

Profile of patients and factors related to the clinical staging of oral squamous cell carcinoma

Perfil de pacientes y factores relacionados con la clasificación clínica del carcinoma de células escamosas en la cavidad oral

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ABSTRACT

Objective The aim of the present study was to identify the profile of patients diagnosed with oral squamous cell carcinoma (SCC) and factors associated with the clinical stage of the disease.

Materials and Method A cross-sectional study was conducted with a sample of 293 medical charts of patients with SCC treated at an oncology reference center in the city of Campina Grande (Brazil) between 2000 and 2006. Descriptive and inferential statistics were performed with robust Poisson regression ($\alpha=5\%$).

Results Males (56.6%), non-white individuals (49.0%) and individuals over than 60 years of age (74.1%) were the most affected by SCC. The tongue (35.1%) and palate (21.5%) were the most common sites. A large portion of the patients were smokers (37.6%) and 60.2% were in an advanced stage of the disease. Clinical staging was not associated with sex, age, skin color or drinking and/or smoking habits.

Conclusion There was a higher incidence of SCC in men, older patients, non-white individuals and smokers. Clinical staging was not associated with the variables analyzed.

Key Words: Squamous cell carcinoma; mouth; neoplasm staging (*source: MeSH, NLM*).

RESUMEN

Objetivos Identificar el perfil de los pacientes con diagnóstico de carcinoma de células escamosas (CCE) de la boca y los factores asociados a la estadificación clínica de la enfermedad.

Métodos Estudio transversal con muestra de 293 historias de pacientes portadores de CEC, atendidos en un Centro de Referencia de Oncología del municipio de Campina Grande (PB), de 2000 a 2006. Se utilizó estadística descriptiva e inferencial por medio de la Regresión Robusta de Poisson ($\alpha=5\%$).

Resultados El sexo masculino (56,6%), los no blancos (49,0%) y el grupo de más de 60 años (74,1%) fueron los más afectados por la neoplasia; la lengua (35,1%) y el paladar (21,5%) fueron los sitios más afectados; la mayoría poseía hábito de tabaquismo (37,6%) y el 60,2% presentaba etapa avanzada de la enfermedad. La estadificación clínica no se asoció al sexo, la edad, el color de la piel y a los hábitos de beber y/o fumar.

Conclusiones Se observó una mayor ocurrencia de CEC en hombres, en pacientes con edad más avanzada, no blancos y que poseían hábitos de tabaquismo, pero sin asociación estadística.

Palabras Clave: Carcinoma de células escamosas; boca; estadificación de neoplasias (*fuentes: DeCS, BIREME*).

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Cancer refers to a set of chronic, degenerative diseases with disorderly cell growth that can spread to other parts of the body (1). This is an important public health problem worldwide, with an estimated annual incidence of 14 million cases, accounting for approximately 8.2 million deaths per year (2).

Mouth cancer is among the ten most frequent types of cancer in the Brazilian population and is the sixth leading cause of cancer in the world (2). Squamous cell carcinoma (SCC) is a malignant tumor that originates in the stratified squamous epithelium; it is the most common tumor of the head and neck region, accounting for approximately 90% of malignant tumors in the oral cavity (3,4). SCC is more common in men between the fifth and seventh decades of life and the tongue is the most commonly affected anatomical site (5-7).

SCC has a multifactor etiology that has not yet been fully clarified (8). Smoking and alcoholism are considered the main etiopathogenic factors and the combination of these two habits increases the risk of developing cancer (9-11). However, oral SCC can also develop in individuals without either of these habits (12,13).

Even though examining the oral cavity is easy, most cases of mouth cancer are detected in late stages. (8) This situation affects the type of treatment used, as therapeutic procedures vary depending on the stage and histological factors (14). Thus, the early detection of a malignant tumor increases the odds of patient survival (15).

The aim of the present study was to identify the profile of patients diagnosed with oral SCC and treated at an oncology reference center, and the factors associated with the clinical staging of the disease in a six-year period in the city of Campina Grande (northeastern Brazil).

MATERIALS AND METHODS

A descriptive, analytical, cross-sectional study was conducted with a census sample nested in a global, accumulated survival study of patients with oral SCC in a six-year period. A total of 293 medical charts of patients treated at an oncology reference center (Paraíba Assistance Foundation Hospital) in the city of Campina Grande (Paraíba, Brazil) between 2000 and 2006 were analyzed.

An individual clinical chart designed specifically for this study was used to collect data. The data on the patient charts were duly recorded, including socio-demographic profile, tumor characteristics, clinical staging and proposed treatment. The inclusion criteria were a diagnosis of oral SCC at the aforementioned reference center between 2000 and 2006, registration at the hospital and patient records with the results of the histopathological exam.

Oral SCC with confirmation by histopathological exam was the dependent variable. The independent variables were location of the tumor, socio-demographic factors, lifestyle habits, clinical staging (TNM) and grouping based on the recommendations of the American Joint Committee on Cancer (16). Initial staging or early diagnosis was recorded for cases in which the tumor was in Stage I or II at the time of diagnosis. Advanced staging or late diagnoses were recorded for cases in which the tumor was in Stage III or IV at the time of diagnosis (16).

This study was approved by the Human Research Ethics Committee of the State University of Paraíba (Brazil) under process number 0223.0.133.000-11 in compliance with Resolution 196/96 of the Brazilian National Board of Health. Data were collected with the authorization of the department chief and the hospital administration.

A simple descriptive analysis was performed to characterize the sample. Bivariate Poisson regression with robust variance was used to determine associations between the independent variables (sex, age, race and lifestyle habits) and clinical staging of the tumor ($p < 0.05$). Multivariate Poisson regression models were constructed with variables achieving a p-value of < 0.20 in the bivariate analysis, as well as variables considered epidemiological determinants. The Statistical Package for Social Sciences (SPSS for Windows, version 18.0, SPSS Inc, Chicago, IL, USA) was used for the organization and analysis of the data.

RESULTS

Fourteen patient charts (4.8%) were excluded from the sample due to the lack of histopathological results that confirmed the diagnosis of oral SCC. Out of 279 cases analyzed, 158 (56.6%) were men and 121 (43.4%) were women (ratio: 2 to 1.5, respectively). The mean age was 65 years in men and 71 years in women. In 206 cases (74.1%), age was over 60 years. The overall mean age was 67 years (range: 27 to 94 years). Non-white individuals predominated in the sample (49.0%). At the time of diagnosis, a large part of the sample smoked (37.6%) and 36.5% used both tobacco and alcohol. The tongue was the most frequently affected anatomical site (98 cases; 35.1%) (Table 1).

A total of 52% cases were classified at T1 and T2; 48% of cases presented metastasis in adjacent lymph nodes (N1 and N2) and only one case of distant metastasis was found. Most cases were in advanced stages: 41.6% in Stage III and 18.6% in Stage IV (Table 2).

In the bivariate analysis, the following variables were associated with clinical staging: sex, age, race and lifestyle habits. However, none of these variables remained in the final multiple Poisson regression model (Table 3).

Table 1. Distribution of oral SCC cases according to sex, age, ethnicity, anatomical site and smoking and alcohol use

Variable	Total N°	Total%
Sex		
Male	158	56.6
Female	121	43.4
Total	279	100
Age		
0-59	72	25.9
60+	206	74.1
Total	278	100
Ethnicity		
White	106	38.0
Non-White	137	49.0
No information	38	13.0
Total	279	100
Habits		
Smoking	105	37.6
Alcohol use	04	1.4
Both	102	36.5
Neither	16	5.7
No information	52	18.6
Total	279	100
Anatomical site		
Floor of mouth	40	14.3
Lower gingival tissue	7	2.5
Upper gingival tissue	6	2.2
Lower lip	35	12.5
Upper lip	0	0.0
Tongue	98	35.1
Buccal mucosa	15	5.4
Hard palate	24	8.6
Soft palate	36	12.9
Retromolar region	18	6.5
Total	279	100

Table 2. Clinical characteristics of SCC according to staging reported on patients' charts

Variable	N° of individuals	% at risk
Tumor size (T)		
1 and 2	145	52.0
3 and 4	98	35.1
No information	36	12.9
Lymph node involvement (N)		
0	104	37.3
1 and 2	134	48.0
3	5	1.8
No information	36	12.9
Metastasis (M)		
0	188	67.4
1	1	0.4
X	54	19.4
No information	36	12.9
Staging		
Stage I	37	13.3
Stage II	44	15.8
Stage III	116	41.6
Stage IV	52	18.6
No information	30	10.8

DISCUSSION

Squamous cell carcinoma is the most frequent malignant tumor found in the oral cavity and affects more men than women (15,17,18). In the present study, the male to female ratio was 2:1.5. The larger proportion of men is explained by the more frequent use of alcohol and smoking in this population (8), although, the literature commonly describes an even larger sex difference (19-21). In the

Table 3. Bivariate and multivariate Poisson regression models for clinical staging and sex, age, ethnicity and habits

Variable	Staging		Bivariate		Multivariate	
	I – II	III - IV	p-value	PR	p-value	PR
	N (%)	N (%)		(95% CI)		(95% CI)
Gender						
Male	40 (28.0)	103 (72.0)	0.084	1.175 (0.979-1.410)	0.516	1.050 (0.907-1.216)
Female	41 (38.7)	65 (61.3)		1.00		1.00
Age						
27-67	15 (22.7)	51 (77.3)	0.034	1.202 (1.014-1.425)	0.103	1.120 (0.977-1.283)
68-94	65 (35.7)	117 (64.3)		1.00		1.00
Ethnicity						
White	43 (40.6)	63 (59.4)	0.032	1.00	0.320	1.00
Non-white	37 (27.0)	100 (73.0)		1.228 (1.018-1.481)		1.075 (0.932-1.240)
Habits						
Smoking	36 (36.4)	63 (63.6)	0.299	1.379 (0.752-2.527)	0.452	1.120 (0.834-1.504)
Alcohol	1 (33.3)	2 (66.7)	0.468	1.444 (0.535-3.897)	0.705	1.108 (0.650-1.889)
Both	26 (28.0)	67 (72.0)	0.146	1.561 (0.856-2.846)	0.426	1.133 (0.832-1.543)
Neither	7 (53.8)	6 (46.2)		1.00		1.00

absence of tobacco abuse, the female sex has a greater prevalence rate of cancer of the head and neck (13), but women generally also have a greater survival rate because such tumors are often diagnosed earlier (22).

The mean age in the overall sample was 67 (65 in men and 75 in women) and the most affected age group was 60 to 79 years. A small number of cases occurred in younger individuals, which is coincides with data described

in the literature (23,24). The lower rate of occurrence among younger individuals is explained by shorter exposure time to risk factors, such as alcohol and tobacco, in comparison to older patients, as the increase of age leads to a greater accumulation of the harmful effects of carcinogenic agents (7,8).

In this study, non-white individuals were more affected by SCC (55%) than whites (45%), which differs from what is commonly described in the literature. (25,26) However, information on ethnicity was missing in a significant number of cases, which hinders the interpretation of this finding. Nonetheless, race does not appear to be a determinant factor for mouth cancer (27).

On the other hand, 105 individuals (37.6%) were smokers, 36.5% used both tobacco and alcohol, and 5.7% of cases had neither of the two habits. The combination of tobacco and alcohol is common (28) and a risk factor for mouth cancer. Indeed, patients who are not smokers have tumors with a lower frequency of genetic alterations (9). Therefore, the control of these habits is the best strategy regarding the long-term perspective of this disease (3).

The tongue was the most affected anatomical site (35.13%), followed by the palate (21.50%), floor of the mouth (14.34%) and lip (12.54%). These findings are in agreement with data described in previous studies (7,20,29-30).

A total of 65.5% of the patients received a late diagnosis (Stages III and IV), while 32.5% were diagnosed early (Stages I and II). This situation is common with regard to oral SCC. (5,8,30) The larger number of patients in advanced stages is caused by the fact that such tumors are asymptomatic in early stages, as well as several difficulties of a social nature and a lack of awareness (31).

Clinical staging at the time of treatment was not significantly associated with sex, age, ethnicity, smoking or alcohol use. These findings may be related to the fact that clinical staging does not depend on these variables (30). An advanced tumor stage at the time of diagnosis may be explained by the delayed seeking of treatment due to the absence of pain or minimal pain in the early phase of tumor growth, unawareness of the disease, fear of the diagnosis, socioeconomic difficulties and the lack of knowledge among some healthcare professionals regarding clinical aspects related to oral SCC, leading to a delayed or mistaken diagnosis (32,33).

Although not all patients charts had been filled out correctly, which may have led to information bias, these findings demonstrate that the late diagnosis of oral SCC is common. Thus, there is a need to implement public policies directed at periodic prevention campaigns, greater awareness on the part of the population regarding mouth

cancer and the importance of early diagnosis. Moreover, investments should be made to train healthcare professionals to correctly identify or treat oral SCC or refer the patient to an appropriate center.

The results of the present study demonstrate a higher incidence of SCC in men, older patients, non-white individuals and smokers. Clinical staging was not associated with any of the variables analyzed •

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REFERENCES

1. World Health Organization. Cancer [Internet]. Available at: <https://goo.gl/gtLZdF>. Consulted in January 2015.
2. World Health Organization [Internet]. Global battle against cancer won't be won with treatment alone: effective prevention measures urgently needed to prevent cancer crisis. Available at: <https://goo.gl/zTw5PT>. Consulted January 2015.
3. Grimm M. Prognostic value of clinicopathological parameters and outcome in 484 patients with oral squamous cell carcinoma: microvascular invasion (V+) is an independent prognostic factor for OSCC. *Clin Transl Oncol*. 2012; 14(11):870-80.
4. Moergel M, Kämmerer P, Kasaj A, Armouti E, Alshihri A, Weyer V, et al. Chronic periodontitis and its possible association with oral squamous cell carcinoma - a retrospective case control study. *Head Face Med*. 2013; 9:39.
5. Brandwein-Gensler M, Teixeira MS, Lewis CM, Lee B, Rolnitzky L, Hille JJ, et al. Oral squamous cell carcinoma: histologic risk assessment, but not margin status, is strongly predictive of local disease-free and overall survival. *Am J Surg Pathol*. 2005; 29(2):167-178.
6. Montebugnoli L, Gissi DB, Flamminio F, Gentile L, Dallera V, Leonardi E, et al. Clinicopathologic parameters related to recurrence and loco-regional metastasis in 180 oral squamous cell carcinomas. *Int J Surg Pathol*. 2014; 22(1):55-62.
7. Troeltzsch M, Knösel T, Eichinger C, Probst F, Troeltzsch M, Woodlock T, et al. Clinicopathologic features of oral squamous cell carcinoma: do they vary in different age groups? *J Oral Maxillofac Surg*. 2014; 72(7):1291-1300.
8. Fronie A, Bunget A, Afrem E, Preotescu LL, Puscu DC, Strela L et al. Squamous cell carcinoma of the oral cavity: clinical and pathological aspects. *Rom J Morphol Embryol*. 2013; 54(2):343-8.
9. Loyha K, Vatanasapt P, Promthet S, Parkin DM. Risk factors for oral cancer in northeast Thailand. *Asian Pac J Cancer Prev*. 2012; 13(10):5087-5090.
10. Radoj L, Paget-Bailly S, Cyr D, Papadopoulos A, Guida F, Tarnaud C, et al. Body mass index, body mass change, and risk of oral cavity cancer: results of a large population-based case-control study, the ICARE study. *Cancer Causes Control*. 2013; 24(7):1437-48.
11. Sousa FB, Freitas e Silva MR, Fernandes CP, Silva PG, Alves AP. Oral cancer from a health promotion perspective: experience of a diagnosis network in Ceará. *Braz Oral Res*. 2014; 28:1-8.
12. Kruse AL, Bredell M, Gratz KW. Oral squamous cell carcinoma in non-smoking and non-drinking patients. *Head e Neck Oncol*. 2010; 2:1-3.
13. Qaisi M, Vorrasi J, Lubek J, Ord R. Multiple primary squamous cell carcinomas of the oral cavity. *J Oral Maxillofac Surg*. 2014; 72(8):1511-1516.

14. Lawaetz M, Homøe P. Risk factors for and consequences of inadequate surgical margins in oral squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2014; 118(6):642-6.
15. Shah JP, Gil Z. Current concepts in management of oral cancer--surgery. *Oral Oncol.* 2009; 45(4-5):394-401.
16. Greene FL, Page D, Morrow M, Balch C, Haller D, Fritz A, et al. *AJCC Cancer Staging Manual.* 6th ed. New York: Springer; 2002.
17. Bagan J, Sarrion G, Jimenez Y. Oral cancer: clinical features. *Oral Oncol.* 2010; 46(6):414-7.
18. Martins JD, Andrade JOM, Freitas VS, Araújo TM. Determinantes sociais de saúde e a ocorrência de câncer oral: uma revisão sistemática de literatura. *Rev. salud pública (Bogotá).* 2014; 16(5): 786-798, 2014.
19. Camisasca DR, Silami MA, Honorato J, Dias FL, de Faria PA, Lourenço S de Q. Oral squamous cell carcinoma: clinicopathological features in patients with and without recurrence. *ORL J Otorhinolaryngol Relat Spec.* 2011; 73(3):170-6.
20. Pires FR, Ramos AB, Oliveira JB, Tavares AS, Luz PS, Santos TC. Oral squamous cell carcinoma: clinicopathological features from 346 cases from a single oral pathology service during an 8-year period. *J Appl Oral Sci.* 2013; 21(5):460-7.
21. Teixeira AKM, Almeida MEL, Holanda ME, Sousa FB, Almeida PC. Oral squamous cell carcinoma: an epidemiological study conducted at Santa Casa de Misericórdia Hospital of Fortaleza - Ce, Brazil. *Rev Bras Cancerol.* 2009; 55(3):229-36.
22. Rikardsen OG, Bjerkli IH, Uhlin-Hansen L, Hadler-Olsen E, Steigen SE. Clinicopathological characteristics of oral squamous cell carcinoma in Northern Norway: a retrospective study. *BMC Oral Health.* 2014; 14:103.
23. Lubek JE, Dyalram D, Perera EH, Liu X, Ord RA. A retrospective analysis of squamous carcinoma of the buccal mucosa: an aggressive subsite within the oral cavity. *J Oral Maxillofac Surg.* 2013; 71(6):1126-31.
24. Udeabor SE, Rana M, Wegener G, Gellrich NC, Eckardt A. Squamous cell carcinoma of the oral cavity and the oropharynx in patients less than 40 years of age: a 20-year analysis. *Head e Neck Oncol.* 2012; 4:1-7.
25. Mendez M, Carrard VC, Haas AN, Lauxen Ida S, Barbachan JJ, Rados PV, et al. A 10-year study of specimens submitted to oral pathology laboratory analysis: lesion occurrence and demographic features. *Braz Oral Res.* 2012; 26(3):235-41.
26. Mosele JC, Stangler LP, Trentin MS, Silva SO, Carli JP. Epidemiological Survey of Cases of Squamous Cell Carcinoma in the Oral Cavity Recorded in the Histopathological Diagnosis Department in the Institute of Biological Sciences at the University of Passo Fundo/RS. *Rev Odontol.* 2008; 16(32):18-24.
27. Durazzo MD, Araujo CEN, Brandão Neto JS, Potenza AS, Costa P, Takeda F et al. Clinical and epidemiological features of oral cancer in a medical school teaching hospital from 1994 to 2002: increasing incidence in women, predominance of advanced local disease, and low incidence of neck metastases. *Clinics.* 2005; 60(4):293-98.
28. Arrais-Ribeiro GL, Clementino MA, Cesarino-Gomes MN, Firmino RT, Dantas-Siqueira MBL, Granville-García AF. Smoking, behavioral factors and familial environment: a population based study with Brazilian adolescents. *Rev. salud pública. (Bogotá)* 2013; 15(3):342-53.
29. Biron VL, O'Connell DA, Seikaly H. The impact of clinical versus pathological staging in oral cavity carcinoma: a multi-institutional analysis of survival. *J Otolaryng - Head and Neck Sugery.* 2013; 42(1):1-4.
30. Seoane-Romero JM, Vázquez-Mahía I, Seoane J, Varela-Centelles P, Tomás I et al. Factors related to late stage diagnosis of oral squamous cell carcinoma. *Med Oral Patol Oral Cir Bucal.* 2012; 17(1):35-40.
31. Santos LCO, Batista OM, Cangussu MCT. Characterization of oral cancer diagnostic delay in the state of Alagoas. *Braz J Otorhinolaryngol.* 2010; 76(4):416-22.
32. Pinheiro SMS, Cardoso JP, Prado FO. Oral Cancer Knowledge and Diagnosis among Dentists from the City of Jequié, Bahia. *Rev Bras Cancerol.* 2010; 56(2):195-205.
33. Tucci R, Borges FT, Castro PHS, Aburad A, Carvalhosa AA. Evaluation of 14 cases of oral squamous cell carcinoma with delayed diagnosis. *Rev Sul-Bras Odontol.* 2010; 7(2):231-8.