Prognostic significance of the anatomical location and TNM clinical classification in oral squamous cell carcinoma

Raimundo Fernandes de Araújo Júnior [1], Carlos Augusto Galvão Barboza [1], Naianne Kelly Clebis [1], Sergio Adrianne Bezerra de Moura [2], Antônio de Lisboa Lopes Costa [3]

(1) Disciplines of Oral Histology, Embriology and Anatomy, Morfology Department, Federal University of Rio Grande do Norte, Natal, RN, Brazil
(2) Disciplines of Histology and Pathology, Federal University of Campina Grande, Cajazeiras, PB, Brazil
(3) Discipline of Oral Pathology, Faculty of Dentistry, Federal University of Rio Grande do Norte, Natal, RN, Brazil

Correspondence:
Dr. Raimundo Fernandes de Araújo Júnior
Departamento de Morfologial/ Centro do Biociências
Campus Universitário da Universidade Federal do Rio Grande do Norte.
BR 101 Bairro: Bairro Lagoa Nova;
CEP: 59072-970 / Cidade: Natal/
Estado: RN/ País: Brasil
E-mail: araujojr@cb.ufrn.br

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Abstract
Objetives: The aim of this study was to investigate the existence of correlation between the TNM clinical classification, anatomical location and prognosis of oral squamous cell carcinoma. Study design: A total of 130 oral squamous cell carcinomas were selected from the files of the Dr. Luiz Antonio Hospital (Natal, Rio Grande do Norte, Brazil). Data concerning TNM clinical classification, anatomical location and prognosis were obtained. Pearsons correlation test was applied for the statistical analysis of data. Results: It revealed a statistically significant correlation ($p = 0.01$) between TNM clinical classification and prognosis. It also revealed correlation between TNM classification and the anatomical location of oral squamous cell carcinomas ($p = 0.01$). Conclusions: We concluded that TNM classification presented correlation with prognosis and with the different anatomical locations of oral squamous cell carcinomas.

Key words: *Oral squamous cell carcinoma, anatomical location, prognosis, TNM clinical classification.*

Introduction
The TNM clinical staging system is very effective, mainly for assessing the fundamental characteristics of a cancer, such as local extent, regional dissemination and distant metastasis (1,2). Advanced TNM stages (III and IV) are related to poor prognosis in patients with oral squamous cell carcinoma (3).
Bilateral metastases of the cervical ganglia in patients with oral oral squamous cell carcinoma have poorer prognosis than those with unilateral metastasis (4). The level of lymph node involvement is an important prognostic factor, given that it diminishes significantly patient survival when multiple contralateral lymph nodes are involved (5, 6).
TNM stages III and IV are more closely related to the presence of neural infiltration and lymphatic embolization in patients with oral oral squamous cell carcinoma, thus showing that patients with clinical stage IV present with active or recurring disease (7, 8) and have lower survival time, whereas, those with TNM I and II are disease-free after 5 year follow-up (9).
The anatomic location of the lesion must also be considered as a prognostic indicator, since the tumors behave differently depending on anatomic location (10,11). Any region of the oral cavity can be affected by in oral squamous cell carcinoma, mainly the tongue (12,13), the floor of the mouth (4,11,12) and the lower lip (13).
T2 lesions of the tongue are more likely to recur and are more intimately related to cervical lymph node metastases,

thus showing the close relation between histopathological findings (mainly form and stage) and prognoses (11). Oral squamous cell carcinoma of the tongue has greater risk of metastasis to the cervical lymph nodes due to the lesion's proximity to this anatomic site. In addition, the histological malignancy score of most of these lesions was high (between 2.5 and 4.0) (14).

The TNM clinical classification record and anatomic location of the oral squamous cell carcinoma are of utmost importance in determining prognosis and treatment, since tongue and the floor of the mouth lesions are associated with higher risk of developing the advanced stage and consequent recurrence (1,4,15).

The most important challenge to the TNM system is how it deals with the large number of non-anatomic prognostic factors that are being widely used. The role of the TNM system when associated to other prognostic factors is to determine the therapeutic choice, select patients for therapeutic studies, in addition to assessing non-anatomic prognostic factors in specific anatomic stages and communicating the extent of the disease (16).

Chen et al. (17) suggested that predictive factors in oral and pharyngeal carcinoma survival are: ethnic groups, period of diagnosis, gender, diagnostic age, anatomic site, morphologic type, and therapy. These data are useful to researchers investigating the long-term survival trends for subjects diagnosed with oral and pharyngeal cancer.

The purpose of this study was to correlate clinical TNM staging with prognosis and anatomic location in 130 cases of oral squamous cell carcinoma.

Material and Methods

1- Population

It consisted of all the cases of oral squamous cell carcinoma on file at Dr. Luiz Antônio Hospital in Natal/RN, Brazil from 2000 to 2005.

2- Sample

The sample selected consisted of 130 cases of oral squamous cell carcinoma in patients treated and recorded in the files of Dr. Luiz Antônio Hospital. With the analysis of the medical records, data were obtained relative to the patient's sex, age group, anatomic location of the lesion and TNM clinical classification. These data were selected according to the following parameters:

*Sex and skin color: men and women with white, brown or black skin.

* Age: in age groups, from the 4th decade.

* Location of the lesion: the lesion was analyzed if it was located on the tongue, lower lip, the floor of the mouth, the orapharynx or jugal mucosa, alveolar mucosa and retromolar area.

*TNM clinical staging: according to the version established by the International Union Against Cancer (UICC) (Hermaneck et al. (18), 1996; Neville et al. (19), 2004): Stage I = T1N0M0; Stage II = T2N0M0; Stage III = T3N0M0, or T1, T2 or T3N1M0; Stage IV = any T4, N2, N3 or M1 lesion.

* Prognosis: We analyzed, after a maximum period of 5 years, if the patients were disease free, had the disease (stable or ongoing), had recurring lesions (after treatment) or had died. We also divided them into two groups: the first group, consisting of disease-free patients, was considered to have the best prognosis and the second, formed by those with the disease (stable, recurring and ongoing) or who had died as a result of the neoplasias, to have the worst prognosis.

Medical records that contained incomplete or confusing information on clinical variables were excluded.

Statistical analysis

We used Pearson's paired t-test to determine the correlation between clinical TNM classification and prognosis and anatomic location of the lesion. In all the tests applied, a level of 5% was set to reject the null hypothesis.

Results

- *Quantitative results*

Based on the analysis of the data of patients with oral squamous cell carcinoma, we observed that of the 130 case analyzed, 70 (53.84%) were of men (M) and 60 (46.15%) were of women (W), with a ratio M/W of 1.16/1. The brown people (65%) were more commum in our sample. Ages varied from 40 to 93 years with 15 cases (11.53%) in the 41- 50- year group, 20 cases (15.38%) in the 51- 60-year group, 30 cases (23.07%) in the 61-70-year group, 40 cases (30.76%) in the 71-80-year group, 20 (15.38%) in the 81-90-year group and 05 cases (3,84%) in the 91-93-year group.

According to clinical TNM classification, our sample was distributed as follows: 29 cases (22.3%) were classified as T1, 17 cases (13.07%) as T2, 33 cases (25.38%) as T3 and 51 cases (39.23%) as T4.

By grouping the clinical stages into I/II and III/IV, we observe the following results for clinical staging (TNM) and prognosis.

1) A correlation between clinical staging (TNM) and prognosis.

2) Of the 46 cases classified as stage I and II, 5 patients had recurring lesions, 3 had active lesions, 1 had died and 37 were disease-free.

3) Of the 84 cases classified as stage III and IV, 38 were disease-free, 11 had active lesions, 16 had recurring lesions and 19 had died.

With respect to anatomic location, the area most affected by oral squamous cell carcinoma was the side of the tongue with 52 cases (40%), followed by the lower lip with 26 cases (20%) and palate with 16 cases (16.2%). Squamous cell carcinoma lesions on the side of the tongue were present in 38 cases (45.2%) of the patients with clinical stages III/IV, while 19 cases (41.3%) with stages I/II presented with oral epidermoid carcinoma on the lower lip.

Table 1. Correlation between TNM clinical staging and prognosis in oral epidermoid carcinoma. Dr. Luis Antônio Hospital, Natal, Brazil (2007).

			Prognosis			
			Disease free	Disease and death	Total	p
TNM clinical staging	I	Count	25	4	29	0.01
		% with TNM clinical staging	86,2%	13,8%	100,0%	
		% with prognosis	33,3%	7,3%	22,3%	
	II	Count	12	5	17	0.01
		% with TNM clinical staging	70,6%	29,4%	100,0%	
		% with prognosis	16,0%	9,1%	13,1%	
	III	Count	16	17	33	0.01
		% with TNM clinical staging	48,5%	51,5%	100,0%	
		% with prognosis	21,3%	30,9%	25,4%	
	IV	Count	22	29	51	0.01
		% with TNM clinical staging	43,1%	56,9%	100,0%	
		% with prognosis	29,3%	52,7%	39,2%	
Total		Count	75	55	130	0,001
		% with TNM clinical staging	57,7%	42,3%	100,0%	
		% with prognosis	100,0%	100,0%	100,0%	

Table 2. Correlation between anatomic location of oral epidermoid carcinoma and TNM clinical staging. Dr. Luis Antônio Hospital, Natal, Brazil (2007).

		TNM clinical staging						
		I/II		III/IV		Total		
Anatomic location	The floor of the mouth	N	%	N	%	N	%	p
		1	2,2	6	7,1	7	5,4	0.01
	Tongue	14	30,4	38	45,2	52	40	0.01
	Lower lip	19	41,3	7	8,3	26	20	0.01
	Orapharynx	1	2,2	10	11,9	11	8,5	0.01
	Palate	6	13	15	17,9	21	16,2	0.01
	Maxillary alveolar mucosa	4	8,7	3	3,6	7	5,4	0.01
	Retromolar area	1	2,2	5	6,0	6	4,6	0.01
Total		46	100	84	100	130	100	0.01

- *Statistical analysis results*

Pearson's test showed a statistically significant correlation between TNM clinical classification and prognosis of oral squamous cell carcinoma when the second group variable is analyzed (group I – disease-free and group II- with the disease and death) ($p = 0.01$) (Table 1). The correlation between TNM clinical staging (I/II; III/IV) and anatomic location also shows a correlation at the 1% level ($p = 0.01$) (Table 2).

Discussion

It was observed that 33.3% of the cases clinically classified as TNM stage 1 were disease-free, as were 16.0% of the patients with TNM stage II after 5 years follow-up. We found that 30.9% of patients with TNM stage III had the disease or had died. Stage IV was present in 52.7% of the patients who had the disease or who had succumbed to it. The results were statistically significant ($p = 0.01$) when the correlation was performed with grouped prognosis variables. TNM clinical staging I and II were most observed in

disease-free patients whereas individuals with ongoing or recurring disease or who had died were the most prevalent in TNM clinical staging III and IV. Woolgar et al. (6), Numata et al. (7), and Dib et al. (8) report a strong correlation between TNM clinical classification and survival in patients with oral squamous cell carcinoma.

Many authors consider TNM clinical staging to be one of the best prognostic indicators of oral squamous cell carcinoma (9,14,18). Other studies have shown a strong correlation between TNM clinical classification and the survival of patients with oral epidermoid carcinoma (6,7,8,15). However, other prognostic parameters should be used, such as the biological properties of the tumor, to corroborate the prognostic value of the TNM system and the treatment plan (2,3).

Our results showed a statistically significant correlation at 1% ($p = 0.01$) between TNM clinical staging and anatomic location of the lesion. Stage I clinical cases occurred mostly in patients with lower lip lesions, whereas most of the tongue lesion cases were stage III or IV. Most of the floor of the mouth and soft palate cases were classified as T4. Our findings suggest that these locations (tongue, soft palate and floor of the mouth) present the worst prognosis for oral squamous cell carcinoma. These data corroborate those of Costa et al. (1,14), who consider anatomic location an important prognostic indicator, given that the lower lip lesions are generally well differentiated from those that affect the tongue and roof of the mouth.

Costa et al. (1) found that lower lip tumors often have better prognosis when compared to other oral cavity locations. According to Dib et al. (8) and Urist et al. (10), squamous cell carcinoma carcinomas of the tongue and floor of the mouth generally have poor prognosis due to the frequent presence of cervical metastases. Chen et al. (17) consider anatomic sites to be significant predictors for survival in Hokkien (Taiwan). Tongue and mouth sites elevated risks of death compared with oropharyngeal, but lip sites had a significantly better prognosis (17).

Our results show that some factors such as the anatomic location of the lesion and TNM clinical classification are important prognostic indicators in patients with Oral squamous cell carcinoma, since there was a statistically significant correlation between TNM clinical classification, prognosis and anatomic location. For this reason, early diagnosis of this neoplasia, along with improved awareness on the part of dental surgeons, may contribute to better survival rates and quality of life in patients with oral squamous cell carcinoma.

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