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Oral squamous cell carcinoma: an analysis of 1,564 cases showing advances in early detection

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Abstract: The present study aimed to detect possible differences in the data of oral squamous cell carcinomas (OSCC) cases diagnosed in a Dental School in São Paulo city over the last 40 years. The records of patients diagnosed as having OSCC between the years 1960 and 2008 were retrieved. The whole period was divided into four time periods. A total of 1,564 cases were reviewed. The variables analyzed were: sex, age, race, anatomical site, lesion duration, and lesion size. The chi-square test was used for statistical analysis. Overall, males were more affected than females (3:1), but when comparing the first and last time periods, the ratio decreased significantly (5.8:1 to 2.8:1). A significant increase in the rate of OSCC in patients over 80 years was observed in the last time periods. The gingiva was the most affected site, but the frequency of lower lip involvement increased in the last time period. Regarding lesion size and duration of symptoms at the time of diagnosis, there was a significant difference between the first and last time periods. Smaller lesions were found and the time of lesion development was shorter in the last few years of the study. These findings support the optimistic view that, in recent years, earlier diagnosis has resulted from early oral cancer detection in São Paulo city. (J Oral Sci 52, 267-273, 2010)

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Introduction

Oral cancer ranks from the sixth to eighth most common cancer around the world, with a great variability in incidence among countries (1). This incidence varies in the most and the least developed regions: 65,000 and 111,000 for male patients (2), respectively. The highest male age-standardized incidences (per 100,000 habitants) are present in Melanesia (31.5) (2). In South America, Brazil has the highest incidence (8.3 per 100,000 habitants) (3).

In Brazil, when only men are considered, oral cancer is the sixth most common neoplasm, representing 2.6% of all malignancies, and it is the ninth most lethal cancer (3). The highest incidence of oral cancer in Brazil is found in the population of the southeastern and southern regions in low-income areas (4,5). Among these regions, the highest incidence rate is found in the city of São Paulo (25.3 per 100,000) (4).

OSCC accounts for about 90% of oral cancers, and affects mostly adult males, predominantly alcohol and tobacco users, between the sixth and seventh decades of life (3). The most affected sites in decreasing order are the tongue, oropharynx, lip, floor of mouth, gingiva, hard palate, and buccal mucosa (3-7). Small lesions are often asymptomatic or may present with vague symptoms. On the other hand, locally advanced lesions usually present with pain, halitosis, and difficulty with speaking, swallowing, and chewing (3,6-10).

Presenting case data from locations with high oral cancer incidence, such as São Paulo city, is important in order to identify the most prevalent risk factors. The identification of these risk factors in various populations can bring more directed research funding to the development of health initiatives (9).

Therefore, in the present study, data of OSSC cases diagnosed in São Paulo, Brazil, over a 48-year period, from 1961 to 2008, were evaluated with the aim of detecting possible differences in a chronological perspective, and also to compare to the current results in the world literature.

Materials and Methods

From a total of 63,000 records, all cases diagnosed histologically as OSCC were retrieved from the files of the Surgical Oral Pathology Laboratory at the University of São Paulo, Brazil – from 1961 to 2008. Demographic data and clinical aspects of the lesions, as reported in the forms, were analyzed. These data included: sex, race, age, and city of residence of the patient, as well as anatomical site, size (in mm) and duration (in months) of the lesion.

Information was collected and categorized according to the most prevalent variables and organized in a spreadsheet according to the period of the diagnosis: 1961-1980, 1981-1990, 1991-2000, 2001-2008. Due to the small number of cases found in the first two decades, they were considered together (1961-1980). Among races, the item "other races" included a constellation of possible races that represent the ethnic diversity observed in Brazil, where a mixture of different races, White, Black, Asian, and Indian populations are possible. Age was classified in decades until 80 years, with 81 years or more grouped as a single category. The term "lips" was used for lesions of the upper and lower lip and lesions affecting the vermillion border, and the term "tongue" was used for lesions localized in all regions of the tongue, except for the lateral border, which constituted a separate category. The term "two or more associated sites" was used for lesions whose extension involved multiple anatomical sites in the oral cavity. Lesion size was divided into groups according to the most prevalent sizes; lesions of more than 60 mm formed a single group. Duration of lesion (in months) was grouped as 0 to 2, 3 to 6, 7 to 12, and 13 months or more. This variable represented the duration of the symptoms as reported by the patient during the history taken prior to the biopsy. Relative frequency (%) was used for the comparison between the periods and variables.

Statistical tests (Chi-square test and equality of proportions test with Bonferroni correction) were used to verify significant differences in proportions between periods. The frequency of absent data was not considered in the statistical analysis when it exceeded the value of any variable. The software used for this analysis was Microsoft Excel® and SPSS®.

The study was performed in accordance with the ethical principles of the World Medical Association Declaration of Helsinki. The study was independently reviewed and approved by an institutional ethical board (IEB).

Results

A total of 1,564 OSCC cases were collected. Divided into periods, 263 cases were diagnosed between 1961 and 1980, 159 cases between 1981 and 1990, 463 between 1991 and 2000, and 679 between 2001 and 2008. These numbers represented respectively 3.8%, 2.0%, 2.8%, and 2.1% OSCC/total number of biopsies in each period.

Most biopsies (97%) came from dental institutions and hospitals located in São Paulo city. Only 2% of the cases were from other cities of São Paulo State and 1% from other Brazilian states. These biopsies were mostly incisional (98%).

Male patients were more affected in all periods (Table 1), but the ratio of females increased significantly in the last two periods when compared to the 1961-1980 period ($P < 0.001$).

White patients were more affected (74.1%), followed by Blacks (11.0%) and Asians (2.6%) (Table 2). This tendency occurred in all periods. Statistically significant differences were observed when comparing the first period with the third and fourth periods for the three races ($P <$

Table 1 Frequency of OSCC by sex for all surveyed periods

Gender	1960-1980 *n* (%)	1981-1990 *n* (%)	1991-2000 *n* (%)	2001-2008 *n* (%)	Total *n* (%)
Male	220 (83.6)	117 (73.6)	326 (70.4)	495 (72.9)	1158 (74.0)
Female	38[c,d] (14.4)	34 (21.4)	124[a] (26.8)	179[a] (26.3)	375 (24.0)
AD	5 (2.0)	8 (5.0)	13 (2.8)	5 (0.8)	31 (2.0)
Total	263 (100.0)	159 (100.0)	463 (100.0)	679 (100.0)	1564 (100.0)

AD = absent data, Chi-square statistical test, $P < 0.05$, a = significant difference to 1960-1980 period; b = significant difference to 1981-1990 period; c = significant difference to 1991-2000 period; d = significant difference to 2001-2008 period.

Table 2 Frequency of OSCC by race for all surveyed periods

Race	1960-1980 *n* (%)	1981-1990 *n* (%)	1991-2000 *n* (%)	2001-2008 *n* (%)	Total *n* (%)
White	209[c,d] (79.5)	118 (74.2)	335[a] (72.4)	498[a] (73.3)	1160 (74.1)
Black	12[c,d] (4.5)	17 (10.7)	64[a] (13.8)	78[a] (11.5)	171 (11.0)
Yellow	4[c,d] (1.5)	1 (0.6)	15[a] (3.2)	21[a] (3.1)	41 (2.6)
Others	28[c,d] (10.7)	9 (5.6)	11[a,d] (2.4)	33[a,c] (4.9)	81 (5.1)
AD	10 (3.8)	14 (8.9)	38 (8.2)	49 (7.2)	111 (7.2)
Total	263 (100.0)	159 (100.0)	463 (100.0)	679 (100.0)	1564 (100.0)

AD = absent data, Chi-square statistical test, $P < 0.05$. a = significant difference to 1960-1980 period; b = significant difference to 1981-1990 period; c = significant difference to 1991-2000 period; d = significant difference to 2001-2008 period.

Table 3 Frequency of OSCC by age for all surveyed periods

Decades	1960-1980 *n* (%)	1981-1990 *n* (%)	1991-2000 *n* (%)	2001-2008 *n* (%)	Total *n* (%)
1-10	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
11-20	1 (0.4)	1 (0.6)	3 (0.6)	5 (0.7)	10 (0.6)
21-30	7 (2.7)	2 (1.3)	6 (1.3)	7 (1.0)	22 (1.4)
31-40	17 (6.5)	17 (10.7)	33 (7.1)	36 (5.3)	103 (6.6)
41-50	72 (27.4)	31 (19.5)	108 (23.3)	133 (19.6)	344 (22.0)
51-60	79 (30.0)	49 (30.8)	109 (23.5)	184 (27.1)	421 (26.9)
61-70	53 (20.2)	38 (23.9)	107 (23.1)	158 (23.3)	356 (22.8)
71-80	30 (11.4)	15 (9.4)	62 (13.4)	80 (11.8)	187 (12.0)
> 80	2[c,d] (0.8)	4[c,d] (2.5)	28[a,b] (6.0)	42[a,b] (6.2)	76 (4.9)
AD	2 (0.8)	2 (1.3)	7 (1.5)	33 (4.9)	44 (2.8)
Total	263 (100.0)	159 (100.0)	463 (100.0)	679 (100.0)	1564 (100.0)

AD = absent data, Chi-square statistical test, $P < 0.05$, a = significant difference to 1960-1980 period; b = significant difference to 1981-1990 period; c = significant difference to 1991-2000 period; d = significant difference to 2001-2008 period.

Table 4 Frequency of OSCC by anatomical site for each period

Anatomical sites	1960-1980 *n* (%)	1981-1990 *n* (%)	1991-2000 *n* (%)	2001-2008 *n* (%)	Total *n* (%)
Gingiva	74[d] (28.0)	55[c,d] (34.6)	111[b] (24.0)	121[a,b] (17.8)	361 (23.1)
Floor of mouth	36 (13.7)	17 (10.7)	70 (15.1)	105 (15.5)	228 (14.6)
Tongue - lateral border	23[c,d] (8.7)	14[c,d] (8.8)	70[a,b] (15.1)	115[a,b] (16.9)	222 (14.2)
Lips	25[d] (9.5)	10[c,d] (6.3)	55[b,d] (11.7)	123[a,b,c] (18.1)	213 (13.6)
Tongue	16 (6.0)	7 (4.4)	23 (5.0)	52 (7.7)	98 (6.3)
Palate	10[d] (3.8)	11 (6.9)	26 (5.6)	50[a] (7.4)	97 (6.2)
Buccal mucosa	7 (2.8)	9 (5.7)	11 (2.3)	19 (2.8)	46 (2.9)
Association of two or more sites	67[b,c,d] (25.5)	22[a] (13.8)	54[a] (11.6)	66[a] (9.7)	209 (13.4)
Other sites	2 (0.9)	6 (3.8)	14 (3.0)	18 (2.7)	40 (2.6)
AD	3 (1.1)	8 (5.0)	29 (6.6)	10 (1.4)	50 (3.2)
Total	263 (100.0)	159 (100.0)	463 (100.0)	679 (100.0)	1564 (100.0)

AD = absent data, Chi-square statistical test, $P < 0.05$, a = significant difference to 1960-1980 period; b = significant difference to 1981-1990 period; c = significant difference to 1991-2000 period; d = significant difference to 2001-2008 period.

0.001). The category of "other races" also showed significant differences among the four periods.

Most patients were between 50 and 60 years of age in all periods (Table 3). A high proportion of OSCC was also observed in the fifth and seventh decades. Patients 81 years of age or older were found mainly in the last periods, with a frequency of 6.2% ($P < 0.001$).

The gingiva was the most affected OSCC site (23.1%) in all periods (Table 4), mainly involving the retromolar region. Regarding this anatomical site, significant

Table 5 Frequency of OSCC by anatomical site and sex for each period

Site of the lesion	1960-1980 *n* (%)		1981-1990 *n* (%)		1991-2000 *n* (%)		2001-2008 *n* (%)	
	Male	Female	Male	Female	Male	Female	Male	Female
Gingiva	59 (26.8)^{c,d}	11 (28.9)	42 (35.9)^{c,d}	12 (35.3)	79 (25.9)^{a,b}	35 (29.4)	88 (18.0)^{a,b}	42 (23.9)
Floor of mouth	35 (15.9)	7 (18.4)	19 (16.2)	2 (5.9)	71 (23.3)	10 (8.4)	93 (19.1)	16 (9.1)
Tongue- lateral border	20 (9.1)^{d}	2 (5.3)^{c,d}	13 (11.1)	5 (14.7)	59 (19.3)	26 (21.8)^{a}	83 (17.0)^{a}	35 (19.9)^{a}
Lips	24(10.9)^{c,d}	2 (5.3)^{c,d}	13 (11.1)	1 (2.9)^{c,d}	39 (12.8)^{a}	15 (12.6)^{a,b}	88 (18.0)^{a}	32 (18.2)^{a,b}
Tongue	12 (5.5)^{d}	1 (2.6)	3 (2.6)	2 (5.9)	15 (4.9)	9 (7.6)	19 (3.9)^{a}	12 (6.8)
Palate	7 (3.2)	2 (5.3)	3 (2.6)	2 (5.9)	6 (2.0)	6 (5.0)	34 (7.0)	10 (5.7)
Buccal mucosa	4 (1.8)	3 (7.9)	2 (1.7)	3 (8.8)	3 (1.0)	3 (2.5)	24 (4.9)	14 (8.0)
Association of two or more sites	57 (25.9)^{c,d}	9 (23.7)	20 (17.1)	6 (17.6)	30 (9.8)^{a}	13 (10.9)	44 (9.0)^{c}	10 (5.7)
Other sites	2 (0.9)^{b,c}	1 (2.6)	2 (1.7)^{a,d}	1 (2.9)	3 (1.0)^{a}	2 (1.7)	15 (3.1)^{b}	5 (2.8)
TOTAL	220 (100.0)	38 (100.0)	117 (100.0)	34 (100.0)	305 (100.0)	119 (100.0)	488 (100.0)	176 (100.0)

Chi-square statistical test, $P < 0.05$, a = significant difference to 1960-1980 period; b = significant difference to 1981-1990 period; c = significant difference to 1991-2000 period; d = significant difference to 2001-2008 period.

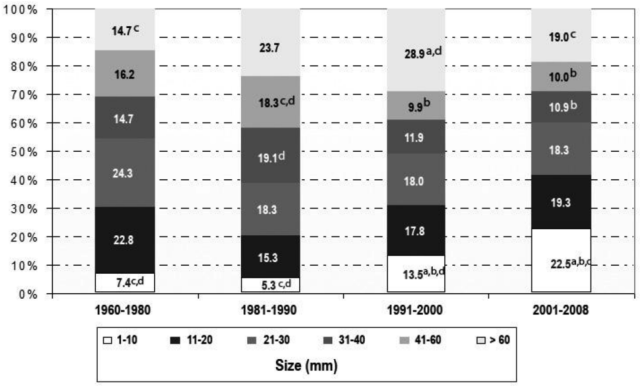

Fig. 1 Bar graph showing size (in mm) of OSCC in all surveyed periods. Chi-square test, $P < 0.05$. a = significant difference compared to 1960-1980 period; b = significant difference compared to 1981-1990 period; c = significant difference compared to 1991-2000 period; d = significant difference compared to 2001-2008 period.

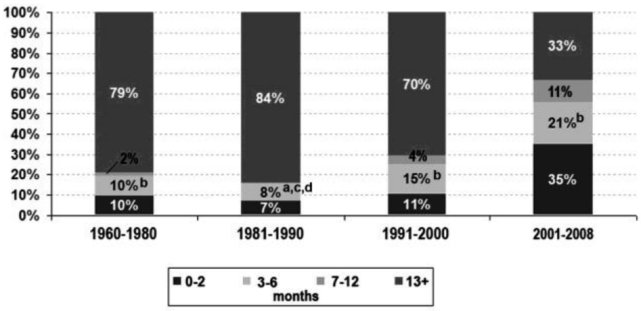

Fig. 2 Bar graph showing duration (in months) of OSCC in all surveyed periods. Chi-square test, $P < 0.05$. a = significant difference compared to 1960-1980 period; b = significant difference compared to 1981-1990 period; c = significant difference compared to 1991-2000 period; d = significant difference compared to 2001-2008 period.

differences were observed in the first two periods when compared to the two last periods ($P < 0.001$). The lateral border of the tongue also showed significant differences between the first two and the last two periods, with a higher frequency in the latest periods ($P < 0.003$). The lower lips also had a significant increase in 2001-2008 in relation to the other periods ($P < 0.001$). The frequency of lesions on the palate was also increased in the last period compared with the first period ($P = 0.034$). Two or more associated anatomical sites (13.4%) occurred with a high frequency in the first period, but it decreased significantly in the last periods ($P < 0.001$). Comparison of sex and anatomical site (Table 5) showed that both men and women had a significant increase in the frequency of lip lesions and in the lateral border of the tongue in the two last periods ($P < 0.001$). In men, two or more associated anatomical sites decreased significantly in the 2001-2008 period compared to 1960-1980 ($P = 0.029$). Considering the frequency of lesions in the gingiva of men, the two last decades showed a significant decrease in relation to the first two periods ($P < 0.040$).

Lesion size was generally between 1 mm and 30 mm. The medium frequency of lesions over 60 mm was high (21.5%) (Fig. 1). However, in the last period, there was a significant increase in the incidence of lesions measuring 1-10 mm (22.5%) compared to the first periods ($P <$

0.001), and a significant decrease of lesions of more than 60 mm compared to the third period ($P = 0.001$).

The duration of symptoms at the time of diagnosis was reported as more than 12 months in most cases in the first three periods, but in the last period, most lesions were present for 3 to 6 months at the time of diagnosis ($P < 0.001$, Fig. 2).

Discussion

During the period of 48 years from 1961 to 2008, 1,564 cases of OSCC were diagnosed at the Surgical Oral Pathology Laboratory in the University of São Paulo. It is important to note that this service belongs to a Dental School, so that most of the biopsies received there were incisional, and the patients, after diagnosis, were sent to different hospitals for treatment. Thus, the aim of the present study, unlike most reported studies, was to identify the profile of OSCC patients when they first seek help. In order to check for possible changes in incidence trends, the whole period was grouped according to decades. Since it was clear that the absolute number of cases increased in the last decades, as did the total number of biopsies, we decided to group the first two decades as a single period.

Taking into account the total number of biopsies in each period, a higher incidence of OSCC was found in the first period (3.8%). The relatively smaller number of OSCC cases in the last three periods could be the result of the increase in the total number of biopsies, because dentists are much more aware of their role as health professionals today, and as a result, they are more careful with their patients and conscious that they can detect oral cancer early. Therefore, more biopsies of oral lesions are performed. Recent studies have presented variable results regarding oral cancer frequency. A decrease or increase in the incidence of head and neck cancer in men and, in general, an increase in woman has been shown. But differences among countries or regions, and in tumor sites (intra-oral, pharynx, larynx or lip) have been observed (10,11). Nonetheless, based on our results, there was a decrease in the relative number of OSCC cases diagnosed at our service in the last decades. However, further epidemiological studies are necessary to confirm this trend, which must focus on the incidence of OSCC in the population of São Paulo city as a whole.

Of the total number of cases, 74% occurred in men (1,158/1,564). This finding of approximately a 3:1 male/female ratio is in agreement with data found around the world for oral cancer incidence (2), and with data from the Brazilian National Cancer Institute (INCA) (3). However, if only the first period of the study is considered, the male to female ratio was 5.8:1, showing a significant increase in the incidence among women in the last two decades. Other studies around the world have also shown an increase in incidence among women in the last decades (4,6,12-16). This increase has been mostly attributed to changes in women's habits such as smoking and alcohol consumption, as well as their increased life expectancy (12,17).

Regarding age, most patients of this study were in the sixth decade of life, which is in accordance with the literature (1,8). A high incidence was also observed in the fifth and seventh decades. Although it is classically postulated that OSCC is a disease of older age, and that aging is a factor that increases its risk (4,6,8,13,17-19), 8.7% of the cases occurred in patients under 40 years, and, as shown in other studies, although in small numbers, cases under 40 years were found in all periods studied (17). Young patients presenting with OSCC have been increasingly noted worldwide since the 1990s, and some studies have shown an increase of these cases only in specific oral sites (17-19). In the present study, patients between 1 and 20 years old were found mainly in the last period. With respect to the third and fourth decades, there was no increase in the incidence of cases in these decades, contrary to other studies that reported a marked increase in OSCC frequency in these ages in the United States and United Kingdom (20).

The present study also showed that the incidence of OSCC in patients over 80 years old increased significantly in the two last periods, a fact that is expected due to an increase in life expectancy in Brazil, especially in São Paulo (21).

Considering race, 74.1% of the cases occurred in Whites, as reported in another study also conducted in São Paulo (12), where the authors state that, to compare the incidence of OSCC among races in Brazil can be a difficult task due to the large amount of miscegenation in the Brazilian population. The present data showed a great predominance of oral cancer among Whites, followed by Blacks and Asians, in all periods studied. There was a significant increase in incidence among Blacks and Asians from the 1990s. This finding could be the result of an increase in the Black and Asian populations in São Paulo over the years due to migration from the northeast of Brazil and from other countries, such as Korea, Japan, and China.

Regarding lesion sites, a greater number of cases occurred in the gingiva, followed by the floor of the mouth, the lateral border of the tongue, and the lips. Most studies (6,8,17) have shown that the tongue is the most prevalent site of OSCC, approximately 45% for the posterior lateral border and 25% for the posterior one-third or base. Some recent surveys have demonstrated a high incidence in the alveolar

ridge, suggesting the effect of factors other than alcohol and tobacco (22,23). It is important to note that the exact site of the lesion can sometimes be confused or classified differently as the base of the tongue or the floor of the mouth (10,17). Despite the absence of standardization in anatomical site description, it was our desire to categorize the different anatomical sites, especially the tongue, where the lateral border was considered separately from the rest of the tongue. Another important tendency observed in this study was the significant increase of cases occurring in the lips in the last two periods, mainly in the lower lip and especially in females. In tropical countries, such as Brazil and Australia, OSCC in this specific anatomical site is associated with solar irradiation (11,13,23,24). Furthermore, in our sample, most patients were White, and lip cancer has a predilection for this race (6,12,13). Some studies have shown the lip as the major site of occurrence of OSCC (25,26). However, even though the incidence of lip cancer is generally high, most lip cases are first seen by physicians and not by dentists, as were most of the cases in the present study. This fact could be responsible for the low incidence of lip OSCC in this study compared to other studies.

The size of the tumor at the moment of the first biopsy was evaluated, and the results were quite variable. The size of the lesion may reflect the social conditions of the population and their ability to obtain healthcare (1,9,13). Although São Paulo has a great social discrepancy, and most patients who seek health care in the Universities or Public hospitals are of a lower socioeconomic status, we observed mostly lesions with a size between 11 to 31 mm or more than 60 mm. In the last years, there was a significant increase in the diagnosis of lesions measuring 1-10 mm (22.5%). This fact, associated with the significant reduction in the duration of the lesion in the same period, can indicate a tendency to earlier detection, which results in a better prognosis.

In conclusion, the present series of OSCC cases showed some important trends for São Paulo city. Although White adults, aged 41 to 60 years, had the highest frequency, a significant increase in the rate of individuals 80 years old or older was observed. Despite the fact that males were more affected, females had a significant increase. The large number of cases occurring in the gingiva can lead to the assumption that factors such as poor oral hygiene can act as coadjutant factors. Further clinical and epidemiologic investigations are needed to confirm these trends. The most important finding in this study was that size and duration of the symptoms at first diagnosis in the last two periods show a tendency to earlier OSCC detection in the studied population.

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