

Epidemiological profile and survival analysis of oral and oropharyngeal squamous cell carcinomas: a 10-year retrospective study

Perfil epidemiológico e análise de sobrevivência de carcinomas espinocelulares orais e orofaríngeos: estudo retrospectivo de 10 anos

Perfil epidemiológico y análisis de supervivencia de los carcinomas de células escamosas orales y orofaríngeos: un estudio retrospectivo de 10 años

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Abstract

The aim of this study is to identify the epidemiology profile of oral squamous cell carcinoma in a population of patients treated at the Bom Pastor FHOMUV Hospital of Varginha, in the state of Minas Gerais, Brazil. To this end, the medical records of patients admitted between 2004 and 2014 were collected and analyzed. The variables analyzed were: age, gender, habits, tumor location, histological grade, tumor size, presence of lymph nodes and metastasis, staging, treatment and relapse. The population studied consisted of 310 patients. Men represent the majority of cases – 79.68% - with ages varying around 60 years. The most common tumor locations were tongue (40.32%), oropharynx (21.29%) and floor of mouth (12.90%). Regarding staging, 54.25% of patients were in stage IV, of which 41.92% reached 5-year survival. Radiation combined with chemotherapy was the most prescribed treatment (32.90%). Statistically significant correlations were found between gender and age, gender and tumor location, and tumor location and age. Results suggest a need for the implementation of public policies to prevent and control oral cancer in the state of Minas Gerais, aiming at reducing the number of new cases, promoting early diagnostics and improving prognosis and treatment of such neoplasias.

Keywords: Squamous cell carcinoma; Oral cancer; Epidemiology.

Resumo

O objetivo deste trabalho foi identificar o perfil epidemiológico dos pacientes portadores de Carcinomas Espinocelulares Oraais tratados no Hospital Bom Pastor FHOMUV de Varginha, em Minas Gerais. Foram buscados e revisados registros nos arquivos do período de 2004 a 2014. Foram observadas as variáveis: idade, gênero, hábitos, localização, grau histológico, tamanho do tumor, presença de linfonodos e metástases, estadiamento, tratamento e recidiva. A população pesquisada foi de 310 casos. Observou-se que 79,68% dos casos prevaleceram em homens, com idade variando acima e abaixo de 60 anos. Os sítios mais acometidos foram língua (40,32%), orofaringe (21,29%) e assoalho de boca (12,90%). Sobre o estadiamento, 54,25% dos pacientes apresentaram-se em estágio IV, sendo que 41,92 % destes apresentaram uma sobrevida de 5 anos. Radioterapia associada a quimioterapia foi o tratamento mais realizado (32,90%). Encontrou-se relação estatisticamente significativa entre as variáveis sexo e idade, entre sexo e local acometido, e deste com idade. Os resultados sugerem a necessidade de implantação de uma política de prevenção e controle do câncer bucal no Estado de Minas Gerais, com o intuito de viabilizar a redução no número de casos novos, melhor prognóstico e diagnóstico precoce e, tratamento dessas neoplasias.

Palavras-chave: Carcinoma espinocelular; Câncer bucal; Epidemiologia.

Resumen

El objetivo de este estudio fue identificar el perfil epidemiológico de los pacientes con Carcinomas Orales de Células Escamosas atendidos en el Hospital Bom Pastor FHOMUV en Varginha, Minas Gerais. Se buscaron y revisaron los registros en los archivos desde 2004 hasta 2014. Se observaron las siguientes variables: edad, sexo, hábitos, ubicación, grado histológico, tamaño del tumor, presencia de ganglios linfáticos y metástasis, estadificación, tratamiento y recurrencia. La población estudiada fue de 310 casos. Se observó que el 79,68% de los casos predominó en hombres, con edades que van desde arriba y abajo de 60 años. Los sitios más afectados fueron lengua (40,32%), orofaringe (21,29%) y piso de boca (12,90%). En cuanto a la estadificación, el 54,25% de los pacientes se encontraban en estadio IV, y el 41,92% de estos tenían una supervivencia de 5 años. La radioterapia asociada a quimioterapia fue el tratamiento más realizado (32,90%). Se encontró una relación estadísticamente significativa entre las variables sexo y edad, entre sexo y sitio afectado, y entre edad y género. Los resultados sugieren la necesidad de implementar una política de prevención y control del cáncer oral en el Estado de Minas Gerais, con el fin de posibilitar la reducción del número de casos nuevos, mejor pronóstico y diagnóstico y tratamiento precoz de estas neoplasias.

Palabras clave: Carcinoma de células escamosas; Câncer oral; Epidemiología.

1. Introduction

The estimated number of new cases in 2020, worldwide, both sexes and all ages for all cancers at Cancer today (International Agency for Research on Cancer) described 18 million human cancers excepted non-melanoma skin cancer. The lip and oral cavity cancers account 377 713 malign tumors. The men (16.7) show 2.14 higher risk than women (7.8) for developing lip and oral cavity cancers. Lip and oral cavity cancer is ranked 16th for incidence and mortality in both sexes and 11th for incidence and for mortality 12th in men. In other hand, the incidence of lip and oral cavity cancers for women ranked 18th and 17th for mortality. Oral Squamous Cell Carcinoma (OSCC) or Epidermoid Carcinoma is 90-95% of oral cavity cancer (Carvalho et al., 2001).

Due to the uncertainty surrounding oral cancer evolution, researchers seek for factors that may influence its prognosis. Usually, such pathologies are directly related to genetics; however, this has not been appointed as a determinant factor for the neoplasia (Montoro et al., 2008).

The incidence of oral cancer is growing for the past decades, following an increase in tobacco and alcohol consumption (Guerra et al., 2005). Among intrinsic factors are general or systemic state, such as malnourishment, iron-deprived anemia, and vitamin A deficiency (Freitas et al., 2016; Marchioni et al., 2007). Environmental factors related to industrialization and factors related to social inequities influence the epidemiology of cancer types in Brazil (Marchioni et al., 2007; Guerra et al., 2005). In addition to that, HPV has been recently associated to oral malignancies. This relationship is stronger in 30–45-year-old non-smokers and non-alcoholic men, who engage in unprotected oral sex. (Montenegro et al., 2015).

Studies carried out in different countries and regions of the world searched for data similar to those of the present work and important results were obtained to be analyzed and compared. Goldenberg et al. (2009) analyzed the survival results of patients with squamous cell cancer of the oral cavity in the United States. And, it could conclude that younger patients had a significantly better five-year survival. Meanwhile in Denmark, Larsen et al. (2009) sought to assess the prognostic value of histological features

related to the primary tumor. It was observed that tumor depth and grade were strong prognostic factors for nodal metastasis, regardless of other histological features. Meanwhile, in Brazil, Pithan et al. (2004) also sought to evaluate the epidemiological profile of squamous cell carcinoma of the mouth in patients at the Service of Stomatology and Oral and Maxillofacial Cancer Prevention at Hospital São Lucas, PUCRS. This present study presents very important data that complement the world data when analyzing age, gender, habits, tumor location, histological grade, tumor size, presence of lymph nodes, presence of metastasis, staging, treatment and relapse. These analyzed topics are substantially larger than those of other researches (Pithan et al., 2004), bringing data that have been little discussed so far. In addition, this present study goes further, as it brings an expressive number of 300 patients surveyed, a number greater than most articles present in the literature (Larsen et al. 2009; Huang et al., 2007) and little found in national studies (Mosele et al., 2008). Finally, this study brought complete data, analyzing the regions of lip and oral cavity.

Treatment is surgical with the complete removal of the lesion with the margin of safety, or with radiation for early-stage tumors. For advanced stage tumors, treatment may consist of surgery combined with chemotherapy and radiation. (Souza et al., 2019).

Cancer is a disease with high incidence worldwide and is considered a public-health concern due to its incidence and severity (Santos et al., 2015). Therefore, epidemiology investigations are key for the definitions of effective control measures. (Neville et al., 2004).

The aim of the study was to describe the epidemiological profile of patients with squamous cell carcinoma of the oropharynx and oral cavity and its associations with age, sex, habits, tumor location, histological grade, tumor size, locoregional metastasis, distant metastasis, staging, treatment and recurrence of tumor.

2. Methods

Ethical approval

This study was approved by the Institutional Research Ethics Committee of School of Dentistry, São Paulo State University (UNESP), Araraquara, SP – Brazil (#4545832). All procedures performed in this study, involving human biological material (paraffin-embedded tissue blocks), were in accordance with the law and the national ethical guidelines of the country, and in compliance with the Helsinki Declaration.

Patients

310 cases of OSCC treated at Bom Pastor FHOMUV Hospital of Varginha, from 2004 to 2014, were included. OSCC demographic and clinicopathologic data were collected from patients between January 2004 and December 2014. The inclusion criteria were a histopathologic diagnosis of primary SCC, no preoperative therapy, and demographic and clinicopathologic data.

Data and sample collection

Demographic and clinicopathologic information on each case were obtained retrospectively from the medical records, i.e., age, gender, tumor size, clinical stage and histologic grade at diagnosis, type of treatment, margin and nodal involvement (locoregional metastasis), surgical resection of lymph nodes, presence of extracapsular spread, and patient's status at the last follow-up. The OSCC staging and grading were performed following the American Joint Committee on Cancer (AJCC) ²⁴ and the International Classification of Tumors of WHO criteria ²⁵, respectively.

Statistical analysis

The Pearson's chi-squared test was used to analyze the association between the clinicopathological variables. A Kaplan-Meier analysis was performed to estimate the median overall survival (OS) and disease-specific survival (DSS), while a Log-rank

test was used to compare the survival curves. OS was calculated from the beginning of the primary therapy until death from any cause or the last follow-up (December 2014). DSS was calculated from the primary surgical treatment until cancer-related death or the last follow-up. Patients who did not reach this endpoint were censored at the last follow-up. For multivariate analysis, the Cox proportional-hazards model was used to estimate the independent prognostic impact factors on the survival of patients with TSCC. A P value <0.05 was considered statistically significant for all the analyses, which were performed with Graph pad prism 9.0 (EMPRESA).

3. Results

Patient Data

The demographical, clinical, and histopathological characteristics are presented in Table 1. Three hundred and ten patients with OSCC (247 males and 63 females) with a mean age of 60±11.2 years (range, 21-98) were included. 184 (60,9%) patients were treated with local surgery, and 83 (26.7%) patients received adjuvant radiotherapy, and 82 (26.4%) patients received adjuvant radioter+chemotherapy. 100 (32.2%) patients were treated with radiotherapy+chemotherapy. Eleven (6.1%) patients received curative radiotherapy. 237 (76.4.2%) of the patients were diagnosed with stages IV and IV, 52 (16.7%) with stage II, and 21 (6.7%) with stage I of SCC. No lip SCC patients died and 94 (30.3%) patients died of oral SCC, 29 (9.3%) developed local recurrence, and 55 (17.7%) presented distant metastasis during the study period. The most common arise location was tongue with 125 (40.3%) patients followed by oropharynx 66 (21.2%) and floor of mouth (12.9%).

One hundred and sixty-two (52.2%) of the tumors were classified as moderate-differentiated, 38 (12.2%) as well-differentiated, and 32 (10.3%) as poor-differentiated. Others 78 (25.1%) were classified as non-specified grade. 146 (47%) percent of the patients had loco-regional metastasis (lymph nodes, N1, N2 and N3).

Table 1. Clinical data.

		N	%
Gender	Female	63	20,3%
	Male	247	79,7%
Habits	Smoker	1	0,3%
	Alcohol consumer	40	12,9%
	Smoker and alcohol consumer	110	35,5%
	Non-smoker and non-alcohol consumer	159	51,3%
Location	Tongue	40	12,9%
	Floor of mouth	21	6,8%
	Hard palate	125	40,3%
	Soft palate	4	1,3%
	Lower lip	66	21,3%
	Upper lip	2	0,6%
	Jugal mucosa	20	6,5%
	Retromolar trigone	14	4,5%
	Alveolar ridge	18	5,8%
Staging	Stage I	21	6,8%
	Stage II	52	16,8%
	Stage III	68	21,9%
	Stage IV	169	54,5%

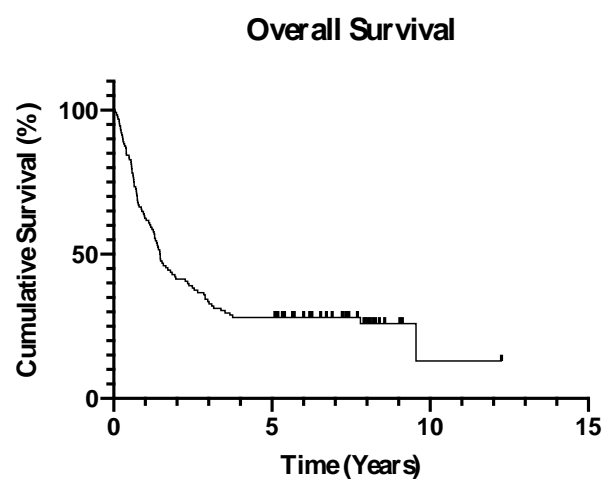
Clinical Tumor Size (T)	T1	30	9,7%
	T2	69	22,3%
	T3	72	23,2%
	T4	139	44,8%
Lymph nodes (N)	N0	162	52,3%
	N1	50	16,1%
	N2	65	21,0%
	N3	33	10,6%
Metastasis (M)	M0	270	87,1%
	M1	2	0,6%
	MX	38	12,3%
Histological	Well Differentiated	38	12,3%
	Moderately Differentiated	162	52,3%
	Not specified	78	25,2%
	Poorly differentiated	32	10,3%
Recidiva	No	55	17,7%
	Location	29	9,4%
	Distant	226	72,9%
Treatment	Surgery	24	7,7%
	Surgery + RT	165	53,2%
	Radioterapy	19	6,1%
	RT + QT	102	32,9%

Source: Authors.

Survival

184 patients without follow-up of 05 years was considered an outlier for the survival analysis. A total of 126 patients were analyzed, 98 male (76.56%) and 30 female (23.44%). The mean age was 58 years (SD 11.81). Of these patients, 94 died and the 5-year overall survival was 28.12%. Figure 1 illustrates the overall survival of the patients analyzed.

Figure 1 - Overall Survival of the analyzed patients.



Source: Authors.

Among the variables analyzed, the location showed statistical significance for the survival curves ($P=0.038$, $\chi^2= 16.84$). Patients who had tongue tumors accounted for the majority of deaths ($n=44$). Table 2 illustrates the distribution and survival of cases classified by location and Figure 2 illustrates patient survival curves according to tumor location.

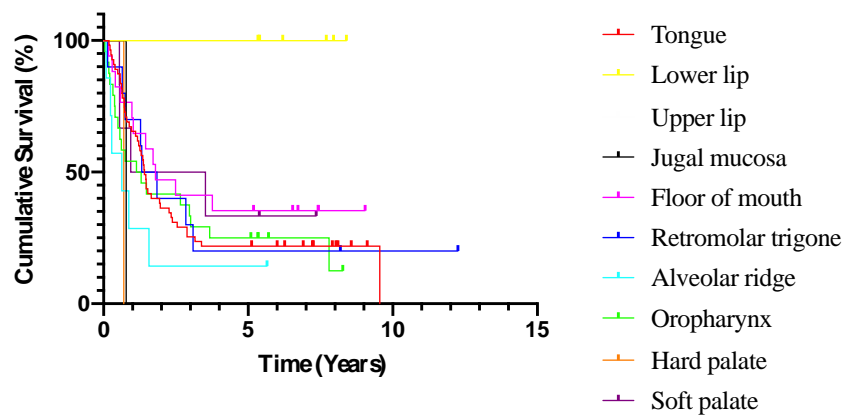
Table 2 - Location of the tumors of the analyzed patients.

Location	N	%	Deaths	Survival of 5 years (%)
Tongue	55	42,97%	44	21.81
Floor of mouth	17	13,28%	11	35,29
Hard palate	1	0,78%	1	0
Soft palate	6	4,69%	4	33.33
Lower lip	7	5,47%	0	100
Upper lip	0	0,00%	0	100
Jugal mucosa	1	0,78%	1	0
Retromolar trigone	10	7,81%	8	20
Alveolar ridge	7	5,47%	6	14.28
Oropharynx	24	18,75%	19	25

Source: Authors.

Figura 2 - Patients survival rate according to tumor location.

Survival Proportions: Tumor Location



Source: Authors.

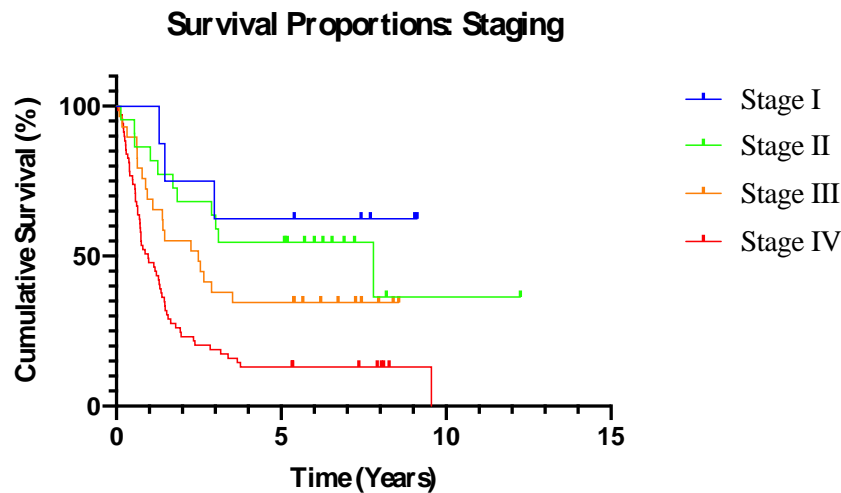
Patients were evaluated according to staging at diagnosis and presented significance for survival ($P< 0.0001$ $\chi^2= 23.12$). The majority (53.91%) of the patients were in stage 4 ($n=69$), followed by stage 3 (22.66%, $n=29$). There were 61 deaths in stage 4 patients and 19 deaths in stage 3. Distributions and survival according to stage are illustrated in Table 3 and Figure 3 shows the survival curves according to stage classification.

Table 3 - Distribution of patients according to staging.

Staging	N	%	Deaths	Survival of 5 years (%)
Stage 1	8	6,25%	3	62,5
Stage 2	22	17,19%	11	54,54
Stage 3	29	22,66%	19	34,48
Stage 4	69	53,91%	61	13,04

Source: Authors.

Figure 3 - Survival curves according to staging.



Source: Authors.

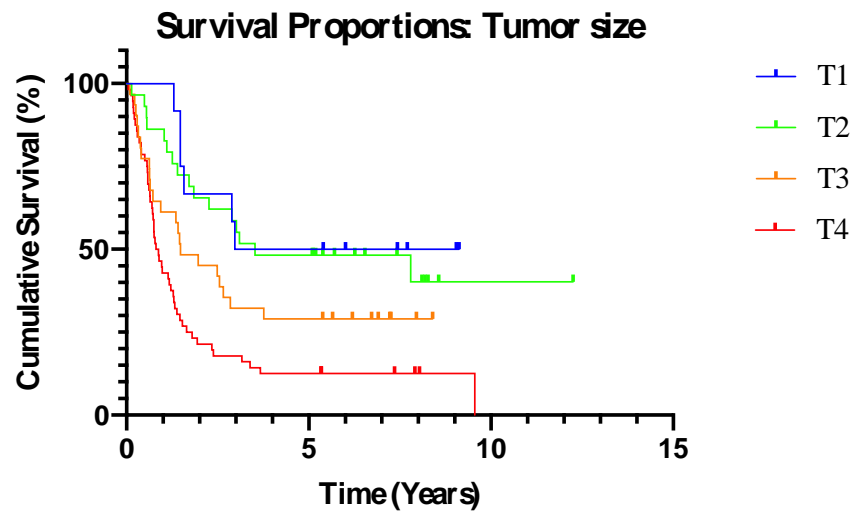
The clinical size of the tumor was another variable analyzed, which has statistical significance in survival ($P < 0.0001$, $\chi^2 = 22.24$). A greater number of T4 ($N=156/43.75\%$) and T3 ($N=31/24.22\%$) tumors were observed. T4 tumors had a higher incidence of deaths ($N=56$), followed by T3 tumors, which had 22 cases of death. Table 4 indicates the distribution of cases and survival, Figure 4 illustrates the survival curves according to tumor size.

Table 4 - Distribution of cases according to tumor size.

Clinical tumor size	N	%	Deaths	Survival of 5 years (%)
T1	12	9,38%	6	50
T2	29	22,66%	16	48,27
T3	31	24,22%	22	29,03
T4	56	43,75%	50	12,5

Source: Authors.

Figura 3 - Survival rate according to tumor size.



Source: Authors.

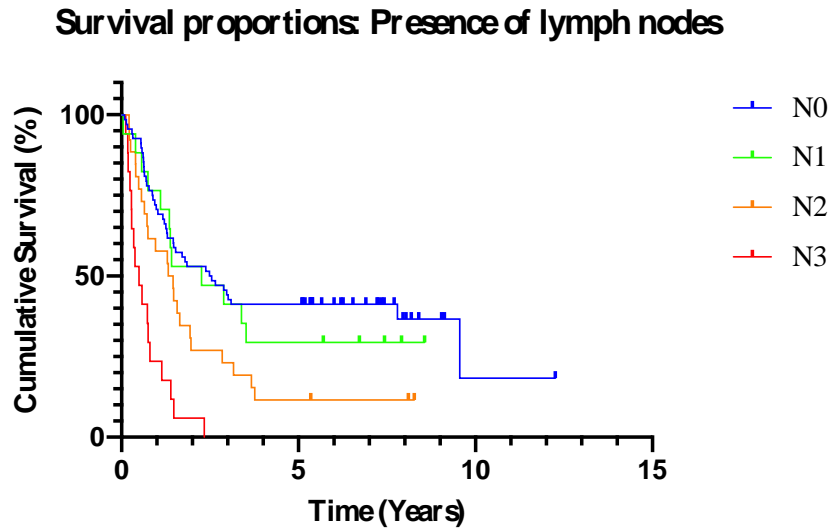
The presence of lymph nodes also influences the survival rate of the studied population ($P < 0.0001 / \chi^2 = 36.54$). Most patients were N0 (N=68/ 53,13%) N1 ((N=17/13,28) and N3 (N= 17/ 13,28%). Most death outcomes (n=42) occurred for patients with no lymph nodes detected at the moment of the diagnostic (N0). Table 5 shows the distribution of cases and Figure 5, the survival rate according to presence of lymph nodes.

Tabela 1 - Distribution of cases according to presence of lymph nodes.

Lymph nodes	N	%	Deaths	Survival of 5 years (%)
N0	162	52,26%	42	41,17
N1	49	15,81%	12	29,41
N2	64	20,65%	23	11,53
N3	33	10,65%	17	0

Source: Authors.

Figura 5 - Survival rate curve according to presence of lymph nodes.



Source: Authors.

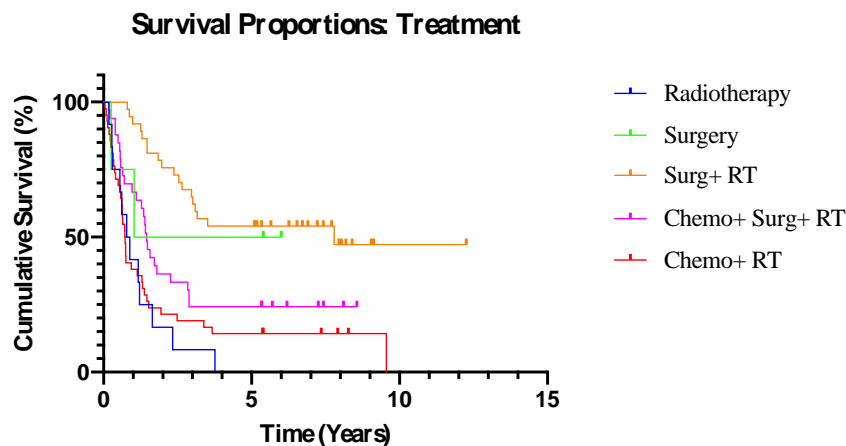
Treatment is another factor influencing survival ($P < 0.0001/x^2 = 32.69$). Most patients ($N=42$) received a combination of chemotherapy and radiation (32.81%), which is the treatment type with the largest number of death outcomes ($N=37$). Radiation alone showed the worst prognosis, with median survival of 1.17 years. Table 6 and Figure 6 show number of cases and the survival rate according to treatment, respectively.

Tabela 2 - Distribution of cases according to treatment.

Treatment	N	%	Deaths	Survival of 5 years (%)
Radioterapy	19	6,13%	12	0
Surgery	24	7,74%	3	50
Surgery + RT	83	26,77%	18	54,05
Surgery + RT + QT	82	26,45%	25	24,24
RT + QT	102	32,90%	37	14,28

Source: Authors.

Figura 6 - Survival rate curves according to treatment.



Source: Authors.

4. Discussion

Most epidemiology studies report squamous cell carcinoma as the most common among male patients between 50 to 60 years old (Pithan et al., 2004; Oliveira et al., 2006; Goldenberg et al., 2009; Oliveira & Mussalen, 2008). The present study corroborates these studies since 79.68% of the studied population were men. The most common age range is 51-60 years old (Oliveira & Mussalen 2008; Mosele et al., 2008), which was also true for the population studied here.

According to the information available at the medical records of the patients treated at the Stomatology healthcare of the Bom Pastor FHOMUV Hospital of the city of Varginha, the most common tumor location was tongue, comprising 40.32% of the cases. This finding agrees with the findings in Oliveira et al. (2006), Oliveira and Mussalem (2008), Fardin et al. (2004) and Antunes et al. (2003). On the other hand, Mosele et al. (2008), Abreu et al. (2009) and Pereira et al. (2003) report the lower lip as the most common location, comprising 23.70%, 66% and 33.54% of the cases, respectively. In the present study, the incidence of cases in the lower lip was 6.77%. Abdo et al. (2002), Larsen et al. (2009) and Teixeira et al. (2009) report larger incidence of tumors in the floor of mouth, comprising 27.9, 39% and 22.7% of cases, respectively. In the present study, the floor of mouth was the third most frequent location, with 12.90% of cases.

Losi-Guembarovski et al. (2009) found that 62.6% of patients had regional lymph nodes compromised and 3.3% had distant metastasis. Our study showed that the presence of lymph nodes is a significant predictor for survival. Patients in our sample were mostly classified as N0 (N=162/ 52.26%) and N2 (N= 64/ 20.65%).

Treatment for squamous cell carcinoma is determined by the disease stage. Therapies of choice are usually surgery, radiation and chemotherapy. For this type of cancer, chemotherapy is usually palliative. In Huang et al. (2007), in a population of 150 squamous cell carcinoma patients, 94 were treated with surgery alone, and 56 with a combination of surgery and radiation. In the present study, surgery was the treatment of choice in 61.50% of the cases. Based on results found in this study, the main treatment of choice is radiation combined with chemotherapy, comprising 32.90% of cases.

In Oliveira et al., 2006, relapses occurred in 24.7% of cases and, according to the authors, despite the high frequency of use of tobacco and alcohol in the population of study, this factor did not influence relapses and metastasis. In the present study, local relapses occurred in 9.35% of the cases and distant metastasis in 17.74%.

New epidemiology investigations should be carried out to allow comparison studies and a more robust basis for assessment and control of causal factors and possible treatments for this type of tumor.

5. Conclusion

In this study, we show that most patients with squamous cell carcinoma are admitted with advanced clinical staging, requiring more aggressive treatment choices. Data suggest the need for the implementation of public policies for the prevention and control of oral cancer in the region, aiming at diminishing the number of cases, favoring early diagnosis and improving the prognosis of such neoplasias.

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