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Oral squamous cell carcinoma: survival, recurrence and death

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ABSTRACT. This paper was based in data survey from macro and microscopic oral lesions characteristics, personal data and medical history of patients diagnosed with oral squamous cell carcinoma in the Lab of Pathological Anatomy from the Federal University of Alfenas from January 2000 to December 2010, establishing comparative parameters among clinical data, type of treatment, recurrence, survival and anatomic pathological characteristics of the lesions. Were analyzed the histopathological reports, dental and hospital records. The highest incidence was in white men, age between 50 and 60 years, married, with low education and socioeconomic levels. The beginning of treatment occurred in average 67 days after the histopathological diagnosis. The estimated survival of patients at five years was 42%. The consumption of alcohol and tobacco and the occurrence of metastasis were statistically significant for the increase of recurrence and lethality.

Keywords: squamous cell carcinoma, oral cancer, oral pathology, epidemiology, prognosis, analysis of survival.

Carcinoma de células escamosas da boca: sobrevida, recidiva e óbitos

RESUMO. O estudo realizou levantamento das características macro e microscópicas das lesões bucais, dados pessoais e históricos dos pacientes diagnosticados com carcinoma de células escamosas da boca no Laboratório de Anatomia Patológica da Universidade Federal de Alfenas entre janeiro de 2000 e dezembro de 2010. Estabeleceram-se parâmetros comparativos entre os dados clínicos, tipo de tratamento, recidivas, sobrevida e características anatomopatológicas das lesões. Foram analisados os laudos histopatológicos e os prontuários odontológicos e hospitalares. A maior incidência ocorreu em homens brancos, com idade entre 50 e 60 anos, casados, com baixa escolaridade e nível socioeconômico. O início do tratamento ocorreu, em média, 67 dias após o diagnóstico histopatológico. A sobrevida estimada dos pacientes aos cinco anos foi de 42%. O consumo de álcool e tabaco e a presença de metástases foram estatisticamente significativos para o aumento da recidiva e da letalidade.

Palavras-chave: carcinoma de células escamosas, câncer da boca, patologia bucal, epidemiologia, prognóstico, análise de sobrevida.

Introduction

Although, there is no clear comprehension of cancer etiology, a lot of determinants factors had been detected and researched (OLIVEIRA et al., 2006). Takács et al. (2011) checked that the excessive alcohol consumption is an important risk factor for both sexes. However, the moderate alcoholic intake is a risk factor for men and decreases the risks in women.

Even though, mouth cancer is a multifactorial disease, the alcohol and the tobacco are the most important risk factors, not only for neoplasias development, but also for prognostics related or not to chronic trauma, poor oral hygiene, low carotene intake and family history of cancer (BUNDGAARD et al., 1994).

There is a tendency of increase in the number of smokers in Latin America, among young people and mostly among women. In Ibadan, Nigeria, most of the patients that presented oral squamous cell carcinomas (OSCC) did not use tobacco or ingested alcohol beverages, having in common to belong to a low income class (ADEYEME et al., 2011).

The localization of the lesion has direct relation to diagnostic and prognostic. The lip cancer has good prognosis (DEMATHE et al., 2011), is easily seen, being able to early, diagnosed. The tumors located on the hard palate and in the cheek mucosa according to Honorato et al. (2009) presents worse prognostic.

The prognostic is usually based in clinical classification TNM that asses the fundamental

characteristics of a cancer such as local extension, regional spreading and metastases at distance (COSTA et al., 2002).

Camisasca et al. (2011) compared the pathologic clinical profile of OSCC in groups with and without recurrence. It was found that the tumor location, tobacco consumption and the pathological characteristics are related in recurrence and should be considered for treatment and attendance.

The time of development of the lesions in the oral cavity influences directly in the disease prognostic. Collected data in Brazil, by Gervásio et al. (2001), showed that although the time of development is a below one year, in the most part of it, the stage is already advanced. Groome et al. (2011) carried out a population based research in Ontario, Canada, and it was verified that there are some groups of patients that are most likely to be diagnosed with the disease already advanced.

The cancer biological behavior that is developed in young people is different from the one found in patients with advanced age. In Brazil, carriers of squamous cell carcinoma (SCC) of the tongue and floor of the mouth from the Amazon region, the only prognostic factors that affect the survival rate at five years was the age at the moment of the diagnostic and treatment with surgical procedure (PONTES et al., 2011). Davidson et al. (2001) analyzed that the SCC of the tongue and verified a 10 years age increasing in patients correspond to 18% increase in the risk of death.

The choice for the most adequate treatment depends on factors like: local, primary tumor extension, age and ganglionic involvement. The five years of overall survival can be influenced by the treatment method according to Kawakita et al. (2012) research, analyzing the impact of smoking on the clinical results in patients with cancer in the oral cavity treated at the Center of Cancer of Aichi, in Japan. Researchers from the Dentist School from the University of Manchester demonstrated that chemotherapy, besides radiotherapy and surgery, is associated to an improvement in the overall survival rate in patients with cancer in the oral cavity and oropharynx (FURNESS et al., 2011).

The mainly causes of failure in the treatment are: local recurrence, regional recurrence and distance metastasis. The regional recurrence in the cervical lymph nodes is the most predominant modality. The survival rate decreases with the increasing of the number of metastatic lymph nodes involved and how much farther are from the primary lesion, worse is the prognostic (RAPOPORT, 1976). The primary site, initial staging, recurrence place, disease-free survival and palliative cares, did not influence the survival after the recurrence (AMAR et al., 2005). The longest survival is presented by the patients that did not present an impairment lymph node during the diagnosis and were submitted to surgery at the initial stages.

The low survival rates and the high percentage of advanced stages reflects the need of bigger attention to oral cancer (DAHER et al., 2008). Therefore, this study proposes to conduct a survey of the macroscopic and microscopic features of oral lesions of patients diagnosed with OSCC. Identify the type of treatment to which they were submitted and establish parameters for comparison between the clinical data, the type of treatment, recurrence, patient survival and the pathologic features of the lesions biopsied.

Material and methods

The research project was approved by the Ethical Committee in Researches from the University Sagrado Coração in October 28, 2010 under the number 197/2010.

This study made a survey data retrospective epidemiological of patients diagnosed with oral squamous cell carcinoma (OSCC) by the lab of pathological anatomy of the Federal University of Alfenas from January 2000 to December 2010. All patients that have hospital and/or dental records found were included. The patients that had histopathological diagnosis of OSCC different from the slides review and/or biopsy surgical specimen were excluded.

From the anatomopathological reports, hospital and dental patients' records were collected the following information: age, gender, skin color, marital status, profession, alcohol and/or tobacco consumption, lesion location, cancer's evolution time, professional clinical suggested diagnosis, histopathological diagnosis, grading, staging, treatment, exams results from surgical specimen, recurrence, survival and death. The social economic and cultural condition was obtained from the social assistance report indexed with the hospital record or analysis of personal data of patients, respecting the established parameters of social assistance. The collected data were used to verify the influence of each factor on the mortality index.

In order for defining the anatomical location, it was adopted as reference the International Classification of Diseases - 10th edition (ICD - 10) by World Health Organization (WHO) of SCC. It was considered the anatomic sites: lips (ICD. C00), tongue (ICD. C02), gums (ICD. C03), floor of the mouth (ICD.C04), palate (ICD.C05), buccal

mucosa (ICD.C06.0), vestibulum (ICD.C06.1) and retromolar area (ICD.C06.2).

The tumors received the histopathological grading recommended by the WHO (LOURENÇO et al., 2007): less differentiated; moderately differentiated; well differentiated. The clinical stage TNM obeys the version established by the Union for International Cancer Control (UICC), considering each staging separately for statistical analyze.

The Fisher's exact test was used to analyze variables with two categories and Chi-Square Test for the three or more categories. The mean time elapsed between the diagnosis and the treatment start was analyzed by the Student's *t* test. It was used the box plot for the cases of death and survivals.

The overall survival was calculated starting from the initial diagnosis determinate by biopsy until the last follow or patients' death, considering a significance level of 5%. The survival curve was estimated by the method of Kaplan-Meier and the Log-Rank test was used to compare of survival curve considering the variables. The statistical tests were made using the software R 2.14.

Results

In the considered time, it was made 3610 oral lesions exams, being 2.33% diagnosed with oral squamous cell carcinoma. The study analyzed 54 patients, 38 men (70.4%) and 16 women (29.6%). The patients' ages during the time of the diagnosis are from 24 to 91 years.

The influence of demographic (Table 1) and socioeconomic characteristics on mortality was not statistically significant (Table 2).

Table 1. Demographic characteristics.

Variable	Deaths		Test	p value
	Yes	No		
Gender				
Female	5	11	Fisher'sexact	0.622
Male	12	26		
Age group				
< 50 years	2	8	Chi-square	0.793
50 a 60 years	10	15		
> 60 years	5	14		
Skin color				
Leucoderma	13	24	Chi-square	0.476
Melanoderm	1	6		
Feoderma	3	4		
Marital status				
Married	4	19	Chi-square	0.309
Single/maiden	5	6		
Widower/widow	3	4		
Divorced	2	5		

The absolute values show a higher incidence in white patients, male, with age between 50 and 60 years, single, low social and economic levels, farmers or housekeepers that took only the primary school.

Table 2. Socioeconomic and culture profile.

Variable	Death		Test	P value
	Yes	No		
Education				
Illiterate	0	5	Chi-square	0.364
Basic education	7	18		
High school/college education	1	5		
Socioeconomiclevel				
Low	13	21	Chi-square	0.342
Medium	1	7		
High	1	1		
Profession				
Farmer	5	7	Chi-square	0.586
Housekeeper	4	6		
Mason/carpenter/ general services	2	9		
Other	5	13		

The anatomic regions distribution affected by OSCC is shown in the Table 3. There was no validating statistical for association between the lesion site, recurrence and lethality rate.

Table 3. Distribution of lesions in the sample recording the anatomical site.

Anatomical sites	Óbitos	Vivos	Total
CID C00 Lips	0	4	4
CID C02 Tongue	2	9	11
CID C03Gums	3	6	9
CID C04Floor of de mouth	5	12	17
CID C05 Palate	1	1	2
CID C06.0Buccal mucosa	3	2	5
CID C06.1 Vestíbulum	1	1	2
CID C06.2 Retromolar area	2	2	4
Total	17	37	54

Smoking or drinking habits were told by the patients themselves during the anamneses. The Fisher's exact test showed statistical significance of smoking and drinking on the lethality rate (Table 4).

Table 4. Risk factors.

Variable	Deaths		Test	p value
	Yes	No		
Alcoholism				
Alcoholic	13	18	Fisher'sexact	0.047
Abstemious	3	16		
Tobacco				
Smoker	16	25	Fisher'sexact	0.021
Not smoking	0	10		

It was register a mean time of 71.17 days for the treatment beginning for the patients that died later (standard deviation 50.34) and 62.19 days (standard deviation 36.73) for survives. There was no significance dispersion and most of patients had the treatment initiated in 60 and 90 days (Figure 1).

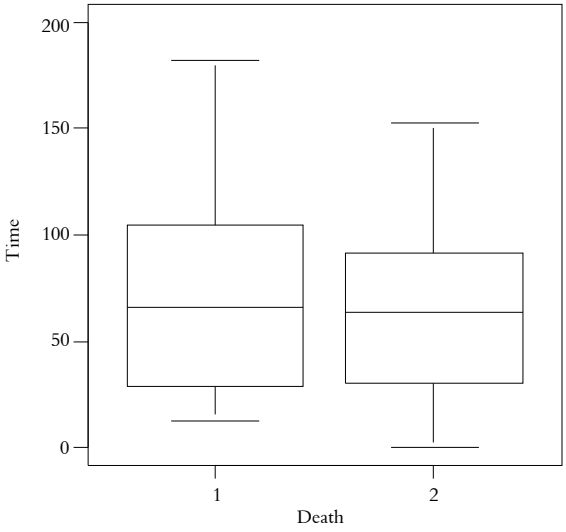

Figure 1. Elapsed time between histopathological diagnosis and beginning of treatment. Subtitle: 1- Yes; 2- Not; Time in days

This study did not register a poorly differentiated tumor. Among tumors classified as well and moderately differentiated, there was no significant influence of histological grading on lethality (Table 5).

Table 5. Gradation, staging, treatment and recurrences.

Variable	Deaths		Test	P value
	Yes	No		
Grading				
Well diferenciated	6	9	Fisher'sexact	0.747
Moderately diferenciated	11	23		
Stading T				
T1	1	9	Notvalid	
T2	3	9		
T3	2	3		
T4	6	6		
Stading N				
N0	3	21	Chi-square	0.008
N1	3	5		
N2	6	3		
Stading M				
M0	5	26	Fisher'sexact	0.040
M1	2	0		
Treatment				
Surgery	1	14	Chi-square	0.0100
Surgery + radiotherapyand/ orchemotherapy	5	16		
Radiotherapyand/ orchemotherapy	7	5		
Recurrence				
Yes	12	1	Fisher'sexact	<0.0001
No	4	26		

The existence of mild and moderate lymph nodes metastasis raised the number of deaths and the presence of distant metastasis was determinant for the raising in the lethality rate (Table 5).

About the OSCC treatment, it was analyzed the effectiveness of different therapeutics resorts, used isolated or associated. It was verified that the surgery used as the only therapeutic resort or associated presented better results (Table 5).

In this study were related 17 occurrences and no cases included escaped observation. The last follow occurred in May and June of 2011. The overall survival rate in five years was 42%. The survival curve comparing the alcoholics and the abstainers was not statistical significant ($p = 0.245$) for lethality. The smokers survival ($p = 0.0342$) at five years is 39%, while for the not smokers there is no such occurrence. The occurrence of recurrences ($p < 0.001$) affected expressively the lethality rate (Figure 2).

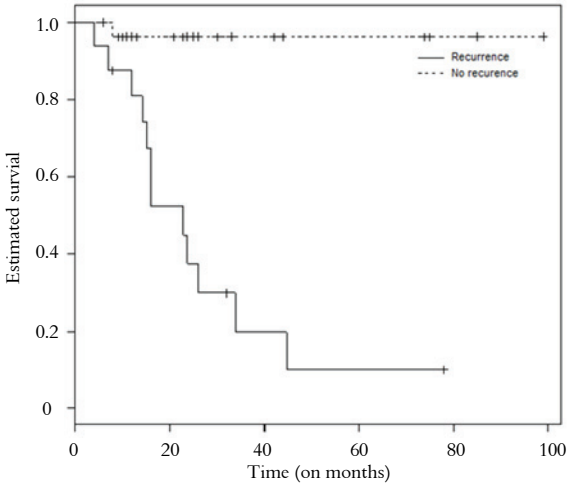

Figure 2. Survival curves in relation to recurrence.

Discussion

The results obtained follow other national studies, like Oliveira et al.(2006), that in a 10 years period, found 340 cases, 84.4% were men and 15.6% were women, and Perez et al. (2007) that in a retrospective observational study related 522 cases in five years, with male predominance, following a ratio of 5:1.

The analysis of the demographic and socioeconomic characteristics shows similar results to those found by Perez et al. (2007) in patients with SCC treated from years 2000 to 2004 at the Heliopolis Hospital in São Paulo and Daher et al. (2008) at the hospital of Uberaba during the years of 1999 to 2003. Elderly patients presented different cancer biological behavior and a death risk increase (DAVIDSON et al., 2001; PONTES et al., 2011).

The location of the tumor has an impact on the perception of the Quality of Life (SILVEIRA et al., 2012). Oliveira et al. (2006) did not find significant differences analyzing the anatomic regions and the occurrence of recurrences and distant metastasis. It was verified the higher incidence of lesions in the floor of the mouth and tongue with lethality rate of

29.4 and 27.3% respectively, and lower incidence in the vestibulum and palate, with rate of 50% of lethality. Patients with lip cancer presented the lowest lethality rate, and there were no deaths, results that agree with Demathe et al. (2011) papers that show only one case of death in a study of 30 cases. The highest lethality rate occurred in the cheek mucosa with 60% of lethality, confirming Honorato et al. (2009) studies. In Table 3, it was verified a higher number of deaths between patients with SCC classified as T4 (50%) and the lowest with T1 (11.1%), similar results were found in Camisasca et al. (2011) studies.

This study confirms Takács et al. (2011) papers showing that alcohol is an expressive risk factor for both sexes. Bundgaard et al. (1994) affirms that tobacco and alcohol are the two most important risk factors for the development and prognosis of neoplasms usually being associated to other factors (TAKÁCS et al., 2011). The isolated use of alcohol or tobacco is rather frequent, so, there is an association between the carcinogenic effects (PEREZ et al., 2007). Studies show that smoking and drinking habits establishing a synergism between these two factors, increasing thirty times the risk for development of this kind of cancer (BRASIL, 2011). Although, Adeyeme et al. (2011) related that in Ibadan, most of the patients with SCC of the mouth did not make use of tobacco or alcoholic beverages.

The time of initiation of treatment for patients, who died later, has upper and lower limits higher than the limits of the patients that survived, demonstrating a relation between the time to the beginning of the treatment after the histopathological diagnosis and lethality. In Brazil, in 2011, o Court of Audit, found an average superior to 70 and 100 days for the chemotherapy and radiotherapy beginning respectively. It is consensus that the lesion time of development and its stage influences directly the prognosis (GERVÁSIO et al., 2001), existing more willing groups to be diagnosed with the advanced disease (GROOME et al., 2011).

In this study, the analysis of the gradation differs from the results found by Costa et al. (2002) that showed a relation between the queratinization grade, nuclear pleomorfism, lymphocytic infiltration and clinical TNM classification, that in this study, influencing the lethality rate. The staging was significant, all patients that presented distant metastasis died. These results are similar to Rapoport (1976).

The effectiveness of therapeutic resorts are checked according to Pontes et al. (2011) studies, made in Amazon region. The chemotherapy isolated or associated with radiotherapy is related to a higher number of deaths (Table 5). However, according to Furness et al. (2011) the chemotherapy associated to surgery improves the overall survival.

The determined survival (42%) is higher than the one found by Oliveira et al. (2006) (24%). Daher et al. (2008) found rates of 24.53% for patients rout by the public health and 69.51% of patients rout by private practice. These rates can be influenced by the treatment methods (KAWAKITA et al., 2012). In this study the expressive number of patients included in the last years in the analyzed time cut, may have influenced the result.

The survival compared between drinkers and abstainers may have been influenced by the difficulty of getting more precise information about the time of consumption and alcohol quantity ingested. However, in the five years was verified a higher survival (70%) for abstainers than alcoholics (40%). Studies indicate alcohol abuse corresponds to nearly 16% of deaths (BRASIL, 2011). The survival rate of 39% determined for smokers confirms the data from the National Institute of Cancer (BRASIL, 2011) that attribute to the smoking habits are responsible for 42% of deaths for oral cancer, agreeing with Kawakita et al. (2012) papers that show a worse clinical result for smokers patients.

The straight relation verified between the occurrence of recurrence and lethality rate is agrees to Camisasca et al. (2011). The Kaplan-Meier curves show a survival rate accumulated at five years of 10% for patients with recurrence and 95% for not recurrence cases. According to Amar et al. (2005) the survival after a incurable recurrence is similar to that related for untreated patients. The palliative cares did not increase the survival of these patients.

This study agree with Honorato et al. (2009),that the best way to express the prognosis tumor's is to analyze the mortality rate, establishing severity index, both in terms of clinical and public health.

Conclusion

The epidemiological data shows patients with a profile similar to other description in the literature. The results found for the most effective form of treatment, percentage of the estimated recurrence and survival are confirmatory of other studies on the subject.

The high number of deaths found reflects the need of campaigns to combat the alcohol and tobacco consumption and investments in human resources and infrastructure that allows earlier diagnosis and early time for the treatment beginning.

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References

ADEYEME, B. F.; OLUSANYA, A. A.; LAWOVIN, J. O. Oral squamous cell carcinoma, socioeconomic status and history of exposure to alcohol and tobacco. **Journal of the Medical Association**, v. 103, n. 6, p. 498-502, 2011.

AMAR, A.; ORTELLADO, D. K.; FRANZI, A. S.; CURIONI, A. O.; RAPOPORT, A. A sobrevida após recidiva intratável do carcinoma epidermóide de cabeça e pescoço**. Revista do Colégio Brasileiro de Cirurgiões**, v. 32, n. 5, p. 267-269, 2005.

BRASIL. Ministério da Saúde, Secretaria de Atenção à Saúde, Instituto Nacional do Câncer, Coordenação de Prevenção e Vigilância, Divisão de Informação. **Estimativa 2012**: incidência de câncer no Brasil. Rio de Janeiro: INCA, 2011. p. 40-41.

BUNDGAARD, T.; BENTZEN, S. M.; WILDT, J. The prognostic effect of tobacco and alcohol consumption in intra-oral squamous cell carcinoma. **European Journal of Cancer Part B: Oral Oncology**, v. 30, n. 5, p. 323-328, 1994.

CAMISASCA, D. R.; SILAMI, M. A. N. C.; HONORATO, J.; DIAS, F. L.; FARIA, P. A. S.; LOURENÇO, S. Q. C. Oral Squamous Cell Carcinoma: Clinicopathological Features in Patients with and without Recurrence. **Journal for Otorhinolaryngol and its Related Specialties**, v. 73, n. 3, p. 170-176, 2011.

COSTA, A. L. L.; PEREIRA, J. C.; NUNES, A. A. F.; ARRUDA, M. L. S. Correlação entre a classificação TNM, gradação histológica e localização anatômica em carcinoma epidermóide oral. **Pesquisa Odontológica Brasileira**, v. 16, n. 3, p. 216-220, 2002.

DAHER, G. C. A.; PEREIRA, G. A.; OLIVEIRA, A. C. A. Características epidemiológicas de casos de câncer de boca registrados em hospital de Uberaba no período 1999-2003: um alerta para necessidade de diagnóstico precoce. **Revista Brasileira de Epidemiologia**, v. 11, n. 4, p. 584-596, 2008.

DAVIDSON, B. J.; ROOT, W. A.; TROCK, B. J. Age and survival from squamous cell carcinoma of the oral tongue. **Head Neck**, v. 23, n. 4, p. 273-279, 2001.

DEMATHE, A.; GARCIA, J. F.; MATTAR, N. J.; SIMONATO, L. E.; MIYAHARA, G. I. Human papillomavirus (HPV) detection in lip squamous cell carcinoma: correlation with clinical aspects and risk factors. **Revista Brasileira de Epidemiologia**, v. 14 n. 1, p. 98-105, 2011.

FURNESS, S.; GLENY, A. M.; WORTHINGTON, H. V.; PAVITT, S.; OLIVER, R.; CLARKSON, J. E.; MACLUSKEY, M.; CHAN, K. K.; CONWAY, D. I. Interventions for the treatment of oral cavity and oropharyngeal cancer: chemotherapy. **Cochrane Database Systematic Reviews**, v. 13, n. 4, 2011.

GERVÁSIO, O. L.; DUTRA, R. A.; TARTAGLIA, S. M.; VASCONCELLOS, W. A.; BABOSA, A. A.; AGUIAR, M. C. Oral squamous cell carcinoma: a retrospective study of 740 cases in a Brazilian population. **Brazilian Dental Journal**, v. 12, n. 1, p. 57-61, 2001.

GROOME, P. A.; ROHLAND, S. L.; HALL, S. F.; IRISH, J.; MACKILLOP, W. J.; O'SULLIVAN, B. A population-based study of factors associated with early versus late stage oral cavity cancer diagnoses. **Oral Oncology**, v. 47, n. 7, p. 642-647, 2011.

HONORATO, J.; CAMISASCA, D. R.; SILVA, L. E.; DIAS, F. L.; FARIA, P. A. S.; LOURENÇO, S. Q. C. Análise de sobrevida global em pacientes diagnosticados com carcinoma de células escamosas de boca no INCA no ano de 1999. **Revista Brasileira de Epidemiologia**, v. 12, n. 1, p. 69-81, 2009.

KAWAKITA, D.; HOSONO, S.; ITO, H.; OZE, I.; WATANABE, M.; HANAI, N.; HASEGAWA, Y.; TAJIMA, K.; MURAKAMI, S.; TANAKA, H.; MATSUO, K. Impact of smoking status on clinical outcome in oral cavity cancer patients. **Oral Oncology**, v. 48, n. 2, p. 186-191, 2012.

OLIVEIRA, L. R.; RIBEIRO-SILVA, A.; ZUCOLOTO, S. Perfil da incidência e da sobrevida depacientes com carcinoma epidermóide oral em uma população brasileira. **Jornal Brasileiro de Patologia e Medicina Laboratorial**, v. 42, n. 5, p. 385-392, 2006.

LOURENÇO, S. Q. C.; SCHUELER, A. F.; CAMISASCA, D. R.; LINDENBLATT, R. C.; BERNARDO, V. G. Classificações histopatológicas para o carcinoma de células escamosas da cavidade ora: revisão de sistemas propostos. **Revista Brasileira de Cancerologia**, v. 55, n. 3, p. 325-333, 2007.

PEREZ, R. S.; FREITAS, S. M.; DEDIVITIS, R. A.; RAPOPORT, A.; DENARDIM, O. V. P.; SOBRINHO, J. A. Estudo epidemiológico do carcinoma espinocelular da boca e orofaringe. **International Archives of Otorhinolaryngology**, v. 11, n. 3, p. 271-277, 2007.

PONTES, F. S. C.; CARNEIRO JR., J. T.; FONSECA, F. P.; SILVA, T. S. P.; PONTES, H. A. R.; PINTO, D. S. Squamous Cell Carcinoma of the Tongue and Floor of the Mouth: Analysis of Survival Rate and Independent Prognostic Factors in the Amazon Region. **The Journal of Craniofacial Surgery**, v. 22, n. 3, p. 925-930, 2011.

RAPOPORT, A. The importance of metastic cervical lymph nodes on the prognosis and therapy of malignant neoplasias of the head and neck. **Tumori**, v. 62, n. 5, p. 473-484, 1976.

SILVEIRA, A.; GONÇALVES, J.; SEQUEIRA, T.; RIBEIRO, C.; LOPES, C.; MONTEIRO, E.; PIMENTEL, F. L. Oncologia de Cabeça e Pescoço: enquadramento epidemiológico e clínico na avaliação da Qualidade de Vida

Relacionada com a Saúde. **Revista Brasileira de Epidemiologia**, v. 15, n. 1, p. 38-48, 2012.

TAKÁCS, D.; KOPPÁNY, F.; MIHÁLYL, S.; SUBA, Z. Decreased oral cancer risk by moderate alcohol consumption in non-smoker postmenopausal women. **Oral Oncology**, v. 47, n. 6, p. 537-540, 2011.

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