.2% of the tumors as T1 and T2 and 59% had no regional involvement. Most tumors were found in the mouth, and the tongue was the most frequent site. Histopathological examination revealed that 57.7% of the tumors were classified as moderate and poor prognosis. **Conclusion:** The profile of patients with HNSCC was similar to that found in other populations, but there is a decline in clinical stage at the time of diagnosis, and detecting this tumor at an early stage can be an effective mean to determine a better prognosis for patients.

Keywords: carcinoma; diagnosis; epidemiology; head and neck neoplasms; squamous cell.

INTRODUCTION

Among oral diseases, head and neck squamous cell carcinoma (HNSCC) leads to the highest rate of mortality and morbidity. The main etiologic factors of HNSCC are tobacco and alcohol use, and the association of these two habits significantly increases the risk of developing the tumor¹⁻⁶. Human papilloma virus, oral hygiene and social inequalities also may play an etiologic role^{5,7-10}.

Developing countries have a high incidence of HNSCC^{7-8,11-12}. In South America, the highest incidence of this tumor is found in the region that includes Argentina, southern Brazil and Uruguay, with the highest rates found in Brazil^{1,2}.

Survival rates are very poor and have not improved in last decades despite advances in therapeutic interventions. One aspect responsible for this low survival rate

is that most tumors are still diagnosed late, when the disease is at an advanced stage^{2,12}. This contributes to low five-year survival rates and demands more aggressive treatments^{2,8,9,13}.

In addition to the late-stage diagnosis, prognoses depend on histopathological grade, exposure to risk factors, patient age and type of treatment¹⁴. The aim of this study was to evaluate the sociodemographic profile and oral health of patients with HNSCC and determine the clinical and histopathological characteristic of the tumor at the time of diagnosis.

METHODOLOGY

Study sample

This study recruited 78 patients seen in the Head and Neck Surgery Clinic (Otolaryngology Department) of Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, Brazil. All participants were recruited during the period of October 2009 to October 2010. Men and women were included in the study if they were 18 years or older, had a primary diagnosis of head and neck squamous cell carcinoma, without any previous treatment.

Interview

Subjects who consented to participate were informed of the objective and methods of the study and signed

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a document of terms of informed consent approved by the Ethics in Research Committee of HCPA (Protocol number: 09-315). The patients were interviewed using a structured questionnaire to collect sociodemographic and behavioral data, such as sex, age, skin color, marital status and education, as well as oral hygiene habits, smoking, alcohol consumption, perception of oral health, socioeconomic status and medical and dental history.

Oral health

An intraoral examination collected data about the presence of prostheses and dental conditions. Records included the presence of full or partial removable prosthesis on the maxillary, mandibular, or both arches. The prevalence of dental caries and the number of missing teeth were recorded using the Decayed, Missing, Filled Teeth (DMFT) index, as recommended by the World Health Organization¹⁵.

Tumor characteristics

Hospital records were reviewed to collect information about clinical tumor features, such as pTNM¹⁶ and the treatment protocol used. Two years after the beginning of the study, the medical charts of participating patients were reviewed.

Histopathological grade

Histopathological tumor grade was defined by two pathologists (A.C. and L.H.) using hematoxylin-eosin (HE) stained slides according to the criteria described by Bryne et al.¹⁷. Reproducibility was confirmed along the study: after each 20 slides were examined, one slide was chosen randomly to be re-examined 7 days later ($kappa > 0.7$).

Statistical analysis

Age was categorized in three age individuals groups (< 50, 50-59 and ≥ 60 years). Skin color was defined as "white" or "non-white" since the study population included only a small percentage of patients in other racial or ethnic group. Economic status was assessed using the Brazilian Criterion of Economic Evaluation (CCEB)¹⁸ and was categorized into high and low strata using the median of CCEB scores. Education was classified into three categories according to number of years: ≤ 4 , 5-8 and ≥ 9 years.

Lifetime exposure to cigarette smoking was calculated for current and formers smokers combined. Pack-years of smoking was calculated by multiplying the number of packs of cigarettes consumed per day by the number of years of habit. Smoking exposure was categorized according to tertiles of pack-years into never smoked (0 pack-years), light (1-887 pack-years), moderate (888-18250 pack-years) and heavy smokers (> 18250 pack-years).

Daily alcohol consumption was calculated by multiplying the number of drinks consumed in one week by the average content of pure alcohol by volume in a glass of beer, wine or cachaça (typical Brazilian distilled spirit produced from sugar cane) divided by 7 days. The amount of pure alcohol by volume was estimated at 10 ml for a glass of beer (200 ml; 5% alcohol), 12 ml for a glass of wine (100 ml per glass; 12% alcohol) and 10 ml for a shot of cachaça (25 ml per shot; 40% alcohol). To derive the amount of alcohol in grams, pure alcohol by volume was converted to pure alcohol by weight using the standard conversion factor of 0.8. Thus, one glass of beer has 8 g pure ethanol, a glass of wine, 9.6 g, and a shot of cachaça, 8 g. Subjects were categorized according to tertiles of the distribution of daily alcohol consumption into never drank (0 g/day), light (1-8.5 g/day), moderate (8.6-32 g/day) and heavy (> 32 g/day).

Data analysis was performed by STATA software (Stata 10 for Macintosh, Stata Corporation, College Station, TX, USA). Descriptive statistics were reported for each variable. For categorical variables, the number and percentage of subjects are reported. Means and standard deviations (SD) are reported for continuous variables.

RESULTS

Mean patient age was 57.6 years (37 to 78 years) and most were male (80.8%), white (83.3%), current or former smokers (94.8%) and had a history of moderate to high alcohol consumption (82%). Other common characteristics were low socioeconomic status (56.4%), low educational level (80.8%) and interval from last dental visit greater than one year (66.7%). The most frequent treatment for head and neck squamous cell carcinoma was surgery with or without radiotherapy (83.6%). The majority of patients were disease-free at 2 year-follow up. Other data about the patients included in the study are shown in Table 1.

Table 2 describes the oral health of participants according to caries prevalence, missing teeth and prostheses. Oral examination showed that 65.4% of the patients had some type of prosthesis. About one-fourth of the participants were fully edentulous. Mean number of missing teeth in the whole sample was about 17 teeth. In the subgroup of dentate patients, 10.7 teeth were decayed, missing or filled teeth.

According to tumor size, 60.2% of the cases were classified as T1 and T2, whereas 39.7% were T3 and T4. Some degree of regional involvement was found in 42.4% of the cases, and no regional involvement, in 59%. Most tumors were found in the mouth (73%), and the tongue was the most frequent site (26.9%). According to histopathological grade, 57.7% of the tumors were classified as moderate and poor prognosis (Table 3).

Table 1. Sociodemographic profile, clinical behavior, oncologic treatment and findings at 2- year follow-up.

Variable	n	%	Variable	n	%
Age			Smoking status		
Mean age	57.6		Current	37	47.4
< 50 years	20	25.6	Former	37	47.4
50-59 years	21	26.9	Never smoked	4	5.12
≥ 60 years	37	47.4	Smoking exposure		
Sex			Never smoked	4	5.1
Female	15	19.2	Mild	21	27
Male	63	80.8	Moderate	24	30.8
Skin color			Severe	29	37.2
White	65	83.3	Alcohol consumption		
Non-white	13	16.7	Never drank	5	6.4
Marital status			Mild	9	11.5
Married	48	61.5	Moderate	27	34.6
Single/divorced	19	24.4	Severe	37	47.4
Widowed	11	14.1	Oncologic treatment		
Socioeconomic status			Surgery	43	57.3
High	34	43.6	Surgery + radiotherapy	20	26.3
Low	44	56.4	Radiotherapy	4	5.3
Educational level			Surgery + radiotherapy + chemotherapy	4	5.3
High	15	19.2	Radiotherapy + chemotherapy	4	5.3
Medium	28	35.9	No treatment	3	3.8
Low	35	44.9	Follow-up (2 years)		
Brushing frequency			Disease-free	54	69.2
< 1 once/day	39	39	Recurrence	15	19.2
≥ 1 once/day	50	50	Metastasis	2	2.6
Mouthwash use			Death	4	5.1
Yes	21	26.9	No data	3	3.8
No	57	73.1	Total		
Dental visit			Total	78	100.0
< 1 year	26	33.3			
≥ 1 year	52	66.7			
Total	78	100.0			

Table 2. Prosthesis and oral health.

Variable	Estimates
Prosthesis (n/%)	
No	27 (34.6)
Maxillary arch	34 (43.6)
Mandibular arch	1 (1.3)
Maxillary and mandibular arch	16 (20.5)
Edentulous (n/%)	
Yes	20 (25.6)
No	58 (74.4)
Missing teeth (mean ± SD)	17.1 ± 9.7
Caries prevalence (mean ± SD)	
DMFT	10.7 ± 9.1
DFT	2.9 ± 2.9

DMFT: Decayed/Missing/Filled Teeth; DFT: Decayed/Filled Teeth

DISCUSSION

In the Brazilian population, HNSCC is the seventh most common type of cancer, and the distribution of new cases is heterogeneous in the states and capital cities. The southeastern and southern regions, particularly the cities of São Paulo and Porto Alegre, have the highest incidence rates².

Although there is a new tendency to occur more often in patients below the age of 40 years and male-female ratio decrease, HNSCC is still more often found in men older than 50 years^{2,12,19}. In our study, no change in the mean age and sex of the patients with HNSCC was observed.

The association between oral cancer and the combined exposure to tobacco and alcohol can be observed by

Table 3. Clinical and histopathological characteristics of the tumors.

Variable	n	%
Size		
T1	22	28.2
T2	25	32.0
T3	14	17.9
T4	17	21.8
Regional involvement		
N0	46	59.0
N1	20	27.0
N2	7	9.0
N3	5	6.4
Metastasis		
M0	78	100.0
Site		
Tongue	21	26.9
Floor of the mouth	10	12.8
Lip	10	12.8
Palate	11	14.1
Buccal mucosa	5	6.4
Neck	21	27.0
Histopathological grade:		
Not staged	12	15.4
<i>In situ</i>	5	6.4
Good	8	10.2
Moderate	18	23.1
Poor	27	34.6
No data	8	10.2
Total	78	100.0

the proportion of patients exposed to these two risk factors in our study. Alcohol enhances mucosa permeability and facilitates the penetration of carcinogenic substances found in tobacco³. Although the prevalence of smoking among the Brazilian adult population has decreased²⁰, the majority of the patients examined in this study were current or former smokers. The decline in smoking rates does not seem to have already affected the incidence of HNSCC, which may occur in the next decades.

The rate of current and former smokers was similar, according to studies that suggest the damaging effects of tobacco are cumulative³⁻⁴, and that former smokers should also be considered at risk of developing this tumor.

The most frequent sites of HNSCC in the mouth are the tongue, floor of the mouth and lower lip^{8-9,13}. In this study, the most frequent site was the tongue, followed by the palate, floor of the mouth and lower lip. The high incidence of tumors in the palate may be explained by

the association of this anatomic region with the tumors that affect the oropharynx and extend towards the mouth.

The treatment protocols for HNSCC are surgery, radiotherapy and chemotherapy, and all have undergone significant advances¹³. The combination of surgery and radiotherapy results in the highest five-year survival rates⁷. As recommended in the literature, the most frequent treatment in this study was surgery with or without radiotherapy¹³. The follow-up at 2 years showed that over half of the patients were free of the disease, which suggests that the treatment protocol was an appropriated option for HNSCC.

Other common characteristics in this sample were the low socioeconomic status and the limited years of schooling. Low socioeconomic status has been described as a risk factor for the development of HNSCC, but there is no consensus as to the exact reasons for this influence in tumor development, though most experts agree that lower cancer screening rates and a later stage of diagnosis are prominent factors^{6,8,10}. Besides, patient profiles seem to be the same in poor and developing countries, as well as in developed countries⁸.

According to some authors, there is a significant association between lack of dental care and oral cancer development^{9,21}. In our study, caries prevalence was low and mean overall DMFT (10.7) was lower than that found in other groups of Brazilians of similar age (16.3)²². The number of missing teeth in this study was similar to that found in a study of a population in the same region of Brazil²³. This result suggests that lack of dental caries is not related to oral cancer development.

The histopathological grade defines tumor behavior, which affects patient prognosis because undifferentiated tumors have a higher rate of recurrence and development of metastases¹⁷. Most cases in this study had a histopathological classification as moderate and poor prognosis, but more than half of patients were free of the disease at 2-year follow up. This shows that tumor cell population is heterogeneous, and that the tumors clinical behavior cannot be determined using only one isolated parameter; rather, it should be defined according to the sum of clinical and histopathological parameters.

Detection of HNSCC during a non-symptom-driven examination has proved an association to lower stage at diagnosis, in the same way as patients with a regular primary care dentist is significantly more likely to be diagnosed at early stages²⁴⁻²⁵. However, in our study, most participants reported an interval of over one year since their last dental visit and yet the majority of the diagnoses were made at an early-stage of the disease. Therefore, the number of dental visits does not necessarily determine an early-stage diagnosis of the tumor.

Detecting HNSCC at an early stage, when lesions are small, seems to be the most effective means to reduce

death, morbidity and disfigurement from this disease²⁴⁻²⁶. However, HNSCC is painless and asymptomatic in the early stages and prompts the patient's self-referral only when symptoms develop, resulting in late-stages²⁵. At the late stages of the disease, tumors are larger and present regional involvement, which indicates a poor prognosis^{2,14}. In our study, many patients were staged T1N0, this result was the same found in other research studies²⁶. The explanation for this observation may be due an improvement in the training of healthcare professionals to diagnose these lesions, self-examination instructions and improved access to reference healthcare services.

Our results emphasize that, in a reference hospital in southern Brazil, the profile of patients with HNSCC was similar to that found in other populations, but there is a decline in clinical stage at the time of diagnosis, and that detecting this tumor at an early stage can be an effective mean to determine a better prognosis for patients.

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