

<http://dx.doi.org/10.4322/2357-9730.72986>

Original Article

HISTOPATHOLOGICAL DIFFERENCES BETWEEN GENDERS IN PATIENTS WITH ORAL SQUAMOUS CELL CARCINOMA

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ABSTRACT

Introduction: Oral cancer ranks fifth among the most frequent malignant tumors in men in Brazil. The incidence of this tumor among women has grown. It is still controversial whether gender can influence the outcome or the prognostic features of the disease.

Objectives: To compare the histopathological features of oral squamous cell carcinomas between genders among patients undergoing surgical treatment in an oncological hospital of southern Brazil.

Methods: Between 2007 and 2011, 404 patients underwent resection of malignant tumors of the oral cavity in the head and neck department of this institution. A subgroup of 209 previously untreated oral cavity squamous cell carcinoma cases was selected for comparative analysis.

Results: In total, 68 participants were women and 141 were men. The tongue was the most common subsite in both genders. Men presented lower mean age and women presented tumors with smaller depth of invasion. Although among women it was observed a trend towards tumors with less aggressive characteristics, no other variable showed statistically significance.

Conclusion: Women with oral tumors tend to present more superficial primary tumors and at a later age.

Keywords: *Oral neoplasms; carcinoma; squamous cell; prognosis*

According to INCA estimates for the biennium 2016-2017¹, oral cavity cancer represents around 3.6% of incident malignancies in Brazil. Despite its low representativeness, the incidence and mortality from oral cavity cancer has been growing over the years in Brazil, differently from what has been seen in developed countries². Nowadays, this cancer ranks fifth among the most common malignant tumors in men in Brazil, reaching the fourth position in southeast Brazil¹. The squamous cell carcinoma (SCC) remains the most common malignancy of the oral cavity. Alcohol intake and smoking remain the main risk factors for the disease in Brazil¹. Apparently, the disparity in the reduction of alcohol and tobacco abuse among men and women seems to explain the increased incidence and mortality observed among female in some studies³, leading to a gradual reduction in the men:women ratio^{1,4}. Although not included among the most incident malignancies of women in Brazil, about 28% of the new oral cavity cancers affect females in this country⁵.

Although current literature still lacks a consensus, there is a trend towards a better prognosis among women with oral cavity cancer^{1-4,6}. Prognostic variations observed between genders might be explained by clinical and pathological differences between men and women. This study aims to evaluate the histopathological features at initial presentation by analyzing a historical series of patients surgically treated for oral cavity squamous cell carcinoma in an oncological hospital of southern Brazil.

Clin Biomed Res. 2017;37(3):147-150

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METHODS

With the approval of the Research Ethics Committee of the author's Hospital, a retrospective analysis was performed involving all patients undergoing resection of malignant tumors of the oral cavity between the years 2007 and 2011 by the Head and Neck Surgery Department of this institution. During this period, 404 patients had their data reviewed. Patients treated without curative intention, cases previously treated for other head and neck malignant tumors, patients with lip tumors and those with histopathological results different from SCC were excluded from the analysis. Age and histopathological characteristics were compared between genders. In total, 209 patients were included in the final analysis.

It was considered an exiguous margin equal or inferior than 2mm. The seventh edition of UICC staging system was used to classify the clinical stage as either early (I-II) or advanced (III-IV). Histopathological grading of the surgery specimens was performed according to the World Health Organization (WHO)

grading system. Lymph-node metastasis was classified as present or absent.

Descriptive analysis was used to summarize data. Kolmogorov-Smirnov test was performed for assessing normality of continuous variables. Continuous variables were expressed in mean and standard deviation or median, minimum and maximum value, as appropriate. Categorical variables were expressed in relative and absolute frequencies. Authors used student's *t*-test in the comparison of age means; Mann-Whitney test in the comparison of size and depth of invasion medians; and the non-parametric chi-square test in the comparison of categorical variables. Statistical analysis was performed through software SPSS version 15.0 (SPSS Inc., Chicago, IL). All tests considered a significance level of 5%.

RESULTS

Tumors were distributed according to gender, histopathological characteristics and age, as demonstrated in Table 1. In total, there were 68 women

Table 1: Analysis of the clinical-pathological characteristics and survival according to gender among patients with oral squamous cell carcinomas.

	Women		Men		Total		p value
	Mean(SD)		Mean(SD)		Mean(SD)		
Age	62.33(15.25)		58.31(13.17)		59.62(13.97)		0.049
Size	Median(min-max)		Median(min-max)		Median(min-max)		0.6448
Depth of invasion	0.6(0.1-4)		1(0.1-4)		0.9(0.1-4)		0.0203
	N = 68	%	N = 141	%	N = 209	100%	
	WD	24 35.2	39 27.6		63 30.1		
	MD	25 36.7	72 51.0		97 46.4		*0.2393
	PD	9 13.2	17 12.0		26 12.4		
Differentiation	Verrucous	3 4.4	2 1.4		5 2.4		-----
	<i>In Situ</i>	2 2.9	0 0		2 1.0		-----
	Microinvasive	3 4.4	7 4.9		10 4.8		-----
	Basaloid	2 2.9	4 2.8		6 2.9		-----
Growth pattern	Expansive	11 25.5	31 31.1		42 20.1		
	Infiltrative	24 55.8	52 52.5		76 36.4		0.7790
	Mixed	8 18.6	16 16.1		24 11.5		
Neural invasion		8 11.7	22 15.6		30 14.4		0.4584
Vascular invasion		1 1.4	5 3.5		6 2.9		0.3999
T	<i>Tis-T1-T2</i>	51 75.0	89 64.9		140 67.0		0.1460
	T3-T4	17 25.0	48 35.0		65 31.1		
N	N0	51 75.0	97 68.7		148 70.8		0.3552
	N+	17 25.0	44 31.2		61 29.2		
Surgical margins	Free	27 39.7	46 32.6		73 34.9		
	Exiguous	28 41.1	59 41.8		87 41.6		0.4798
	Compromised	13 19.1	36 25.5		49 23.4		

Variables are expressed in absolute (N) and relative (%) values. Mean (standard deviation) or Median (minimum-maximum), as appropriated; Age is expressed in years; T: T Staging; N: N Staging; WD: well differentiated; MD: moderately differentiated; PD: poorly differentiated; Size and Depth of invasion are expressed in centimeters; p: significance level; * authors chose not to include other histological variants in statistical analysis, avoiding false-negative results attributable to low representativeness.

(32.5%) and 141 men (67.4%), with a male:female ratio of 1:2. Tongue tumors were the most prevalent in both genders: 31(44.1%) among women and 60(42.5%) among men. Men presented a lower mean age ($p = 0.049$). Women presented tumors with smaller depth of invasion ($p = 0.0203$). Neck dissection was performed in 43 women (63.2%) and 110 men (78.0%). It was not observed statistically significant differences in size ($p=0.6448$), frequency of metastatic lymph nodes ($p=0.3552$), tumor differentiation ($p=0.2393$), growth pattern ($p =0.7790$), surgical margin status ($p=0.4798$), and neural and vascular invasion rates ($p =0.4584$ and $p =0.3999$, respectively) between genders.

DISCUSSION

There is evidence of an increasing incidence of oral malignant tumors among women over the last decades. In the 1950's, Pinsonneault and Gill⁷ observed that only 3.4% of oral cavity cancer cases in their series were represented by women, reaching 42.8% in the most recent series^{3,4}. Since the 1950's researchers have already observed peculiarities in disease presentation when compared both genders. Despite the technical limitations of those studies, when affecting women, tumors used to present with a less infiltrative form, with lower response to radiotherapy and with lower prevalence of lymph node metastasis when compared to the male oral tumors⁷. During the following decades, few studies have added new information, most of them restricted to tumor subsite analysis, tobacco and alcohol consumption and age disparities.

With some variations in the literature, tongue and lips are the most involved subsites⁷, and SCC, the most common histological diagnosis. Some authors observed a higher prevalence of superior gingiva and hard palate tumors among women, and a higher proportion of tumors of floor of the mouth among men⁴.

Bross and Coombs⁸ observed that women exposed to alcohol and/or tobacco manifested the disease at an earlier age, suggesting that those habits

could "hasten" the onset of the disease in females. Recent studies suggest that the longer life expectancy among females and perhaps the later exposure to risk factors can collaborate with differences in age at onset of the disease in some regions⁴.

Some authors observed a higher prevalence of early T stage among women^{6,9,10}. Divergently, Kruse et al. found no statistically significant differences in T and N stages between genders⁴. Except for depth of invasion, no association between gender and other analyzed histopathological features were found in the author's study, despite the observed tendency of women presenting earlier stages. Even the rate of lymph node metastasis did not differ, suggesting that although women presented more superficial tumors, those findings were not associated with expressive lower regional metastasis rates. Other authors also observed similar results^{6,10,11}. Interestingly, Chen et al. also observed a higher prevalence of earlier stages among women, as well as an association between the presence of IL-6 tumor cytosolic, female gender and lymph node metastasis, demonstrating that other independent factors may also be involved in differences of metastasis risk between genders. It is possible that similar rates of lymph node metastasis may be correlated with similar disease survival curves when comparing men and women, since the N stage is one of the most important prognostic factors in oral cancer^{12,13}.

CONCLUSION

Oral cavity carcinomas among women tend to present with more superficial tumors and at later ages. Nevertheless, there were no statistically difference in the prevalence of lymph node metastasis and other histopathological factors historically associated with the prognosis.

Conflicts of interest

The authors declare no conflicts of interest.

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Received: Apr 28, 2017

Accepted: July 05, 2017