A histological and clinical study on oral cancer: Descriptive analyses of 365 cases

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ABSTRACT

Cancer is the second cause of death in Portugal right after cardio vascular diseases. In Portugal the incidence of oral and pharynx cancer (OPC) is higher than uterus and larynx cancers, and in US its frequency is higher than melanoma or uterus cancer, diseases that concern more population than oral cancer.

Aims

The aim of this paper is to identify preferable anatomic location for oral cancer, mean age of patients, the use of tobacco and alcohol, histological characteristics, staging, type of therapeutics, presence of metastases and 1 and 5 year follow up.

Matherials and Methods

Data was collected from clinical charts of 365 cases from the Centro de Lisboa do Instituto Português de Oncologia with histological confirmation of malign tumor of the mouth. These cases are the total of oral malign tumors in the years of 1997, 1998 and 1999 in that institution.

Results

We observe that despite modern diagnostic and treatment techniques 37,9% of all patients died after first year with evidence of tumor. From all patients just 23,7% were free of disease after 5 years of treatment. Tongue was the principal region affected and the average age was 62, 25 years. It was concluded that 57, 8% of patient were smokers and 43,8% were alcohol drinkers. A high number of patients were submitted to radiotherapy either alone or with other treatment options.

Key words: *Oral cancer, epidemiology, squamous cell carcinoma*

INTRODUCTION

Cancer is the second cause of death in Portugal, right after cardiovascular diseases (CVD), and head and neck cancer accounts for 10% of all malign cancers. In Portugal the incidence of oral and pharyngeal cancer (OPC) is higher than uterus and larynx cancers, and in United States estimated deaths for this cancer are higher than melanoma or uterus cancer, which are more concerning diseases than OPC for population in general, even if OPC has severe consequences, not only functional but also psychologically (1-2).

The death rate for OPC in males starts to rise in mid eighties. Between 1988 and 1998 and an increase of 24% was noticed compared to earlier years. This increase affected mainly middle age and young males following a pattern where the incidence age was decreasing (3-5).

Trends in oral cancer incidence rates that include all oral sites may be misleading. For example, risk factors for lip cancer are different from intraoral sites. Also because there are differences in oral cancer incidence rates by age, anatomic site, treatment and geographic location (6-10). Thus, descriptive oral cancer data for each geographic area are important to understand the extent of the problem (11-13).

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The purpose of this study is to analyze a large case series of oral cancer emphasing risk factors and outcome.

MATERIALS AND METHODS

A total of 365 files with a histopathological diagnosis of primary malignant neoplasm of the mouth were reviewed. Data collected from patient records included patient gender, anatomic location (buccal mucosa, tongue, floor of the mouth, gingival and palate)(ICD-O, International Classification of Disease- Oncology)(14), pre-treatment staging, treatment options, metastases evidence, recurrence, 1 and 5 year follow-up, tobacco and alcoholic habits, association with other tumours of the upper aero digestive tract and outcome. Lip cancer was not considered because it has different risk factors. Descriptive analyses of the variables was made using software SPSS for windows.

Information on alcohol consumption included the type of alcoholic beverage. Taking into account the different alcohol concentrations for each beverage, we considered someone with alcoholic habits who drunk more than 12 g of ethanol a day. At the some time a smoker was define as someone who smoke more than a cigarette a day for more than a year.

RESULTS

Epidemiological research concerning oral cancer is complex due to the existence of multiple anatomic regions and sub-regions. The anatomic location was identified by anatomic sub-regions whenever possible. All results show frequency of each variable.

Eighty percent of the 365 oral cancer cases was diagnosed in males. The overall male-to-female ratio was 4.0. The average age of diagnosis of malignant neoplasm was 62 years old with a standard deviation of nearly 12 years.

Anatomic location was registered and coded according to the recommendations of the ICD-O (International Classification of Disease – Oncology). The anatomic location distribution indicates that the tongue and its sub-regions (C01.9 to C02.9) were involved in about 43% of the cases. Other sites with significant results were: floor of the mouth and its sub-regions (C04.0 to C04.9) with approximately 18,9%; palate (C05.0 and C05.1) with about 6,9%; gum(C03.0 and C03.1) and retromolar pad(C06.2) with 6,6%, and oral mucosa (C06.0) with 6,0% (Table 1).

Lesions involving overlapping regions (C06.8) total 12,3% of the malignancies, what indicates that sometimes due to a late diagnosis it's difficult to determinate the original location of the tumour.

The distribution of the tumour histological types is shown in table 2. Squamous Cell Carcinomas SCC (Non Otherwise Specified = NOS) were the most common type. Non-epithelial tumours were less than 3% of all malignant neoplasm's (8000.3 and 9591.3).

We found that 84,6% of the tumours were SCC (NOS) and that percentage is even higher when considering both the non-keratinized and keratinized spinocellular carcinomas (table 2).

The majority of the tumors were well differentiated – 36,2%. However, the analysis of this variable was not possible in 30,1% of the cases.

Most of oral cancers were diagnosed at advanced stages (T3 and T4) - 48,2% . Lymph node involvement (N) regardless of the tumour size was 40,6%.

Distant metastases were identified in 38 cases which represents 9,3% of the overall sample. The mean time for distant metastasis identification after the diagnosis was 496 days. Distant metastases affected mainly the lung. This organ stands for 47,4% of all the anatomical locations with metastases involvement.

Combined radiation and surgery was provided to 20,8% of the cases. The radiation therapy alone, or combined with surgery or chemotherapy was provided to more than 60%. Radiation therapy included patients treated both with curative or palliative intent.

Clinical or histopathological evidence of recurrence was registered in 22,5% of the cases. Recurrence was not possible to be identified in 31,1% of the subjects due to follow up absence or late diagnosis (in some cases patients were never free of disease, being impracticable to identified recurrence).

At 1 year follow up, of all the cases studied, approximately 36,4% of the patients had deceased with documented tumour, while 38,9% exhibited no such evidence (Table 3). Regardless of the clinical condition about 58,9% of the patients were alive. At 5 year follow up, 26,5% of all the sample cases were disease-free five years after treatment completion. Regarding only the individuals who were alive after the first year follow-up the disease-free group at the fifth year rises to 45,1% (Table 4). A high percentage of cases, 33,6%, were included in a non-applyable category. (These included the patients already dead and the ones that miss follow up appointments).

Of the total sample 57,8% had tabagic habits and 47,9% reported alcoholic habits. To notice is the fact that 43,8% of the patients had both habits.

In 25 cases an association with other primary tumours was established, which represents of 6,8% of the sample. The main regions affected were the larynx and the lungs with percentages of 40% and 16%, respectively.

DISCUSSION

This non-randomized sample is the totality of oral cancer cases diagnosed between 1997 and 1999 at Francisco Gentil Lisbon Centre of Portuguese Institute of Oncology (Centro de Lisboa do Instituto Português de Oncologia Francisco Gentil). We examined the available records of all patients with oral cancer.

This research indicates that 80% of cases affected males. This finding is consistent with other oral cancer demographic reports(2,3,5).However gender is not a risk factor per se for oral cancer. This prevalence indicates the existence of other risk factors associated to the male gender, such as tabagic and alcoholic habits.

The most frequent anatomical location was the tongue. This is supported by other studies that showed the tongue as the

Table 1. Oral cancer cases according to the site of the primary tumor.

Anatomic Site	Number of cases	%
Tongue (C01.9) (C02.0) (C02.1) (C02.2) (02.8) (C02.9)	159	43
Gum(C03.0) (C03.1)	24	6,6
Mouth Floor (C04.0) (C04.1) (C04.8) (C04.9)	69	18,9
Palate (C05.0) (C05.1)	25	6,9
Uvula (C05.2)	8	2,2
Oral Mucosa (C06.0)	22	6,0
Retromolar Pad (C06.2)	24	6,6
Overlapping sites of several anatomic locations (C06.8)	45	12,3
Other locations	5	1,4
Total	365	100,0

Table 2. Histological Distribution of all malignancies.

	Number of cases	%
Malitious Neoplasia (NOS-Not Otherwise Specified) (8000.3)	2	0,5
Carcinoma in situ (8010.2)	2	0,5
Carcinoma NOS (8010.3)	3	0,8
Indiferentiated Carcinoma (8020.3)	1	0,2
Poligonal cells carcinoma (8034.3)	1	0,2
Verrucoso Carcinoma (8051.3)	2	0,5
SquamousCell carcinoma NOS (8070.3)	309	84,6
Non keratinized Squamous Cellcarcinoma (8072.3)	3	0,8
Keratinized Squamous Cellcarcinoma (8071.3)	31	8,5
Neuroendocrine Carcinoma (8246.3)	1	0,2
Acinic cells carcinoma (8550.3)	3	0,8
Melanoma NOS (8720.3)	2	0,5
Non-Hodjkin Lymphoma (9591.3)	5	1,3
Total	365	100,0

Table 3. 1 year follow up.

1 year Follow Up	Number of cases	%
Alive with tumor evidence	51	13,9
Alive with metastasis evidence	5	1,3
Alive without tumor evidence	142	38,9
Alive with tumor recurrence	17	4,6
Deseased with tumor evidence	133	36,4
Others	17	4,5

Table 4. 5 years follow up.

5 years follow up	Number of cases	%
Alive with tumor evidence	3	0,8
Alive with metastasis evidence	2	0,5
Alive without tumor evidence	97	26,5
Alive with tumor recurrence	7	1,9
Deseased with tumor evidence	31	8,4
Deseaced without tumor evidence	25	6,8
Deceased with recurrence	41	11,2
Deseaced with metastasis evidence	4	1,0
Other	155	42,3

main organ involved, when excluding the lip regions(15-17). The existence of approximately 11% tumours involving overlapping regions, 74,3% of which are stage T4 is indicative of late diagnosis.

The patients' average age of 62,2 years-old along with the standard deviation of approximately 12 years were consistent with other reports in general, and confirms the suggestion to adopt screening appointments for patients with certain risk factors. Based on our results, screening appointments targeted to individuals over 50 years old and/or alcohol consumers could raise the number of early diagnosis and therefore increase treatment outcome. Moreover, monitoring pre-malignant lesions may also contribute to early diagnosis of SCC(5). Our research indicates that the most frequent histopathological type of oral tumour is SCC (84,1%) which corroborates other studies findings (18).

Despite the progress in diagnosis and treatment of oral cancer the survival rates are lower in comparison to other types of cancer. This may be related to late diagnosis in the majority of cases. In our report, T3 and T4 tumours were extremely high – 50% and the involvement of regional lymph nodes were present in 40,6% of the patients. Once that lymph nodes involvement is an oral cancer prognosis sign, histological analysis of the sentinel node may provide specific information about ganglia involvement circumventing the limitations of clinical and imaging methods (19-20).

In our sample a great number of patients received radiation treatment. Once that radiotherapy is planned to be used in a great number of patients, a pre-treatment evaluation should be undertaken in order to apply preventive measures to minimize collateral effects (21-22).

At 1 year follow-up 40% of the patients were disease-free. This finding is similar to other authors' studies(23). Our 5 year follow-up indicates that the percentage of disease-free patients, 26,5%, is not as high as in other reports(16-18). These low results may be explained by the fact that our sample is from an oncological hospital, where many patients are referred to palliative treatment for advanced tumours and also because part of the population has no primary oral care assistance.

The majority of patients in this study had a history of tobacco use - 57,8%. The positive association between oral cancer and tobacco use is well documented by various authors who have shown that the risk of developing oral cancer is directly proportional to the number of cigarettes smoked per day and to the number of years as a smoker (24-25).

Alcohol consumers were approximately 50% of the total number of cases. The association between oral cancer and alcohol consumption may be explained in Portugal because it is one of the countries with the highest average alcohol consumption, namely 12,1 litres (25,57 U.S. pints) of pure alcohol per capita(26). Although it seems that alcohol is not a carcinogen per se, once it is metabolised active substances with carcinogenic potential are produced (27).

The interaction between alcohol and tobacco has been studied in order to determine the existence of a synergic mechanism predisposing to oral cancer. We found that 43,8% of the patients were both alcohol consumers and smokers. Excess risk of approximately 10 fold is associated with tobacco and alcohol use. Nowadays it is proposed that tobacco is an initiator while alcohol is a promoter, presumably by either increasing the permeability of mucosa lining cells to tobacco carcinogens or by cellular lesions induced directly by alcohol metabolism (28). Therefore primary prevention must favour a decrease in exposure to tobacco, alcohol and other carcinogenic agents.

The highest incidence of second tumours is found in the larynx and lung, which is in accordance with other author's reports (29-30). However, our total percentage is lower, namely 6,1%. This might be explained by the difficulty in distinguishing between two primary tumours.

Metastatic spread of oral SCC tends to increase with the size of the primary tumor. Metastases were observe after an average time of 16,5 months. Therefore, within this timeframe clinical surveillance of patients with SCC must be scheduled in regular intervals in order to identify metastases.

Because of the magnitude of the oral cancer problem, and because this is a tobacco and alcohol related cancer, serious thought should be given to prevention and early tumour detection.

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