

Original

Survival of Oral Cancer Patients in a Developing Latin American City

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Abstract

Objective: To evaluate overall survival in incident cases of oral cancer notified by the Goiânia population-based cancer registry between 1988 and 2002. **Patients and Methods:** A total of 313 incident cases of squamous cell carcinoma of the oral cavity were identified. The variables studied were: age, gender and clinical staging. Data regarding vital status were obtained from the medical charts of the hospital and clinics and from the Goiânia Mortality Data System. **Results:** Of the 313 incident cases of oral cancer notified between 1988 and 2002 that were identified in this study, 245 (72.7%) occurred in males and 92 (27.3%) in females. The five-year overall survival rate for oral cancer in Goiânia was 35.3% with a mean survival time of 30 months (95%CI, 27-32). There was no statistically significant difference in survival time between males and females (35.8% versus 33.9%; $p=0.750$). In patients with tumors ≤ 4 cm, survival rate was 77%, whereas in patients with tumors >4 cm, survival rate was 39% ($\mu= 35$ months, 95%CI, 31-38, $p<0.001$). **Conclusion:** In patients with oral cancer, survival is associated with gender, age at diagnosis and treatment of these tumors. The low survival rates found indicate that the majority of tumors were at an advanced stage. Training healthcare professionals to clinically examine the oral cavity, to identify abnormalities in oral mucosa and to duly refer patients to a specialized service for early diagnosis would lead to an improvement in survival.

Keywords: Survival; Neoplasms; Mouth; Epidemiology; Latin America

Introduction

Together with cervical, stomach and breast cancer, oral cancer is one of the ten most common forms of malignant neoplasm in the Brazilian population.¹ The estimated rates of oropharyngeal cancer in males in Latin America and the Caribbean may be classified into three groups: $<10/100,000$ in Central America and the Andean countries, $10-15/100,000$ in countries of the Caribbean and southernmost part of South America (Argentina and Uruguay) and $>15/100,000$ in Puerto Rico and Brazil.²⁻⁴

In Goiânia, mortality rates in 2004, classified according to age, were $0.29/100,000$ for men under 45 years of age and $6.54/100,000$ for those over that age. In

women, these rates were $0.61/100,000$ and $2.47/100,000$, respectively.⁵

The estimated rate of oral cancer in Brazil for 2008 was 14,160 new cases, including both males and females, making oral cancer the fifth most common neoplasm in the country. In the state of Goiás, the estimated incidence of oral cancer in 2008 was $7.7/100,000$ for males and $3.8/100,000$ for females. In the state capital, Goiânia, these rates were $12.59/100,000$ and $5.15/100,000$, respectively.⁶

Survival is the parameter most commonly used to

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evaluate the results of treatment and prevention and is based on data obtained from health registries.⁷ Survival in any given population depends on access to diagnosis and treatment and the life expectancy of the population under evaluation. In developing countries, particularly in Latin America, life expectancy in the 1990s was around 70 – 72 years of age. In Goiânia, life expectancy in 2007 was 68.8 years for men and 76.4 years for women.⁸

The 5-year survival rate in oral cancer patients may reach 90% in the case of initial tumors and 40% in advanced cases.⁹⁻¹² In developing countries such as Brazil, the rate of identification of initial malignant lesions of the oral cavity is low, resulting in poor survival rates.¹³⁻¹⁵

The city of Goiânia is situated in the midwestern region of Brazil and has a population of 1,265,394 inhabitants.¹⁶ The principal economic activity of the area is related to agriculture followed by industrial activities. The majority of the population has migrated from rural areas of the state to the cities and towns.

Few studies have been conducted on survival rates in oral cancer in Brazil. Diagnosis of this form of cancer depends on the experience of healthcare professionals in identifying tumors at clinical examination. This study may contribute towards clarifying the prognostic factors related to oral cancer in a developing country.

The present study is a population-based evaluation of survival in oral cancer in the capital city of the state of Goiás in midwestern Brazil, which has a population of 1.2 million inhabitants and an economy that is based on agricultural and industrial activities.

Materials and Methods

Incident cases of oral cancer were identified from the database of the Goiânia population-based cancer registry at the Araújo Jorge Hospital between January 1, 1988 and December 31, 2002. Cases with a diagnosis of squamous cell carcinoma of the oral cavity (ICD C02, C03, C04, C05 and C06) were included. The variables analyzed were: gender, age, clinical staging and date of last contact. Follow-up was performed actively and passively to update information on survival. Follow-up was passive in those cases in which the notification sheet already contained data on the patient's death or when this information was obtainable from existing medical charts at the data collection sources (hospitals and clinics specialized in the diagnosis and treatment of cancer patients), and in the Goiânia mortality data system.

Active follow-up was performed by consulting the mortality system database and contacting the patients

either through their referral physicians or directly by telephone. Clinical staging was classified according to the definitions of the International Union Against Cancer (UICC).¹⁷

A database was constructed in Excel 2003, which was subsequently imported to the Statistical Package for the Social Sciences (SPSS) software package for Windows, version 15. Survival was calculated using the Kaplan-Meier test, including the respective 95% confidence intervals (95%CI). *P*-values < 0.05 were considered statistically significant.

Ethical Issues

This research study was approved by the Internal Review Board of the Araújo Jorge Hospital of the Association for the Combat of Cancer in Goiás on November 11, 2007 under approval number 031/2007.

Results

A total of 313 cases of oral cancer notified between 1988 and 2002 were identified, 245 (72.7%) of which occurred in males and 92 (27.3%) in females, with a male-to-female ratio of 3:1. The age of the individuals ranged from 25 to 94 years (mean $\pm$ SD: 58 $\pm$ 13.44 years); however, the largest group of patients, 54.74% of males and 33.33% of females, were in the 40 – 59-year age-group.

With respect to topography, the tongue was the site most commonly affected (36% of cases) followed by the oral cavity without further specification (31%) and the floor of the oral cavity (16%).

According to the TNM staging system¹⁷, these tumors were classified as T4 (35.1%), N0 (48.9%) and M0 (82%). In 86 cases, (27.5%), tumors were initial ($\leq$ 4 cm), whereas in 172 cases (55%), tumors were $>$ 4 cm and in 55 cases (17.6%) no information was available on tumor size.

Of the 313 cases of oral cancer evaluated in the present study and followed-up for five years, 193 patients (61.7%) died, 87 (27.8%) were still alive at the time of the final evaluation and 33 (10.5%) were lost to follow-up. The highest incidence of loss to follow-up occurred in the first ($n=13$; 39.4%) and fifth years ($n=12$; 36%).

The overall five-year survival rate in oral cancer patients in Goiânia was 35.3% and mean survival time was 30 months (95%CI, 27–32) (Figure 1). No statistically

significant difference was found between males and females with respect to survival (35.8% versus 33.9%, $p=0.750$) (Figure 2). In patients with tumors ≤ 4 cm, survival was 77%, whereas in patients with tumors >4 cm, survival rate was 39% ($\mu=35$ months, 95%CI, 31-38, $p=0.001$) (Figure 3).

In patients clinically evaluated as stage I or II, survival was 58.9% and 58.6%, respectively, while in those who were stage III or IV, survival was 48.1% and 18%, respectively (Figure 4).

When survival rate was classified according to gender and clinical staging, rates were found to be better in male, stage IV patients compared to female patients with the same clinical staging (21.8% versus 6.6%; $p<0.001$) (Figure 5). In stage IV patients under 50 years of age, survival was 24.2% compared to 15.6% in patients over 50 years of age with the same clinical staging.

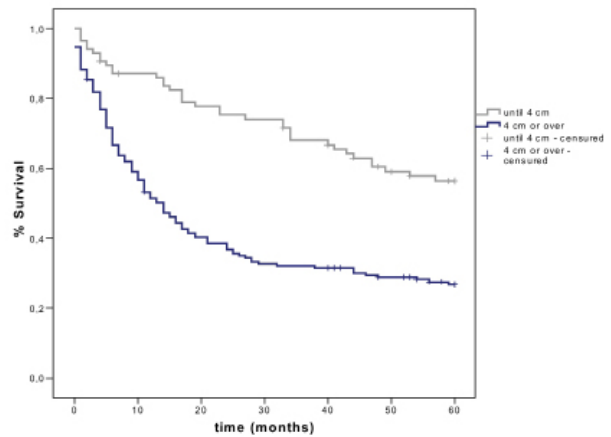


Figure 3 5-year overall survival curve for patients with squamous cell carcinoma of the mouth, according to tumor size in cm, in Goiânia

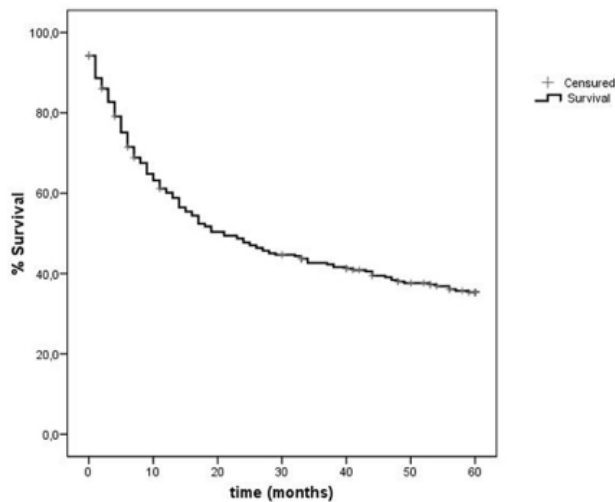


Figure 1 - Five-year overall survival curve for patients with squamous cell carcinoma of the mouth in Goiânia

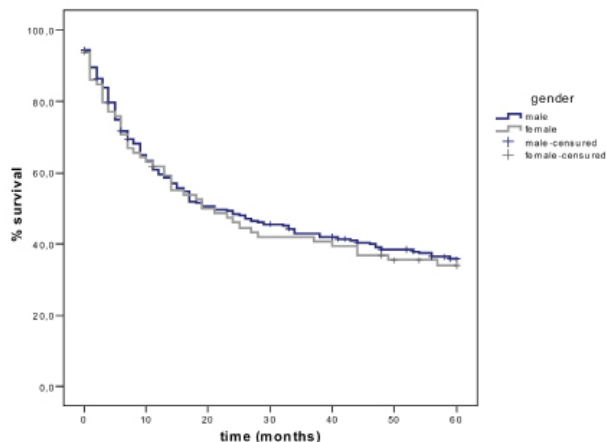


Figure 2 - 5-year overall survival curve of patients with squamous cell carcinoma of the mouth according to gender in Goiânia

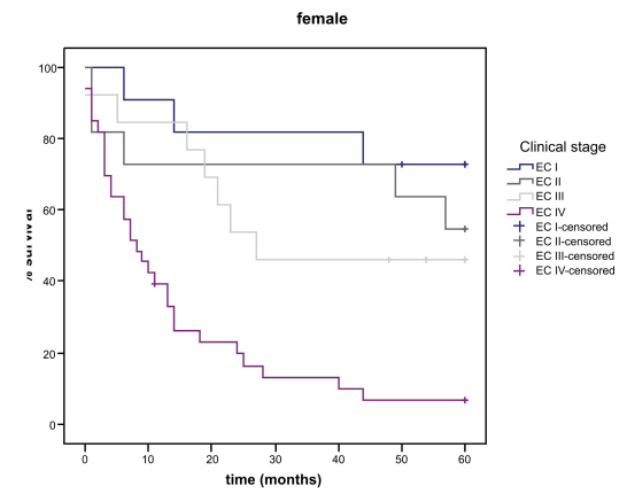
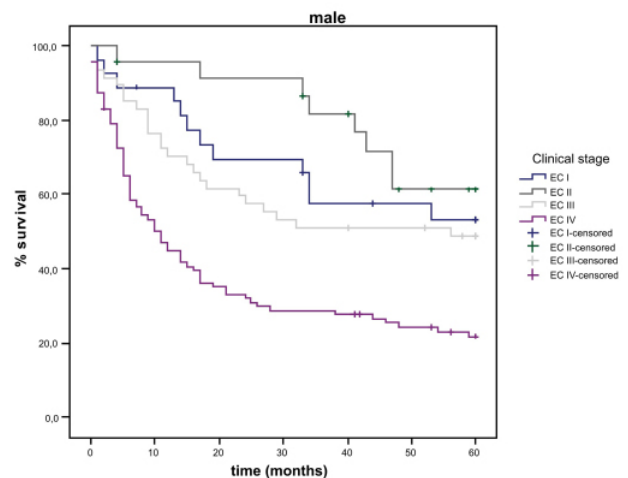


Figure 4 - Overall survival in patients with squamous cell carcinoma of the mouth, according to gender and clinical staging, in Goiânia

Discussion

Studying survival rates in developing countries is a challenge that merits more attention from epidemiologists. One fact to be considered is the difficulty in accessing data on the survival of patients with a diagnosis of malignant neoplasm. In developing countries, specialist centers are located in urban areas. In the 1990s, there was intense movement of the population from rural areas to urban centers in search of better quality of life and work conditions.

In survival studies, individuals are followed-up through the occurrence of an event, death, relapse or loss of follow-up. Cases are included in the study at different times in the calendar year; however, in the analysis, the survival time of each individual is counted from the date of their entry into the study (considered time zero). In the total or overall survival analysis, the final event is death, a variation in another biological parameter or a certain event that indicates a modification in initial status (cure, recurrence, return to work, etc.). The final event is referred to as failure, since it most often refers to undesirable events such as the appearance of disease or the occurrence of death⁷. In the present study, the duration of follow-up was five years from the date of diagnosis.

Recently, the CONCORD study on cancer survival in five continents analyzed survival in incident cases of breast, colon and prostate cancer between 1990 and 1994 and reported that the survival rates for these types of cancer were higher in North America and lower in countries such as Algeria and Brazil and in countries of Eastern Europe.¹⁸ This relatively low survival rate may be due, principally, to migration to regions offering better conditions of work, access to medical treatment and education. In addition, due to economic conditions, there is a constant migration process within cities themselves, with frequent changes of address that hamper adequate patient follow-up.

In the present study, oral cancer was more common in males, with a male-to-female ratio of 3:1.^{5,9,19-20} With respect to age, oral cancer principally affects patients over 50 years of age.^{9,14,21} In this study, 73.2% of patients were found to be over 50 years of age compared to 26.8% below this age, findings that are in agreement with those of other studies.²²⁻²⁵ In agreement with data published in the literature on the distribution of malignant oral tumors, the anatomic sites most commonly affected in this study were the tongue, the floor of the oral cavity and other parts of the oral cavity.^{2,9,26-27}

The overall 5-year survival rate in the present study is similar to rates previously reported in the literature,

which range from 30% to 40%.^{14,28-30}

Comparing hospital-based data between two institutions, one in a developing and one in a developed nation, the survival rates found for patients with oral cancer were 58% and 68%, respectively. The justification given by the authors for the poorer survival rate found in the developing country institute was the greater number of patients with advanced tumors in that institute compared to the greater proportion of initial tumors in the developed country institute.¹⁴

When the survival of patients with oral cancer was analyzed according to gender in the present study, no statistically significant difference was found; nevertheless, when survival rate was associated with both gender and clinical staging, survival rates were found to be poorer in female stage IV patients compared to males with the same clinical staging (6.6% versus 21.8%, respectively; $p < 0.001$). This fact may be related to diagnosis only being made at later stages in the case of women and to a lack of knowledge on the part of healthcare professionals with respect to diagnosis of this disease, hampering their ability to recognize this condition in women. Studies have been published in the literature showing that the disease-free interval is shorter in women compared to men.^{28,30-31}

In a study conducted in the United States with 100 cases and 200 controls, increased rates of cancer of the oral cavity and oropharynx were found to be associated with the human papillomavirus (HPV), principally HPV subtype 16, as a consequence of oral sex, irrespective of alcohol consumption or tobacco use²⁵. HPV infection is associated with poorer prognosis in tumors and reduced survival time.³²⁻³⁷

The survival rate of stage III-IV patients in the present study was low (39%), highlighting the need to encourage early diagnosis by healthcare professionals and implement educational campaigns to standardize the knowledge of these professionals with respect to the identification of premalignant oral cavity lesions and referral to specialists for appropriate treatment.

Tumor size is an important factor in predicting survival. In this study, survival was better in cases of tumors < 4 cm compared to those ≥ 4 cm (77% versus 39%, $p < 0.001$).^{5,14,28,30,38-41}

Conclusion

The survival of patients with oral cancer is related to gender, age at diagnosis and the treatment of these tumors. Survival was poorer in female patients compared

to males with the same clinical staging. The low survival rates found indicate that the majority of tumors were diagnosed at an advanced stage.

Training healthcare professionals in clinical examination of the oral cavity in order to identify abnormalities in oral mucosa and refer patients to a specialist center for early diagnosis would result in better survival rates in these patients.

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