

Clinical features and evolution of oral cancer: A study of 274 cases in Buenos Aires, Argentina

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Abstract

Oral Squamous Cell Carcinoma has a low survival rate, 34 to 66% five-year survival after initial diagnosis, due to late diagnosis. Objectives: The aim of the present study was to examine the clinical features and evolution of oral cancer in the University of Buenos Aires. Study design: 274 patients with primary oral carcinoma, over the 1992-2000 period were included in the study. Results: The survival rate of this population was 80% at 12 months, 60% at 24 months, 46% at 36 months, 40% at 48 months, and 39 % at 60 months (5 years). The tumor localizations with worse prognosis were floor of mouth and tongue, with survival rates of 19% and 27% respectively. Sixty-five percent of the oral carcinomas evaluated were diagnosed at advanced stages (III and IV). Conclusions: The patients under study exhibited the lowest survival rate described for oral cancer (34% five-year survival after initial diagnosis). The population included in this study can be considered representative of the Argentine population. This bad prognosis would be mainly due to the large number of oral cancer cases that were diagnosed at advanced stages.

Key words: Oral cancer, survival.

Introduction

Squamous Cell Carcinoma is the most frequent of oral carcinomas and represents approximately 3 % of all human malignant tumors.(1-3)

The main carcinogenic agents associated to the development of tumors of the upper aerodigestive tract are tobacco and alcohol.(4) Approximately between 75% and 90% of malignant head and neck tumors have been associated to the joint consumption of tobacco and alcohol. However, a recent study revealed that these risk factors act independently, increasing the risk of cancer compared to the non-smoking, non-drinking population.(5) Grinspan et al. (6,7) were the first to describe chronic

traumatic ulcer of dental, prosthetic or functional origin as a precancerous lesion. More recently, chronic trauma has been shown to act as a promoter in the process of oral carcinogenesis. (6) The oncogenic action of viruses is accepted as an important factor in the development of oral carcinomas. The presence of oncogenic human papilloma viruses, in particular types 16 and 18, cytomegalovirus and the Epstein Barr virus has also been associated to the development of oral carcinomas.(8,9) However, the literature is controversial regarding the transformation of the lichen. In a study of 719 patients with oral lichen in Buenos Aires, 32 (6.19%) underwent malignant transformation.(10) Head and Neck Squamous Cell Carcinomas (HNSCC)

frequently present as a heterogeneous disease whose prognosis is difficult to establish. The prognosis of oral cancer is conditioned by multiple variables such as histopathological variety, degree of tumor differentiation, extension and localization of the primary tumor, degree of invasion of neighboring structures, presence of metastatic regional lymph nodes, presence of distant metastases, the choice of therapeutic modality, and the general health status of the patient.(11) Oral cancers are usually diagnosed late at advanced stages of the disease.(12) Between 34 and 66% of the patients die within 5 years from diagnosis. (13-16) In 2005, 29.370 new cases of oral cavity and oropharyngeal cancer were diagnosed in USA. A total of 7.320 patients died(17) due to late diagnosis and disease progression. The aim of the present study was to analyze the clinical features and survival of 274 patients with primary carcinoma of the oral cavity.

Materials and Methods

274 patients with primary oral carcinoma who attended the Faculty of Dentistry, University of Buenos Aires, over the 1992-2000 period were included in the study. Our Service is considered a reference center that attends 4000 new patients per year. Within this context, the population under study would be representative of the population of our country. The initial time-point of this study (t0) was the time of clinical and histopathological diagnosis of oral carcinoma. The following clinical parameters were recorded: age, sex, tumor localization and size, and presence of metastatic adenopathies. Tumor stage was defined in keeping with the clinical classification TNM.(18) The patients were followed clinically at regular intervals in keeping with their need of medical attention. Findings at follow-up were recorded and updated once every six months over the study period. Prognostic assessment of survival was performed employing pre-established categories in keeping with the protocols of Kaplan Meier’s survival analysis.

Results

The mean age of the 274 patients included in the study was 62±13 years, with a range of 19-95 years. The distribution by sex, expressed as the male/female ratio, was 1.24/1. The most frequent tumor sites were tongue (30%, n = 83) and gum (29%, n = 81). 46% (n = 127) of the diagnosed tumors exhibited clinical lesions invading neighboring structures at 2 to 4 cm. 39% (n = 109) of the cases exhibited metastatic, unilateral and mobile adenopathies (Table 1). Of the total number of cases with an early diagnosis, 18% (n = 51) corresponded to stage I and 16% (n = 46) to stage II. 66% of the oral carcinomas evaluated was diagnosed at advanced stages (III and IV).

The most frequently observed histological variant was Squamous Cell Carcinoma (SCC) with an incidence of 86% (n = 237). The incidence of Verrucous Carcinoma (VC) was 7% (n = 19), of SCC and VC combined, 5% (n = 13), and of carcinoma “in situ” (Ci), 2% (n = 5).

Table 1. Analysis of the clinical parameters associated to oral carcinoma.

	%	n=
Age (in years)		
< 40	3	9
40-49	7	19
50-59	18	49
60-69	28	78
70-79	27	73
80-89	16	43
>90	1	3
Distribution by sex		
Male	55	150
Female	45	124
Tumor localization		
Tongue	30	83
Gum or alveolar ridge	29	81
Cheek mucosa	18	50
Floor of mouth	10	26
Palate	9	24
Lip	4	10
Tumor size		
< 2cm	29	81
2 a 4cm	46	127
> 4cm	18	48
Regional invasion	7	18
Presence of metastatic adenopathies		
No adenopathies	40	111
Unilateral, mobile metastases	39	109
Bilateral, mobile metastases	11	29
Metastases fixed to deep structures	10	25
Clinical stage (TNM)		
I	18	51
II	16	46
III	45	120
IV	21	57
Histological diagnosis		
Squamous Cell Carcinoma (SCC)	91	250
Verrucous Carcinoma (VC)	7	19
Carcinoma in situ	2	5

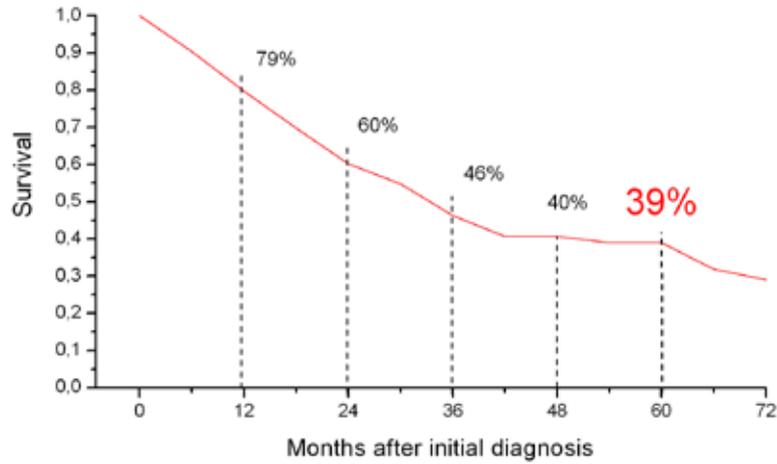


Fig. 1. Survival curve of oral carcinoma (Kaplan Meier test)

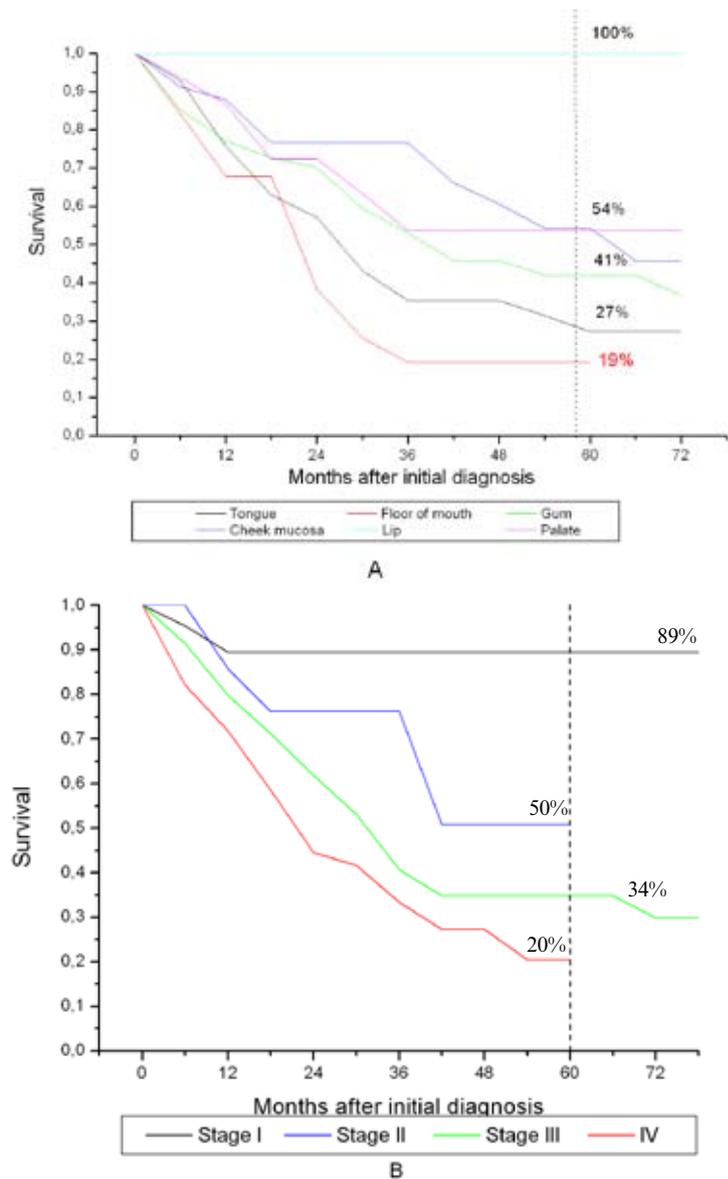


Fig. 2. Survival curve (Kaplan Meier). A: According to the localization of oral carcinomas. B: According to the clinical stage of patients with oral carcinoma (TNM classification).

Table 2. Patient survival according to the test of Kaplan Meier for the different clinical variables.

	* Survival	
Age		
< = 59 years	43%	
> 59 years	43%	
Distribution by sex		
Male	31%	**
Female	45%	
Tumor localization		
Tongue	27%	
Gum or alveolar ridge	41%	
Cheek mucosa	54%	
Floor of mouth	19%	
Palate	54%	
Lip	100%	
Clinical stage (TNM)		
I	89%	
II	50%	
III	34%	
IV	20%	
Histological diagnosis		
Squamous Cell Carcinoma (SCC)	38%	
Verrucous Carcinoma (VC)	90%	
Carcinoma in situ	100%	

* 5 years after initial diagnosis

** Log-rank Mantel-Cox Test $p < 0.05$.

Of the 274 patients included in the study, 210 had a reliable follow-up, with a mean of 12 months and a range of 1 to 120 months. The survival rate of this population was 79% at 12 months, 60% at 24 months, 46% at 36 months, 40% at 48 months, and 39 % at 60 months (5 years). (Fig. 1) Table 2 shows survival data 5 years after initial diagnosis according to the Kaplan Meier test for different clinical variables.

In the present study of oral carcinoma patients, the survival of women was significantly higher (45%) than that of men (31%) (Cox long rang test $p < 0.05$).

The tumor sites with the worst prognosis were floor of mouth followed by tongue, with survival rates 5 years after initial diagnosis of 19% and 27% respectively.

The survival of patients with Squamous Cell Carcinoma was 38%.

The patients with advanced stage disease exhibited a low survival rate (stage III 34% and stage IV 20%, 5 years after initial diagnosis) whereas patients with an early diagnosis had a good prognosis (stage I, 89% survival, 5 years after initial diagnosis). (Table 2)

SCC was the histological variant with the worst prognosis. Survival rate 5 years after initial diagnosis was 38% in the case of SCC and 90% in the case of VC ($p < 0.05$, Log-rank Mantel-Cox Test).

Discussion

Updated studies of significant case series devoted to the analysis of the characteristics of oral cancer in Argentina are lacking. The present section analyzes the clinical features of oral carcinoma in the most representative studies of Buenos Aires city, in the international literature and in our own series.

The literature reports that 95% of oral cancers occur in individuals over 40 years of age and 53 % occur in individuals between 50 and 70 years of age.(19) Our case series shows a similar age distribution. A study by the National Cancer Institute of USA (1973-1984) revealed that oral cancer occurs in men at an earlier age (mean age 40-49 years) than in women (over 65 years).(20,22) Our study revealed statistically significant differences ($p=0.01$) between the mean age of men with oral carcinoma (59 ± 13 years, $n=174$), and the mean age of women with oral carcinoma (63 ± 16 years, $n=154$).

The increase in the incidence of oral cancer in women in the city of Buenos Aires is worrying.(7) The man/woman ratio observed by Silverman and Grinspan et al. (22) corresponding to the 1950-1970 period was 7.1:1 ($n=517$ patients). Schajowicz F et al.(21) reported a rate of 4.3:1 ($n=352$ patients) corresponding to the 1961-1968 period; Brandizzi and Chuchurru et al.(7) reported a rate of 2.3:1 ($n=336$ patients) corresponding to the 1972-1984 period. Our own series corresponding to the 1992-2000 period revealed a ratio of 1.24:1 ($n=274$ patients).

The distribution by sex of oral cancer in societies whose habits are similar to ours is man/woman: 2.5-1.24/1. (19,22)

In keeping with the literature, the tongue was the most frequent localization of oral cancer in our series. A previous study by the National Institute of Radiology (Buenos Aires, Argentina, between 1961 and 1968, $n=78$) reported a prevalence of 35%.(21) In our series prevalence was 30% ($n=60$). In considerably large USA series, these values varied: in a study by the Surveillance, Epidemiology and End Results (SEER) Program, prevalence was 30.3% in the 1973-1979 period and 33.7% in the 1979-1984 period,(22) prevalence was 36.7% in North California(1) and 41.5% in the studies by Silverman S. et al. from University of California(22).

Our study revealed a marked prevalence of gum carcinoma, i.e. 29% ($n=58$), and cheek mucosa carcinoma, i.e. 28% ($n=36$).

Late diagnosis in oral cancer has been reported by several studies.(14) 66 to 80% of oral malignant tumors were diagnosed at stages III and IV whereas only 20-34% were diagnosed at early stages (TNM I and II). (22-24) The results of the present study are in agreement with these findings. Morelatto RA et al. studied the role of the patient and acting professionals in late oral cancer diagnosis in a province of Argentina.(14)

In 2005, 29.370 new cases of oral and oropharyngeal

cancer were reported in the USA and 7.320 patients died. (19)

Evidence of a rise in mortality rate of oral cancer has been reported for Cordoba, Argentina, over the 1997-2001 period.(12)

The literature reports that survival at 5 years after initial diagnosis ranges from 34-56% (13,15,16,24,25) in populations with similar socio-cultural habits to ours. Our series reveals a survival rate of 39% in 186 patients with representative clinical follow-up. This bad prognosis is mainly the result of a late diagnosis in a large number of oral tumors.(14,19)

In our series, 65% of the cases were diagnosed at advanced stages (clinical stages TNM III and IV) and the survival rate in the case of tongue tumors was only 27%.

The small number of patients with oral tumors at stages I and II (early stages of the disease) included in our study was due to the failure to perform an early diagnosis.

References

- Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. *Int J Cancer*. 1999 Mar 15;80(6):827-41.
- Canto MT, Devesa SS. Oral cavity and pharynx cancer incidence rates in the United States, 1975-1998. *Oral Oncol*. 2002 Sep;38(6):610-7.
- Pindborg JJ. Oral cancer and precancer as diseases of the aged. *Community Dent Oral Epidemiol*. 1978 Nov;6(6):300-7.
- Pöschl G, Seitz HK. Alcohol and cancer. *Alcohol Alcohol*. 2004 May-Jun;39(3):155-65.
- Hashibe M, Brennan P, Benhamou S, Castellsague X, Chen C, Curado MP, et al. Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *J Natl Cancer Inst*. 2007 May 16;99(10):777-89.
- Pérez MA, Raimondi AR, Itoiz ME. An experimental model to demonstrate the carcinogenic action of oral chronic traumatic ulcer. *J Oral Pathol Med*. 2005 Jan;34(1):17-22.
- Brandizzi D, Chuchurru JA, Lanfranchi HE, Cabrini RL. Analysis of the epidemiological features of oral cancer in the city of Buenos Aires. *Acta Odontol Latinoam*. 2005;18(1):31-5.
- Koch BB, Trask DK, Hoffman HT, Karnell LH, Robinson RA, Zhen W, et al. National survey of head and neck verrucous carcinoma: patterns of presentation, care, and outcome. *Cancer*. 2001 Jul 1;92(1):110-20.
- Shroyer KR, Greer RO, Fankhouser CA, McGuirt WF, Marshall R. Detection of human papillomavirus DNA in oral verrucous carcinoma by polymerase chain reaction. *Mod Pathol*. 1993 Nov;6(6):669-72.
- Lanfranchi-Tizeira HE, Aguas SC, Sano SM. Malignant transformation of atypical oral lichen planus: a review of 32 cases. *Med Oral*. 2003 Jan-Feb;8(1):2-9.
- Ghoshal S, Mallick I, Panda N, Sharma SC. Carcinoma of the buccal mucosa: analysis of clinical presentation, outcome and prognostic factors. *Oral Oncol*. 2006 May;42(5):533-9.
- Morelatto RA, Herrera MC, Fernández EN, Corball AG, López de Blanc SA. Diagnostic delay of oral squamous cell carcinoma in two diagnosis centers in Córdoba Argentina. *J Oral Pathol Med*. 2007 Aug;36(7):405-8.
- Jones AS, Beasley N, Houghton D, Husband DJ. The effects of age on survival and other parameters in squamous cell carcinoma of the oral cavity, pharynx and larynx. *Clin Otolaryngol Allied Sci*. 1998 Feb;23(1):51-6.
- Morelatto RA, López de Blanc SA. Oral cancer mortality in the province of Cordoba, Argentine Republic in the period 1975-2000. A comparative study with other populations. *Med Oral Patol Oral Cir Bucal*. 2006 May 1;11(3):E230-5.
- Navarro Vila C, Cuesta Gil M, Lopez de Ayala Gutierrez J. Advanced stage (T3-4) squamous cell carcinoma of the oral cavity: Therapeutic results of 375 cases after 5 years of follow-up. *Med Oral*. 1998 Jan; 3(1):7-17.
- Carinci F, Pelucchi S, Farina A, Bonsetti G, Mastrandrea M, Calearo C. Site-dependent survival in cancer of the oral cavity. *J Craniofac Surg*. 1997 Sep;8(5):399-403.
- American Cancer Society. Cancer facts & figures 2005. available from <http://www.cancer.org/downloads/STT/CAFF2005f4PWSecured.pdf>.
- TNM classification of malignant tumors. 5th ed. Book of the International Union Against Cancer (UICC). 1997 ICD-O-COO, 002-6.
- Silverman S. Epidemiology. Oral cancer. 3th ed. Book of The American Cancer Society. Atlanta -The United States of America; 1990. p. 1-6.
- Jones AS. Prognosis in mouth cancer: tumour factors. *Eur J Cancer B Oral Oncol*. 1994 Jan;30B(1):8-15.
- Schajowicz F, Gallardo H, Cabrini RL. Cancer of the mouth mucosa in the city of Buenos Aires. Study of 370 cases at the Municipal Institute of Radiology and Physiotherapy (1961-1968). *Rev Asoc Odontol Argent*. 1969 Jun;57(6):200-5.
- Silverman S, Greenspan D. Early detection and diagnosis of oral cancer. *CDA J*. 1985 May;13(5):29-33.
- Fernández-Martínez JA, Ruiz-Avila I, Bravo M, Ramos MC, Martínez-Lara I, Urquía M, et al. Some histopathological and clinical correlations in oral squamous cell carcinoma. *Bull Group Int Rech Sci Stomatol Odontol*. 1995 Jan-Feb;38(1-2):11-5.
- Leite IC, Koifman S. Survival analysis in a sample of oral cancer patients at a reference hospital in Rio de Janeiro, Brazil. *Oral Oncol*. 1998 Sep;34(5):347-52.
- Vallecillo Capilla M, Romero Olid MN, Olmedo Gaya MV, Reyes Botella C, Bustos Ruiz V. Factors related to survival from oral cancer in an Andalusian population sample (Spain). *Med Oral Patol Oral Cir Bucal*. 2007 Nov 1;12(7):E518-23.