Nodal Metastasis in Oral Squamous Cell Carcinoma: an Analysis of Risk Factors and Influence on Overall Survival

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Metástase Nodal no Carcinoma de Células Escamosas Oral: uma Análise dos Fatores de Risco e Influência na Sobrevida Global

Metástasis Ganglionar en Carcinoma de Células Escamosas Oral: un Análisis de Factores de Riesgo y su Influencia en la Supervivencia Global

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ABSTRACT

Introduction: Oral squamous cell carcinoma (OSCC) presents a high tendency of lymph node metastasis (LNM). **Objective:** Determine which risk factors play a significant role in metastasis to cervical lymph nodes and to evaluate the influence of nodal involvement on overall survival of patients with OSCC. **Method:** Medical records of 350 patients with OSCC were retrospectively reviewed. The data were analyzed using the chi-square, Fisher's exact and log-rank Mantel Cox tests and multinomial and Cox logistic regression. **Results:** Of the 350 medical records evaluated, 251 reported N0, 75 N1, 16 N2 and 8 N3. Male gender, referrals from private health care providers, T3/4 stage and non-surgical treatments were associated with LNM. In multivariate analysis, men and T3/4 tumors were shown to be independent risk factors for LNM. The independent risk factors for survival were male gender, nodal involvement (p = 0.017) and non-surgical treatment. **Conclusion:** Male gender and T-stage are risk factors for LNM in patients with OSCC. Moreover, the presence of LNM and age >65 years are associated with poor overall survival.

Key words: Neoplasm Metastasis; Mouth Neoplasms/epidemiology; Lymph Nodes; Squamous Cell Carcinoma of Head and Neck; Neck Dissection.

RESUMO

Introdução: O carcinoma de células escamosas oral (CCEO) apresenta uma alta tendência de metástase para linfonodos cervicais (MLC). **Objetivo:** Determinar quais fatores de risco desempenham um papel significativo na metastização para linfonodos cervicais e avaliar a influência do envolvimento nodal na sobrevida geral de pacientes com CCEO. **Método:** Os registros médicos de 350 pacientes com CCEO foram revisados retrospectivamente. Os dados foram analisados usando os testes qui-quadrado, exato de Fisher e log-rank Mantel Cox, além de regressão logística multinomial e Cox. **Resultados:** Dos 350 registros médicos avaliados, 251 relataram N0, 75 N1, 16 N2 e 8 N3. Gênero masculino, encaminhamentos de prestadores de cuidados de saúde privados, estágios T3/4 e tratamentos não cirúrgicos estavam associados ao MLC. Foi demonstrado na análise multivariada que homens e tumores T3/4 são fatores de risco independentes para MLC. Os fatores de risco independentes para sobrevida foram gênero masculino, envolvimento nodal (p = 0,017) e tratamento não cirúrgico. **Conclusão:** O gênero masculino e o estágio T são fatores de risco para MLC em pacientes com CCEO. Além disso, a presença de MLC e a idade > 65 anos estão associadas à reduzida sobrevida geral.

Palavras-chave: Metástase Neoplásica; Neoplasias Bucais/epidemiologia; Linfonodos; Carcinoma de Células Escamosas de Cabeça e Pescoço; Esvaziamento Cervical.

RESUMEN

Introducción: El carcinoma de células escamosas oral (CCEO) presenta una alta tendencia hacia la metástasis en los ganglios linfáticos cervicales (MGLC). **Objetivo:** Determinar qué factores de riesgo desempeñan un papel significativo en la metástasis a los ganglios linfáticos cervicales y evaluar la influencia de la participación nodal en la supervivencia general de pacientes con CCEO. **Método:** Se revisaron retrospectivamente los registros médicos de 350 pacientes con CCEO. Los datos se analizaron utilizando las pruebas de ji al cuadrado, exacta de Fisher, log-rank Mantel-Cox, así como regresión logística multinomial y de Cox. **Resultados:** De los 350 registros médicos evaluados, 251 indicaron N0, 75 N1, 16 N2 y 8 N3. El género masculino, las referencias de proveedores de atención médica privados, el estadio T3/4 y los tratamientos no quirúrgicos estaban asociados con el MGLC. Se demostró en análisis multivariado que los hombres y los tumores T3/4 son factores de riesgo independientes para el MGLC. Los factores de riesgo independientes para la supervivencia fueron el género masculino, la participación nodal (p = 0,017) y el tratamiento no quirúrgico. **Conclusión:** El género masculino y el estadio T son factores de riesgo para el MLC en pacientes con CCEO. Además, la presencia de MGLC y la edad >65 años están asociadas con una supervivencia general reducida.

Palabras clave: Metástasis de Neoplasias; Neoplasias de la Boca/epidemiología; Ganglios Linfáticos; Carcinoma de Células Escamosas de Cabeza y Cuello; Disección del Cuello.

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the sixth most common type of cancer in the world, with an incidence of more than 600,000 new cases per year[1]. In Brazil, cancer represents the third leading cause of death, followed by cardiovascular diseases and external causes. In the head and neck region, the tongue is the structure with the highest occurrence of this cancer (32%), followed by oropharynx with 18.5% and the floor of the mouth with 12.4%[2].

The main risk factors related to oral cancer are smoking history and alcohol use, with a synergistic effect among these variables and a directly proportional relationship with the amount consumed and the duration of exposure. Moreover, other risk factors as excessive exposure to solar radiation, which could lead to the development of basal cell carcinoma on the vermilion border of the lip have been associated with OSCC[3].

The prognosis of OSCC depends on several factors, including the compromised area of the oral cavity as well as the TNM classification, which has been used as an international standard to categorize malignancies and to estimate both therapy response and survival. In addition to covering details of local anatomical characteristics, this staging system assists in gathering data on the degree of involvement of surrounding structures and on the detection of metastases in the lymph node chains adjacent to the tumor, outlining patient prognosis and survival[4].

Studies have indicated that approximately 50% of OSCC cases metastasize to lymph nodes, which leads to more aggressive treatments, worse prognosis and lower overall survival[1]. The risk factors for the development of nodal metastasis in patients with OSCC are numerous. Microscopic characteristics as desmoplasia, perineural infiltration, tumor thickness (≥4 mm) and pT4 demonstrate an independent relationship for occult cervical lymph node metastasis[5]. Systemic comorbidities, histologic tumor size pathologic nodal status, tumor differentiation, perineural invasion and extracapsular spread are also considered risk factors[6].

Despite the importance of histological characteristics in predicting lymph node metastases, variables as age, sex and educational level could also significantly influence the occurrence of nodal involvement[6]. Therefore, clinical predictors also play an important role in the prognosis of patients with OSCC. Recent investigations have highlighted the importance of risk factors as low educational levels[4], previous smoking exposure and alcohol use as predictors of poor overall survival[7]. Furthermore, nodal involvement has been described as a determining factor for the development of distant metastases[8], which is the main risk factor for OSCC mortality.

Thus, given the importance of cervical lymph node involvement on the prognosis of OSCC, the aim of this study is to determine which risk factors play a significant role in metastasis to cervical lymph nodes and to evaluate the influence of nodal involvement on overall survival of patients with OSCC.

METHOD

Retrospective and cross-sectional study with data collected from 350 medical records of patients with OSCC.

The inclusion criteria were patients diagnosed and treated at *Hospital Haroldo Juaçaba* between January 1, 2000, and December 31, 2014, whose medical records included pTNM[9] staging, obtained from the institution's digital database. The exclusion criterion were patients diagnosed and treated not within the study period or whose clinical data were unavailable.

Sociodemographic variables included: age, sex, race, educational level, marital status, family cancer history, smoking history, alcohol use and type of health care provider (public or private). Clinical variables included: histological type, tumor site, pT, pN obtained during the initial diagnosis of the patient and treatments. Overall survival (in months) was defined as the time from the beginning of treatment (day/month/year) to date of death (day/month/year) or the last follow-up visit (day/month/year)[4].

Fisher's exact test, Pearson's chi-squared test and multinomial logistic regression model were utilized to evaluate the factors associated with pN. Kaplan-Meier curves were plotted to determine the mean and standard error values of overall survival. The curves were compared between Mantel-Cox test and Cox regression analysis. All the variables were included in the multivariate models. All statistical analyses were performed with the IBM SPSS[10] Statistics software for Windows (v. 20.0), using a 95% confidence interval.

The study was approved by the Research Ethics Committee of "*Hospital Haroldo Juaçaba*", CAAE (submission for ethical review) 06530818.70000.5054, report number 3212746, in compliance with Directive 466/12[11] of the National Health Council. The patient signed the Informed Consent Form (ICF) after being briefed about the study. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology[12] (STROBE) reporting guideline.

RESULTS

The evaluation of the 350 medical records revealed that most patients did not exhibit lymph node metastasis

(n = 251, 71.7%), whereas 75 (21.4%) exhibited N1, 16 (4.6%) N2 and 8 (2.3%) N3. Males were more prevalent (n = 249, 71.1%) and this factor was shown to be directly associated with a higher prevalence of N1, N2 and N3 than females (p = 0.013) (Table 1).

The most prevalent age was ≤ 65 years (n = 184, 52.6%), the majority of the patients were of mixed race (n = 166, 63.1%) and single (n = 302, 86.3%) with incomplete primary education (n = 89, 32.7 %) and no family cancer history (n = 299, 85.4%). One hundred and eighteen patients (33.7%) showed history of alcohol use and 138 (39.4%) reported previous smoking history. Admission to the hospital through referral from private health care providers was reported in 193 (55.1%) of the medical records, the only factor (p = 0.006) associated with increased prevalence of N2 and N3, whereas the other factors did not significantly modify the prevalence of nodal metastasis (Table 1).

Table 1. Metastasis profile in cervical lymph nodes and influence of sociodemographic factors of patients with OSCC diagnosed and treated at *Hospital Haroldo Juaçaba* between 2000 and 2014

	Total	Nodal Status				*p*-value
		N0	N1	N2	N3	
Total	**350 (100.0%)**	**251 (71.7%)**	**75 (21.4%)**	**16 (4.6%)**	**8 (2.3%)**	**-**
Sex						
Female	101 (28.9%)	84 (33.5%)*	15 (20.0%)	2 (12.5%)	0 (0.0%)	***0.013***
Male	249 (71.1%)	167 (66.5%)	60 (80.0%)*	14 (87.5%)*	8 (100.0%)*	
Age						
≤65 years	184 (52.6%)	133 (53.0%)	34 (45.3%)	12 (75.0%)	5 (62.5%)	0.162
>65 years	166 (47.4%)	118 (47.0%)	41 (54.7%)	4 (25.0%)	3 (37.5%)	
Race						
White	129 (36.9%)	89 (35.5%)	30 (40.0%)	7 (43.8%)	3 (37.5%)	0.836
Mixed	221 (63.1%)	162 (64.5%)	45 (60.0%)	9 (56.3%)	5 (62.5%)	
Educational level						
Illiterate	76 (27.9%)	58 (30.1%)	13 (22.4%)	5 (38.5%)	0 (0.0%)	0.206
Elementary (incomplete)	89 (32.7%)	61 (31.6%)	22 (37.9%)	3 (23.1%)	3 (37.5%)	
Elementary (complete)	68 (25.0%)	45 (23.3%)	16 (27.6%)	2 (15.4%)	5 (62.5%)	
High-school (complete)	39 (14.3%)	29 (15.0%)	7 (12.1%)	3 (23.1%)	0 (0.0%)	
Marital status						
Other	302 (86.3%)	218 (86.9%)	62 (82.7%)	16 (100.0%)	6 (75.0%)	0.231
Married	48 (13.7%)	33 (13.1%)	13 (17.3%)	0 (0.0%)	2 (25.0%)	
Family cancer history						
No	299 (85.4%)	217 (86.5%)	63 (84.0%)	13 (81.3%)	6 (75.0%)	0.739
Yes	51 (14.6%)	34 (13.5%)	12 (16.0%)	3 (18.8%)	2 (25.0%)	
Alcohol use						
No	232 (66.3%)	169 (67.3%)	49 (65.3%)	9 (56.3%)	5 (62.5%)	0.819
Yes	118 (33.7%)	82 (32.7%)	26 (34.7%)	7 (43.8%)	3 (37.5%)	
Smoking history						
No	212 (60.6%)	158 (62.9%)	41 (54.7%)	10 (62.5%)	3 (37.5%)	0.321
Yes	138 (39.4%)	93 (37.1%)	34 (45.3%)	6 (37.5%)	5 (62.5%)	
Referral						
Public	157 (44.9%)	122 (48.6%)*	32 (42.7%)*	3 (18.8%)	0 (0.0%)	***0.006***
Private	193 (55.1%)	129 (51.4%)	43 (57.3%)	13 (81.3%)*	8 (100.0%)*	

(*) p <0.05, Fisher's exact test or Pearson's chi-square.

Tongue was the most prevalent anatomical primary tumor site (n = 149), with 42.6% of all cases, followed by the palate (n = 69, 19.7%), the retromolar area (n = 53, 15.1%) and the floor of the mouth (n = 45, 12.9%). Tumor site did not significantly influence the prevalence of nodal metastasis (p = 0.438) (Table 2).

The most prevalent T-stage were T2 (n = 152, 43.4%) and T3 (n = 140, 40.0%). This variable was significantly associated with nodal metastasis (p < 0.001). Surgery associated with adjuvant radiotherapy was the most treatment protocol utilized (n = 96, 27.4%), followed by radiotherapy only (n = 88, 25.1%). Patients treated with surgery and radiotherapy had a higher prevalence of N0, whereas patients who received radiotherapy only had a higher prevalence of N1 and patients treated with both radio and chemotherapy had a higher prevalence of N2 and N3 (p < 0.001) (Table 2).

In the multivariate analysis, male sex (2.21, 95% CI 1.06-4.59, p = 0.034) and T3/T4 stage (2.49, 95% CI 1.40-4.43, p = 0.002) significantly increased the odds ratio of metastasis to cervical lymph nodes (Table 3).

The overall survival of patients with OSCC was 44.0% with an average time of 81.67 ± 4.49 months and a median of 43 months (CI95% = 28.90-57.10). Male patients (p = 0.017), aged >65 years (p = 0.013) and of mixed race (p = 0.041) had worse survival, with a reduction of 67, 22 and 34 months, respectively, in the median overall survival (Table 4).

Educational level (p = 0.604), marital status (p = 0.554), alcohol use (p = 0.204), and smoking history (p = 0.599) did not significantly influence the overall survival. Patients with family cancer history reached significantly higher overall survival than patients with no family history (p = 0.045). The type of referral did not significantly change the overall survival of patients with OSCC (Table 4).

The anatomical site of the primary tumor did not influence the overall survival. T-stage (p = 0.017) and N-stage (p = 0.001) were directly associated with lower survival. Patients treated with surgery only had the best prognosis (p < 0.001) (Table 5).

The results of the multivariate analysis highlight that age over 65 years, the presence of lymph node metastasis,

Table 2. Influence of clinical factors on the metastasis profile in cervical lymph nodes and on the therapeutic profile of patients with OSCC diagnosed and treated at *Hospital Haroldo Juaçaba* between 2000 and 2014

	Total	Nodal Status				*p*-value
		N0	N1	N2	N3	
Primary tumor site						
Tongue	149 (42.6%)	109 (43.4%)	30 (40.0%)	5 (31.3%)	5 (62.5%)	0.438
Retromolar area	53 (15.1%)	34 (13.5%)	13 (17.3%)	4 (25.0%)	2 (25.0%)	
Floor of the mouth	45 (12.9%)	29 (11.6%)	11 (14.7%)	5 (31.3%)	0 (0.0%)	
Gingiva	4 (1.1%)	3 (1.2%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	
Lip	12 (3.4%)	10 (4.0%)	2 (2.7%)	0 (0.0%)	0 (0.0%)	
Jugal mucosa	18 (5.1%)	14 (5.6%)	4 (5.3%)	0 (0.0%)	0 (0.0%)	
Palate	69 (19.7%)	52 (20.7%)	15 (20.0%)	1 (6.3%)	1 (12.5%)	
T						
1	48 (13.7%)	43 (17.1%*)	4 (5.3%)	0 (0.0%)	1 (12.5%)	***<0.001***
2	152 (43.4%)	114 (45.4%)*	32 (42.7%)*	5 (31.3%)	1 (12.5%)	
3	140 (40.0%)	91 (36.3%)	37 (49.3%)*	7 (43.8%)*	5 (62.5%)	
4	10 (2.9%)	3 (1.2%)	2 (2.7%)	4 (25.0%)*	1 (12.5%)*	
Treatment						
None	46 (13.1%)	32 (12.7%)	8 (10.7%)	4 (25.0%)	2 (25.0%)	***<0.001***
Surgery	47 (13.4%)	39 (15.5%)	7 (9.3%)	0 (0.0%)	1 (12.5%)	
Surgery + RT	96 (27.4%)*	80 (31.9%)*	13 (17.3%)	3 (18.8%)	0 (0.0%)	
Surgery + RT + CT	17 (4.9%)	10 (4.0%)	6 (8.0%)	0 (0.0%)	1 (12.5%)	
RT	88 (25.1%)	64 (25.5%)	22 (29.3%)*	1 (6.3%)	1 (12.5%)	
RT + CT	56 (16.0%)	26 (10.4%)	19 (25.3%)	8 (50.0%)*	3 (37.5%)*	

(*) p <0.05, Fisher's exact test or Pearson's chi-square; RT = radiotherapy; CT = chemotherapy.

Table 3. Risk factors for cervical lymph node metastasis in patients with OSCC diagnosed and treated at *Hospital Haroldo Juaçaba* between 2000 and 2014

N+	*p*-value	Adjusted OR (95%CI)
Sex (male)	***0.034**	***2.21 (1.06-4.59)***
Age (>65)	0.195	1.49 (0.81-2.74)
Race (white)	0.875	0.95 (0.52-1.75)
Educational level Complete elementary or high-school	0.285	0.58 (0.21-1.57)
Marital status (married)	0.394	1.40 (0.65-3.04)
Family history of cancer (yes)	0.846	1.09 (0.46-2.57)
Alcohol use (yes)	0.523	0.74 (0.30-1.85)
Smoking history (yes)	0.464	1.39 (0.58-3.35)
Referral (private)	0.063	1.74 (0.97-3.13)
Anatomical site (tongue/floor of the mouth)	1.000	1.02 (0.58-10.52)
T3/4	***0.002***	***2.49 (1.40-4.43)***

(*) $p < 0.05$, multinomial logistic regression.

and non-surgical treatment are associated with a significant increase in the risk of death, regardless of other factors. They demonstrate the statistical significance of the factors, while the adjusted HR with a 95% confidence interval provides an estimate of the mortality risk associated with each factor.

DISCUSSION

In Brazil, the annual incidence of OSCC was 11.54 and 3.92 new cases per 100,000 men and women, respectively. Clinical factors such as nodal involvement and tumor stage play a major role in the prognostic variability of patients with OSCC. Nevertheless, recent studies have pointed out that social factors such as access to health services, educational level, patient occupation, behavioural and cultural aspects also significantly influence the overall survival[2].

The involvement of regional lymph nodes (N) is an important factor with a clear prognostic impact, reducing overall survival by 50%[13]. Most of the patients did not exhibit nodal metastasis at the initial diagnosis of OSCC, as described in other investigations[14]. This prevalence tends to fluctuate considerably among studies; however, nodal involvement has been described at head and neck surgery services with frequency ranging from 25 to 65% of patients diagnosed with OSCC[15-17].

Several variables have been described as risk factors for nodal involvement. Although sex is not described as a risk factor in some studies[15,18,] the present investigation showed that men were almost twice as likely to develop cervical lymph node metastasis than women, which is in accordance with previous studies where male sex is a predictor of nodal metastasis[19]. Nonetheless, occult metastases in low-stage primary tumors in the tongue showed higher prevalence in women[20].

T-stage was also considered a determining factor. Patients with higher staging were directly associated with a higher prevalence of nodal involvement, and this association is directly connected to stage severity. Large tumors usually exhibit extended tumor invasion depth (TID). TID values ≥ 4 mm, even in cases of early OSCC, are risk factors strongly associated with involvement of the cervical lymph node chain[20,21].

TID is the most important factor for metastasis in cervical lymph nodes, often requiring cervical lymph node dissection for better prognosis[21,22]. Other risk factors also related to tumor size such as growth pattern, primary tumor in the tongue, degree of histological differentiation in high-grade tumors and smaller diameter/larger diameter ratio strongly contribute to a higher risk of nodal involvement[17].

Among the survival determinants, age>65 years and nodal involvement were considered strong risk factors in this study, thereby corroborating other data[23]. It is known that OSCC most commonly affects patients over 60 years, and that this could be related to the cumulative effect of extrinsic etiopathogenic factors, as smoking[3]. Studies show that older patients are more frequently diagnosed with advanced tumors and, therefore, usually have worst prognoses[24]. In addition, older individuals generally have associated comorbidities, resulting in less resistance to OSCC treatments, lower immune surveillance and higher risk of disease progression[25].

Table 4. Influence of sociodemographic factors on the overall survival of patients with OSCC diagnosed and treated at the *Hospital Haroldo Juaçaba* between 2000 and 2014

Total	OS	Overall Survival (OS)(months)		*p*-value
		Mean±SEM (95%CI)	Median (95%CI)	
	154 (44.0%)	**81.67±4.49 (72.87-90.47)**	**43 (28.90-57.10)**	**-**
Sex				
Female	57 (56.4%)	90.70±7.74 (75.54-105.87)	106 (52.60-159.40)	***0.017***
Male	97 (39.0%)	75.23±5.10 (65.24-85.21)	39 (29.21-48.79)	
Age				
≤65 years	93 (50.5%)	93.32±6.36 (80.85-105.80)	54 (8.02-99.98)	***0.013***
>65 years	61 (36.7%)	68.71±6.05 (56.85-80.58)	32 (17.89-46.11)	
Race				
White	66 (51.2%)	94.28±7.58 (79.43-109.13)	74 (19.21-128.79)	***0.041***
Mixed	88 (39.8%)	74.35±5.49 (63.59-85.10)	40 (29.92-50.08)	
Educational level				
Illiterate	29 (38.2%)	72.88±7.91 (57.38-88.38)	41 (12.80-69.20)	0.604
Elementary (incomplete)	31 (34.8%)	71.53±7.96 (55.93-87.12)	39 (14.86-63.14)	
Elementary (complete)	37 (54.4%)	83.86±10.08 (64.11-103.61)	48 (15.33-80.67)	
High-school (complete)	19 (48.7%)	88.86±13.75 (61.91-115.81)	48 (7.31-88.69)	
Marital status				
Other	131 (43.4%)	80.67±4.83 (71.20-90.14)	42 (31.16-52.84)	0.554
Married	23 (47.9%)	83.49±10.44 (63.03-103.96)	74 (0-154.92)	
Family cancer history				
No	122 (40.8%)	78.01±4.70 (68.80-87.22)	42 (30.16-53.84)	***0.045***
Yes	32 (62.7%)	109.32±12 (85.80-132.85)	-	
Alcohol use				
No	92 (39.7%)	78.22±5.26 (67.91-88.53)	40 (29.09-50.91)	0.204
Yes	62 (52.5%)	73.54±5.99 (61.80-85.28)	62 (18.11-105.89)	
Smoking history				
No	86 (40.6%)	79.83±5.50 (69.05-90.62)	43 (28.99-57.01)	0.599
Yes	68 (49.3%)	70.41±5.49 (59.66-81.17)	44 (19.08-68.92)	
Referral				
Public	71 (45.2%)	78.16±5.93 (66.54-89.77)	48 (26.87-69.13)	0.708
Private	83 (43.0%)	79.80±6.02 (68.01-91.59)	42 (29.77-54.23)	

* $p < 0.05$ Log-rank Mantel-Cox test; SEM = standard error of the mean of global survival time calculated by Kaplan-Meier curves; 95% CI = 95% confidence interval.

Nodal metastasis is a prognostic modulator frequently observed in the literature. Montoro et al. showed in 2008 that the overall survival for N + patients decrease from 60-70% to 30-50% compared to N0 patients, with extracapsular invasion negatively affecting overall survival. Other studies reported a 10% decrease in the overall survival of patients with OSCC when single lymph node is involved, and 50% when multiple lymph nodes are compromised[26].

Several studies have indicated that cancer cells spread relatively early in the lymphatic and blood vessels[27]. Experimental studies show that the increase in local vascularization, induced by signalling proteins as the vascular endothelial growth factor (VEGF) in response to tumor growth, favours tumor spread and consequent aggressiveness[28,29]. This response leads to poorer prognosis and decreased survival, as observed by Silva et al. in 2020 who described nodal involvement as an independent risk factor for the development of distant metastases.

The retrospective and cross-sectional nature of this research limits data retrieval and patient follow-up, respectively. Moreover, the extended inclusion period leaves data susceptible to updates in the histological classification of the tumours described in the medical records analysed.

Table 5. Influence of anatomical site, clinical staging and therapeutic profile on the overall survival of patients with OSCC diagnosed and treated at the *Hospital Haroldo Juaçaba* between 2000 and 2014

Primary tumor site	OS	Overall Survival (months)		*p*-value
		Mean±SEM (95%CI)	Median (95%CI)	
Tongue	73 (49.0%)	81.35±6.29 (69.01-93.68)	54 (34.67-73.33)	0.454
Retromolar area	27 (50.9%)	93.30±12.28 (69.23-117.36)	35	
Floor of the mouth	19 (42.2%)	85.07±11.10 (63.32-106.82)	48 (0-120.24)	
Gingiva	1 (25.0%)	57.75±27 (4.83-110.67)	29 (18.22-39.78)	
Lip	5 (41.7%)	62.32±15.25 (32.42-92.21)	62 (20.48-103.52)	
Jugal mucosa	8 (44.4%)	84.55±18.48 (48.32-120.77)	47 (5.54-88.46)	
Palate	21 (30.4%)	62.94±8.95 (45.40-80.48)	30 (18.53-41.47)	
T				
1	28 (58.3%)	89.78±9 (72.13-107.43)	95 (56.05-133.95)	***0.017***
2	70 (46.1%)	84.98±7.01 (71.24-98.71)	42 (25.37-58.63)	
3	54 (38.6%)	73.34±6.64 (60.33-86.35)	34 (21.62-46.38)	
4	2 (20.0%)	40.20±17.91 (5.10-75.30)	15 (1.34-28.66)	
N				
0	115 (45.8%)	86.32±5.24 (76.05-96.59)	48 (29.68-66.32)	***0.001***
1	32 (42.7%)	76.45±9.94 (56.98-95.93)	45 (15.41-74.59)	
2	6 (37.5%)	61.36±18.37 (25.36-97.36)	25 (0.00-63.15)	
3	1 (12.5%)	12.50±3.37 (5.90-19.10)	10 (4.46-15.54)	
Treatment				
None	19 (41.3%)	72.96±10.86 (51.68-94.23)	39 (3.59-74.41)	***<0.001***
Surgery	29 (61.7%)	115.36±12.17 (91.51-139.22)	-	
Surgery + RT	49 (51.0%)	97.40±8.24 (81.25-113.54)	86 (36.61-135.39)	
Surgery + RT + CT	6 (35.3%)	31.70±6.67 (18.62-44.78)	19 (13.58-24.42)	
RT	26 (29.5%)	50.31±7.11 (36.38-64.25)	19 (8.26-29.74)	
RT + CT	25 (44.6%)	81.82±11.70 (58.89-104.74)	35 (22.33-47.67)	

(*) $p < 0.05$ Log-rank Mantel-Cox test; SEM = standard error of the mean of global survival time calculated by Kaplan-Meier curves; OS – overall survival; 95% CI = 95% confidence interval.

CONCLUSION

The findings of this study emphasized that male sex and T-stage are significant risk factors for cervical lymph node involvement in patients with OSCC. Furthermore, age >65 years and the presence of lymph node metastasis are factors independently associated with poor overall survival.

CONTRIBUTIONS

Paulo Goberlânio de Barros Silva contributed to the study design. Thinali Sousa Dantascontributed to the study design and final review. Tayane Oliveira Gonçalves, Ana Mirian da Silva Cavalcante, Erick Ibraim Carlos da Costa, João Vitor de Paula Freitas contributed to the wording of the article and Osias Vieira de Oliveira Filho contributed to the wording and review of the article. All the authors approved the final manuscript to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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