

Risk factors for oral squamous cell carcinoma in young and older Brazilian patients: A comparative analysis

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Abstract

Objectives. The aim of this study was to investigate risk factors and clinical aspects associated with oral squamous cell carcinoma (OSCC) in young patients as compared to older ones.

Study design. Data was obtained by retrospective analysis of files of patients with OSCC, who were categorised into two groups: the young group (≤ 40 years old) and the older group (> 40 years old). Clinical data, including habits, familial antecedents, medical records and occupation were collected.

Results. One hundred and twenty-one patients were found to have OSCC; 13 (10.7%) were young individuals and 108 (89.3%) older ones. Consumption of tobacco and/or alcohol was reported by 7 (53.8%) young patients and by 81 (75.0%) older patients, this difference not being statistically significant ($P = 0.18$). However, only 1 young patient (12.5%) was a heavy consumer of tobacco and alcohol as opposed to 49 (60.5%) of the older patients. Familial antecedents of malignant neoplasm were reported by 11 (84.6%) young patients and 32 (29.6%) older ones respectively, this difference being statistically significant ($P = 0.0001$). Medical records and patient's occupation did not show correlation with the aetiology of OSCC.

Conclusion. Although the young and older patients share a similar habit for the consumption of tobacco and/or alcohol, the pattern of consumption and time of exposure to these two risk factors suggested that these etiologic factors are less clearly implicated in the development of oral cancer in the young patients than in older ones. Thus, for young patients with OSCC, the search for predisposing factors should assign greater weight to familial antecedents of malignant neoplasm.

Key words: Oral squamous cell carcinoma, young patients, older patients, risk factors.

Introduction

Oral squamous cell carcinoma (OSCC) typically occurs in elderly men during the fifth through eighth decades of life, and is strongly associated with tobacco and alcohol abuse (1,2). This disease is rare in patients aged 40 years or younger. Several studies indicate that the incidence of OSCC in young adults accounts for 0.4 to 3.6% of all cases of this disease (3-5).

Investigation of the etiologic factors implicated in the development of OSCC in young patients has been of great importance. While in older patients OSCC is commonly associated with prolonged consumption of tobacco and alcohol, in younger patients (≤ 40 years old) the implication of these risk factors is not well established. Some authors (4-8) consider that young patients with OSCC are exposed to the same known risk factors, i.e., tobacco and alcohol,

while others argue that many of the patients in their studies had never smoked or had the habit of consuming alcohol and, moreover, that for patients under 40 years of age their exposure to these carcinogens would be too short to induce oral carcinogenesis (3,9).

The present study compared clinical data of young versus older patients with OSCC, focusing mainly on whether the question of habits and familial antecedents of malignant neoplasm play any role as risk factors for these two groups of patients.

Materials and Methods

This study was carried out by retrospective analysis of files of patients who attended the Clinic of Oral Diagnosis, School of Dentistry, University of São Paulo, between 1994 and 2004. The patients were categorised into two groups: the young group, composed of patients aged 40 and under, and the older group, composed of patients older than 40 years. Only patients with biopsy-proven OSCC were included. This study was approved by the Committee on Ethics of the University of São Paulo.

Data collected for analysis included age, sex, race, habits (tobacco and alcohol consumption), occupation, medical records and familial antecedents of neoplasm. Clinical characteristics of the lesions were also analysed, including the site, duration time, and presence of pain. Smoking was considered heavy, moderate or light depending on the number of cigarettes consumed per day; more than 20 cigarettes was considered heavy, 11 to 20 cigarettes moderate and 1 to 10 light. Alcohol consumption was quantified according to the gram (g) content of alcohol for a can of beer (350 ml), a glass of wine (150 ml) and a measure of distilled liquor (36 ml), which was assumed to be 14 g, 14.4 g and 14.4 g, respectively. A consumption of over 84 g of alcohol per day was considered heavy, from 42 g to 84 g per day moderate, and up to 42 g per day light. Statistical analysis was performed using Chi-square and Fischer's exact test. Significance was set at $P < 0.05$.

Results

One hundred and twenty-one patients were found to have OSCC. Of these, 13 (10.7%) were young patients (mean age 33.6, range 20–40; male/female 1.6:1) and the remaining 108 (89.3%) were older individuals (mean age 57.5, range 41–88; male/female 3.2:1). When the two groups were compared, no statistical difference was found between their male/female ratios ($P = 0.31$). Among the older patients, there were more who habitually consumed tobacco and/or alcohol (81; 75%) than those who did not (27; 25%). Among the younger patients, the number of those who habitually consumed tobacco and/or alcohol (7; 53.8%) was similar to that of those who did not (6; 46.2%). However, there was no statistical difference between the two groups in regard to tobacco and/or alcohol consumption ($P = 0.18$). Table 1 summarises these data.

Analysis of the pattern of tobacco and/or alcohol consumption revealed that only 1 (12.5%) young male patient was a heavy smoker and drinker. The other young patients (6 cases; 92.3%), were light-to-moderate consumers of tobacco or alcohol, or of both. In the older group, of the 24 patients who were habitual users only of tobacco (non-drinkers), 15 (62.5%) were heavy smokers while of the 57 patients who habitually smoked and drank, 49 (60.5%) were heavy consumers. None of the older patients were habitual consumers of only alcohol. In terms of gender, among the younger group the habitual consumption of tobacco or alcohol, or both, was much more prevalent in male patients (75%) than in female patients (20%), although the difference was not statistically significant ($P = 0.10$). Among the older patients, the difference in the rates of habitual consumption of tobacco or alcohol, or of both, between men (79%) and women (61.5%), was not so great and was also statistically non-significant ($P = 0.11$).

The main site of OSCC in both groups was the lateral border of the tongue, with 10 cases (76.9%) in young patients and 28 (25.9%) in older patients, this difference being statistically significant ($P = 0.0004$). The floor of the mouth was also a site frequently affected in older patients (25 individuals; 23.1%). Approximately 62.0% of the young patients and 44.0% of the older patients reported that the lesion had existed for at least 2 months prior to the time of consultation. Presence of the lesion for more than 7 months was reported by 4 (30.7%) young patients and 28 (25.9%) older ones. Pain was reported by 8 (61.5%) young patients and 80 older patients (74.1%). These data are summarised in Table 2.

Analysis of the medical records of the younger group did not reveal any disease in particular that could predispose for the development of OSCC. However, 2 older patients with lip squamous cell carcinoma had been previously affected by skin cancer. Among the younger patients, there was 1 case reported for each of the diseases hypertension and diabetes. In the older patients, hypertension (28 cases; 25.9%), cardiac disease (12 cases; 11.1%) and pneumonia (7 cases; 6.5%) were the main diseases found. In neither group was any patient taking any kind of medication that could suppress the immune system.

Familial antecedents of malignant neoplasms (any site) were reported respectively by 11 (84.6%) patients of the younger group and 32 (29.6%) of the older group, these data being statistically significant ($P = 0.0001$; Table 3). However, malignant neoplasm in first-degree relatives was reported by only 3 out of these 11 young patients (27.3%), while for the older group this factor was reported by 19 out of the 32 patients (59.4%).

The patient's occupation, as a risk factor, was also analysed. None of the occupations reported seemed to represent a hazardous environment that would constitute a predisposing factor for the development of oral cancer.

Table 1. Clinical profile of patients (n = 121).

Patients				
Characteristics	Young (≤ 40 years) n = 13		Older (> 40 years) n = 108	
	Male (%)	Female (%)	Male (%)	Female (%)
Number	8 (61.5%)	5 (38.5%)	82 (75.9%)	26 (24.1%)
Race				
Caucasian	6 (75%)	3 (60%)	69 (84.1%)	19 (73.1%)
Non-caucasian	2 (25%)	2 (40%)	13 (15.8%)	7 (26.9%)
Habits				
<i>Only tobacco</i>				
Light	2 (25.0%)	None	None	3 (11.5%)
Moderate	1 (12.5%)	None	1 (1.2%)	5 (19.2%)
Heavy	None	None	13 (15.8%)	2 (11.5%)
<i>Only alcohol</i>				
Light	None	1 (20.0%)	None	None
<i>Tobacco + alcohol</i>				
Light	None	None	3 (3.7%)	None
Moderate	2 (25.0%)	None	None	5 (19.2%)
Heavy	1 (12.5%)	None	48 (58.5%)	1 (3.8%)
<i>Never</i>	2 (25.0%)	4 (80%)	17 (20.7%)	10 (38.5%)

n = number of patients

Test for statistical differences between the two groups (young versus older):

Male/female ratio: nonsignificant: Fisher's exact test, 2-tailed, P = 0.31

Habit of tobacco and/or alcohol: nonsignificant: Fisher's exact test, 2-tailed, P = 0.18

Test for differential consumption by gender:

Older patients: nonsignificant: Chi-square with Yate's correction, P = 0.11

Younger patients: nonsignificant: Fisher's exact test, 2-tailed, P = 0.10

Table 2. Clinical characteristics of OSCC.

Clinical characteristics	Patient group	
	Young: ≤ 40 years (%)	Older: > 40 years (%)
Site		
Tongue*	10 (76.9)	28 (25.9)
Floor of the mouth	1 (7.7)	25 (23.1)
Lower lip	1 (7.7)	12 (11.1)
Palate	1 (7.7)	11 (10.2)
Retromolar trigone	–	11 (10.2)
Alveolar ridge (lower)	–	10 (9.2)
Alveolar ridge (upper)	–	9 (8.3)
Buccal mucosa	–	2 (1.8)
Duration time (months)		
1–2	8 (61.5)	47 (43.5)
3–4	–	17 (15.7)
5–6	1 (7.7)	16 (14.8)
7–8	–	10 (9.3)
9–12	3 (23.1)	12 (11.1)
13–16	1 (7.7)	6 (5.5)
Presence of pain		
Positive	8 (61.5)	80 (74.1)
Negative	5 (38.5)	28 (25.9)

*Significant: Fischer's exact test, 2-tailed, P = 0.0004

Table 3. Familial antecedents of malignant neoplasm.

Sites	Relatives with Malignant neoplasm	
	Young: ≤ 40 years (%)	Older: > 40 years (%)
Breast	1 (7.7)	12 (11.1)
Intestine	2 (15.4)	8 (7.4)
Prostate	1 (7.7)	4 (3.7)
Stomach	–	3 (2.7)
Oropharynx	–	3 (2.7)
Liver	–	3 (2.7)
Esophagus	–	2 (1.8)
Lung	5 (38.5)	2 (1.8)
Brain	1 (7.7)	1 (0.9)
Bone	–	1 (0.9)
Pancreas	–	1 (0.9)
Skin	2 (15.4)	1 (0.9)
Kidney	–	1 (0.9)
Thyroid	–	1 (0.9)
Uterus	4 (30.8)	1 (0.9)
Mouth	1 (7.7)	–
Ovarian	1 (7.7)	–

Rate of young patients with familial antecedents for malignant neoplasm was 11(84.6%) out of 13

Rate of older patients with familial antecedents for malignant neoplasm was 32 (29.6%) out of 108

The difference between the rates was statistically significant; Fischer's exact test, 2-tailed, P = 0.0001

Discussion

This study confirms that OSCC affects predominantly older patients (89.3%); however, there was a much higher incidence of this disease in the young patients (10.7%) than that reported by other authors, which has varied from 0.4 to 3.6% (3,5,7,10,11).

By and large, the cause of OSCC is complex and multifactorial, and for young patients the cause of OSCC seems to present a different pattern from that found in older patients. As a result, many authors have investigated some risk factors for OSCC in young subjects (8-18). This was also the focus of the present study.

No statistical difference was found between the older and younger patients in regard to being a habitual consumer of tobacco and/or alcohol or not. Therefore, the higher occurrence of OSCC in patients over 40 years old seemed to be due to a longer exposure and heavier consumption of tobacco and/or alcohol than to the habit itself. Although men and women in the older group were almost equally exposed to tobacco and/or alcohol (79.3% men versus 61.5% women), men were more prone (58.5% versus 3.8% for women) to consume tobacco and alcohol heavily, which

might explain the predominance of OSCC in older male patients. These data are in agreement with those found in similar studies (1,19).

Contrary to what was found in respect to the older patients, in whom OSCC was associated predominantly with smoking and/or drinking, for the younger ones the occurrence of OSCC was almost equally distributed among those who were smokers and/or drinkers as compared to those who were not. Although in respect to the consumption of tobacco and/or alcohol no statistical difference was found between young male and female patients, the young male patients – like the older males – were more prone to consume these substances. These data are in agreement with the results of other studies (5,6,13).

Another important finding was that, in the younger patients, the disease occurred with great frequency along the lateral border of the tongue (76.9%), whereas in the older patients this site was affected in only 25.9% of cases. Neither in the present study, nor in others, any factor associated with the predominance of OSCC in the tongue of the young patients could be identified (2,6,8,20-23).

Other risk factors which have been investigated by other authors in patients with OSCC were viral agents (HPV, HSV) (24,25), type of diet (5,26), work environment (12), immunosuppressing drugs (27), Fanconi's anemia (28), and genetic antecedents (familial) (29,30). These investigations, however, did not indicate any consistent link between the risk factors studied and the development of OSCC in young patients.

In the present study, data concerning medical records, use of medication, occupation and familial antecedents of malignancy were analysed in both groups. The analysis revealed that the only factor found to be statistically correlated with OSCC in young patients was familial antecedents of malignant neoplasm.

When investigating familial antecedents of cancer, it is important to analyse whether relatives with malignant neoplasm had any exposure to carcinogenic factors, especially tobacco and alcohol (15). Most of the studies have failed to investigate environmental factors that could be responsible for malignant neoplasm among relatives and descendants. In light of the hereditary nature of carcinogenesis, it is important to analyse sites of occurrence of cancer in parents and offspring (29,30). Large-scale studies are also essential to correlate the frequency of malignant diseases in patients and their relatives.

In the present study, data concerning habits of smoking and/or alcohol consumption among the relatives of both groups were not available because such information was not adequately detailed in the files. In terms of sites, only 1 case in the young group had a relative (a father) with history of OSCC, the other cases with malignancy in relatives involved sites other than the oral mucosa. Also, the number of young patients in this study was not large enough to provide conclusive information in respect to

familial antecedents as an aetiological factor in the occurrence of OSCC in the young patients.

While one must remain aware of these foregoing considerations, the high rate (84.6%) of positive familial history for malignant neoplasm in these young patients (compared to 29.6% in older patients) does appear significant. Such a relationship would presumably be due to the fact that this risk factor carries great weight for young patients since the other risk factors (mainly habitual alcohol and tobacco use) require relatively long periods of exposure.

References

- Chen YK, Huang HC, Lin LM, Lin CC. Primary oral squamous cell carcinoma: an analysis of 703 cases in southern Taiwan. *Oral Oncol.* 1999 Mar;35(2):173-9.
- Martínez-Conde R, Aguirre JM, Burgos JJ, Rivera JM. Clinicopathological factors in early squamous cell carcinoma of the tongue and floor of the mouth, in Biscay (the Basque Country, Spain). *Med Oral.* 2001 Mar-Apr;6(2):87-94.
- Cusumano RJ, Persky MS. Squamous cell carcinoma of the oral cavity and oropharynx in young adults. *Head Neck Surg.* 1988 Mar-Apr;10(4):229-34.
- Friedlander PL, Schantz SP, Shaha AR, Yu G, Shah JP. Squamous cell carcinoma of the tongue in young patients: a matched-pair analysis. *Head Neck.* 1998 Aug;20(5):363-8.
- Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for squamous cell carcinoma of the oral cavity in young people--a comprehensive literature review. *Oral Oncol.* 2001 Jul;37(5):401-18.
- McGregor AD, Rennie JS. Intra-oral squamous cell carcinoma in patients under 40 years of age. A report of 13 cases and review of the literature. *Br J Plast Surg.* 1987 May;40(3):270-3.
- Burzynski NJ, Flynn MB, Faller NM, Ragsdale TL. Squamous cell carcinoma of the upper aerodigestive tract in patients 40 years of age and younger. *Oral Surg Oral Med Oral Pathol.* 1992 Sep;74(3):404-8.
- Mackenzie J, Ah-See K, Thakker N, Sloan P, Maran AG, Birch J, et al. Increasing incidence of oral cancer amongst young persons: what is the aetiology? *Oral Oncol.* 2000 Jul;36(4):387-9.
- Sankaranarayanan R, Mohideen MN, Nair MK, Padmanabhan TK. Aetiology of oral cancer in patients less than or equal to 30 years of age. *Br J Cancer.* 1989 Mar;59(3):439-40.
- Sarkaria JN, Harari PM. Oral tongue cancer in young adults less than 40 years of age: rationale for aggressive therapy. *Head Neck.* 1994 Mar-Apr;16(2):107-11.
- Atula S, Grénman R, Laippala P, Syrjänen S. Cancer of the tongue in patients younger than 40 years. A distinct entity? *Arch Otolaryngol Head Neck Surg.* 1996 Dec;122(12):1313-9.
- Coble JB, Brown LM, Hayes RB, Huang WY, Winn DM, Gridley G, et al. Sugarcane farming, occupational solvent exposures, and the risk of oral cancer in Puerto Rico. *J Occup Environ Med.* 2003 Aug;45(8):869-74.
- Llewellyn CD, Linklater K, Bell J, Johnson NW, Warnakulasuriya S. An analysis of risk factors for oral cancer in young people: a case-control study. *Oral Oncol.* 2004 Mar;40(3):304-13.
- McKaig RG, Baric RS, Olshan AF. Human papillomavirus and head and neck cancer: epidemiology and molecular biology. *Head Neck.* 1998 May;20(3):250-65.
- Ankathil R, Mathew A, Joseph F, Nair MK. Is oral cancer susceptibility inherited? Report of five oral cancer families. *Eur J Cancer B Oral Oncol.* 1996 Jan;32B(1):63-7.
- Schantz SP, Byers RM, Goepfert H, Shallenberger RC, Beddingfield N. The implication of tobacco use in the young adult with head and neck cancer. *Cancer.* 1988 Oct 1;62(7):1374-80.
- Smith EM, Hoffman HT, Summersgill KS, Kirchner HL, Turek LP, Haugen TH. Human papillomavirus and risk of oral cancer. *Laryngoscope.* 1998 Jul;108(7):1098-103.
- Thomas DW, Seddon SV, Shepherd JP. Systemic immunosuppression and oral malignancy: a report of a case and review of the literature. *Br J Oral Maxillofac Surg.* 1993 Dec;31(6):391-3.
- Siriwardena BS, Tilakaratne A, Amaratunga EA, Udagama MN, Ogawa I, Kudo Y, et al. Analysis of histopathological and immunohistochemical differences of oral squamous cell carcinoma in young and old patients in Sri Lanka. *J Oral Pathol Med.* 2007 Jul;36(6):357-62.
- O'Regan EM, Timon C, Sheils O, Codd M, O'Leary JJ, Toner M. Squamous cell carcinoma of the head and neck in young Irish adults. *Br J Oral Maxillofac Surg.* 2006 Jun;44(3):203-6.
- Iype EM, Pandey M, Mathew A, Thomas G, Sebastian P, Nair MK. Oral cancer among patients under the age of 35 years. *J Postgrad Med.* 2001 Jul-Sep;47(3):171-6.
- Jin YT, Myers J, Tsai ST, Goepfert H, Batsakis JG, El-Naggar AK. Genetic alterations in oral squamous cell carcinoma of young adults. *Oral Oncol.* 1999 May;35(3):251-6.
- Amsterdam JT, Strawitz JG. Squamous cell carcinoma of the oral cavity in young adults. *J Surg Oncol.* 1982 Feb;19(2):65-8.
- Scully C. Oral cancer; the evidence for sexual transmission. *Br Dent J.* 2005 Aug 27;199(4):203-7.
- Das CM, Schantz SP, Shillitoe EJ. Antibody to a mutagenic peptide of herpes simplex virus in young adult patients with cancer of the head and neck. *Oral Surg Oral Med Oral Pathol.* 1993 May;75(5):610-4.
- Steinmetz KA, Potter JD. Vegetables, fruit, and cancer prevention: a review. *J Am Diet Assoc.* 1996 Oct;96(10):1027-39.
- Fortina AB, Piaserico S, Caforio AL, Abeni D, Alaibac M, Angelini A, et al. Immunosuppressive level and other risk factors for basal cell carcinoma and squamous cell carcinoma in heart transplant recipients. *Arch Dermatol.* 2004 Sep;140(9):1079-85.
- Kaplan MJ, Sabio H, Wanebo HJ, Cantrell RW. Squamous cell carcinoma in the immunosuppressed patient: Fanconi's anemia. *Laryngoscope.* 1985 Jul;95(7 Pt 1):771-5.
- Foulkes WD, Brunet JS, Kowalski LP, Narod SA, Franco EL. Family history of cancer is a risk factor for squamous cell carcinoma of the head and neck in Brazil: a case-control study. *Int J Cancer.* 1995 Dec 11;63(6):769-73.
- Foulkes WD, Brunet JS, Sieh W, Black MJ, Shenouda G, Narod SA. Familial risks of squamous cell carcinoma of the head and neck: retrospective case-control study. *BMJ.* 1996 Sep 21;313(7059):716-21.