Original Research
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Oral cancer analysis in a Brazilian city: interval between diagnosis and treatment

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Abstract: In Brazil, there are 15,500 incident cases of oral cancer (OC) yearly, and early diagnosis is the main factor for a better prognosis. The objective of this study was to analyze the interval between the first symptoms, diagnosis, and treatment commencement in patients with malignant neoplasms in the oral cavity, lips, and oropharynx diagnosed between 2012–2018. Epidemiological data, duration, history of lesion, biopsy, and diagnosis were obtained from the medical records of these patients, who were then contacted via phone and interviewed about their oncological treatment. The results were analyzed and expressed as mean, median, and SD. Of 184 patients, most were men, white, 50–69 years old, smokers, and alcoholics. The longest interval was between the first symptoms and first evaluation (a mean of 275 days). The interval between the first appointment and the result of the biopsy was shorter (13 days). Among the 85 patients interviewed, the interval between the diagnosis, the first appointment at the oncological clinic and treatment commencement was 55 days (mean) for patients using private-sector health care, and 96 days (mean) for patients using public health care. The interval was twice as long in the public health system compared with the private sector, which highlights the inequality of access to health care in Brazil. Delay in seeking health care after the appearance of the first symptoms remains a major problem.

Keywords: Mouth Neoplasms; Early Detection of Cancer; Delayed Diagnosis; Time-to-Treatment.

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Introduction

Cancer is among the leading causes of death, second only to cardiovascular diseases.[1] Globally, OC accounted for approximately 150,000 deaths in 2015.[2]

In Brazil, OC is the 5th most common cancer in men (11,200 cases/year) and the 12th most common cancer in women (3,500 cases/years).[1] In 2016, it was responsible for 0.46% of deaths in the country (6,088 people)[1]. In Brazil's southeast region, it is the 4th most common cancer in men and the 13th most common cancer in women.[1]

OC are malignant neoplasms of the tongue, gums, floor of the mouth, palate, and other unspecified mouth parts.[3] OC has a multifactorial etiology, with risk factors, such as smoking, excessive alcohol consumption, and

exposure to solar radiation. Initially, the lesions are asymptomatic, which may account for the long time it takes patients to seek professional care.[1]

The risk of death from head and neck tumors increases with the waiting time between diagnosis and treatment.[4] In approximately 4 weeks of waiting for radiotherapy, most patients develop significant signs of tumor progression.[5] So, the interval between diagnosis and treatment is a determinant of the prognosis of the disease.

In Brazil, studies were published evaluating the interval between the first sign or detection of the disease and the search for a professional. The interval ranged from 18 days to 10 years.[6,7,8] The mean interval ranged 197.8[8]–240[9] days. In all the studies, the interval between the detection of the first symptom by the patient and the search for a professional was greater than the interval between diagnosis and treatment.

In Brazil, in 2012, the 60-day law was established, whereby a patient diagnosed with malignant neoplasia has the right to undergo the first treatment in the public health care system, within 60 days.[10]

The objective of this study was to evaluate the interval between diagnosis and treatment of patients diagnosed with cancer in the oral cavity, lips, and oropharynx, evaluated at our stomatology clinic.

Methodology

Patients diagnosed with cancer in the oral cavity, lips, and oropharynx at our stomatology clinic between 2012–2018 were selected. Patients were contacted via phone and, after accepting to participate in the research and authorizing the recording of the call, an interview was conducted. This study was approved by the Research Ethics Committee under reference number 12482919.5.0000.0075.

The following were evaluated: the patient's age, sex, race, predisposing habits (smoking, consumption of alcoholic beverages), systemic diseases, first professional they looked for, history of the lesion (first signs and symptoms), duration of the lesion, staging of the lesion, location of the lesion, date of first appointment, date of biopsy, date of biopsy result, and date of referral. These data were retrieved from the patients' medical records.

In the phone interview, patients were asked to answer the following questionnaire, with their medical data available in their hands, to avoid memory bias:

a. When was the first appointment at the oncological clinic?
b. Where did you have the treatment? Public or private health care?
c. When did you start treatment?
d. What was the proposed treatment?

For patients who died, the questionnaire was answered by family members who agreed to participate in the study. The questions were the same, but two more were added:

a. What was the date of death?
b. What was the cause of death?

The data were divided into four moments: The interval between the first sign/symptom of the lesion and the first appointment at the stomatology clinic, the interval between the first appointment and the biopsy result, the interval between the biopsy result and the first appointment at the referred clinic, and the interval between the first appointment at the oncological clinic and treatment commencement. Whether the interval between the first appointment and treatment commencement satisfied the 60-day law was also assessed.

All medical records accessed by the study had authorization to use patient's information for research and all contacted patients agreed to participate.

Inclusion criteria

Patients diagnosed and treated for cancer in the oral cavity, lips, and oropharynx, with ICD-10 ranging from 0.0 to 10.9, and were willing to participate in the study.

Exclusion criteria

Patients diagnosed with potentially malignant disorders such as leukoplakias. Patients with inconsistency/missing data in their medical records.

Results

Between 2012–2018, 209 patients were diagnosed with cancer in the oral cavity, lips, and oropharynx at the School of Dentistry of the University of São

Paulo. Of these, 184 medical records were available for evaluation and were included in the study, with 25 records excluded due to inconsistency/missing data.

From the 184 cases included in the study, we were able to contact 94 patients. Of these, 9 patients refused to participate in the study, while 85 agreed. Of the 85 cases, 58 were the patients themselves, while in 27 cases, a family member was interviewed, because the patient had died.

According to the epidemiological data in Table 1, more than half of the patients were aged between 50–69 years (58%), male (66%), white (74%), and were exposed to smoking and alcohol (52%). Most of the patients looked for a private care dentist first (60%); the most frequent location of the cancer was the tongue (29%), the first sign was ulcer (54%), and the predominant diagnosis was squamous cell carcinoma (88%). Of the 85 participants, most were treated with only surgery (41%). As regards the stage at the time of diagnosis, patients were predominantly in stage III (29.89%) (Figure).

To assess the interval between diagnosis and treatment, the information was divided into 4 moments: T1 is the interval in days between the first sign/symptom and the first appointment at the stomatology clinic, T2 is the interval in days between the first appointment and the result of the biopsy, T3 the interval in days between the result of the biopsy and the first appointment at the oncological clinic and T4 the interval in days between the first appointment at the oncological clinic and treatment commencement. T1 and T2 were calculated using the average time found in the medical records. Of the 184 medical records, 8 were excluded due to primary diagnosis of leukoplakia, 2 were excluded from T1 and 4 were excluded from T2 due to missing data. Whereas T3 and T4 were calculated using the average time reported by the 85 contacted study participants after consulting their medical records; 11 were treated in private health care, 74 were treated in public health care and 4 did not start the treatment. Data are summarized in Table 2.

Patients took 275 days (mean) (SD = 526.6) to have their first appointment at the Stomatology clinic, which took 13 days (mean) (SD = 8.4) to diagnose these patients. Those treated in private health care

Table 1. Distribution of patients according to epidemiological data and medical history.

Variables	n	%
Age (years)		
0–49	29	16
50–69	107	58
> 70	48	26
Sex		
Male	121	66
Female	63	34
Race		
White	136	74
Black	42	23
Asian	6	3
Habits		
Smoking/alcohol	96	52
Nonsmoker/alcohol	44	24
Only smoking	35	19
Only alcohol	9	5
First professional appointment		
Private care dentist	109	60
Public care dentist	31	17
Physician	24	13
Stomatology clinic	19	10
Location		
Tongue	54	29
Floor of mouth	32	17
Mandible	29	16
Palate	23	13
Lip	19	10
Maxilla	17	9
Buccal mucosa	7	4
Oropharynx	3	2
First signs and symptoms		
Ulcer	54	29
Nuisance / pain / burning	42	23
Nodule	30	16
Non healing oral aphthous ulcer	18	10
Asymptomatic Growth	18	10
White and / or red lesion	18	10
Verrucous lesion	4	2
Diagnosis		
Squamous cell carcinoma	162	88
Mucoepidermoid carcinoma	8	4
Adenoid Cystic Carcinoma	5	2
Verrucous Carcinoma	4	2
Metastatic Carcinoma	2	1
Basal-Cell carcinoma	1	1
Clear-Cell Carcinoma	1	1
Myoepithelial Carcinoma	1	1
Treatment		
Surgery	35	41
Surgery and radiotherapy	22	26
Surgery, radiotherapy and chemotherapy	10	12
Radiotherapy and chemotherapy	10	12
Palliative treatment	4	5
Radiotherapy	3	3
Chemotherapy	1	1

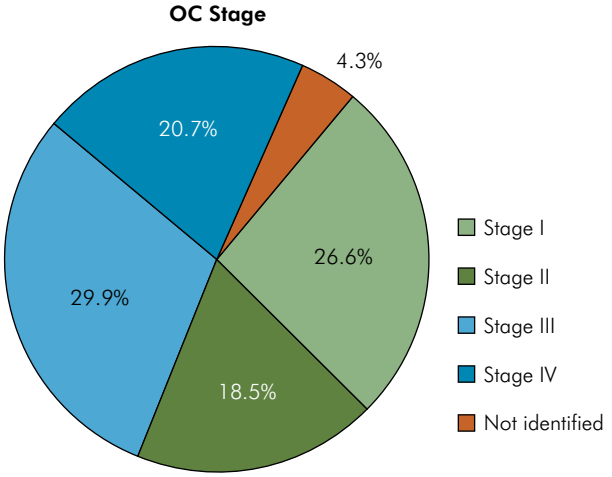

Figure. Distribution of patients according to OC stage at diagnosis.

waited 19 (mean) days (SD = 23.7) to have their first appointment at the treatment center and for 36 days (mean) (SD = 33.6) to start their treatment. Patients treated in the Brazilian public health care system waited for 33 days (mean) (SD = 30) to have their first appointment at the treatment center and for 63 days (mean) (SD = 46.8) to start the treatment.

Of the 27 patients who died, 21 died due to cancer while 6 died due to other health issues not related to cancer. Of the patients who died due to cancer, 67% died within1 year of the diagnosis, 28% died 2 to 3 years after diagnosis, and 5% in 4 to 5 years after diagnosis. About these patients, 48% were diagnosed in stage IV, 43% were diagnosed in stage III, and 9% were diagnosed in stage I.

Discussion

Cancer in the oral cavity, lips and oropharynx in Brazil is considered a public health problem, with more than 1,200 new cases in the city of São Paulo in 2018.[1] At the University of São Paulo's School of Dentistry, the Stomatology clinic diagnoses these and other oral lesions, being one of the largest public centers for oral diagnosis in São Paulo. Biopsies are sent to the Histopathology Service of the institution, facilitating the exchange of information between the professionals involved.

In this study, most patients were men, white, and aged between 50 and 69 years, like other studies.[4,6,8] Most patients were smokers or alcoholics, both of which were risk factors for head and neck cancer, especially if combined.[5] However, 24% denied smoking and drinking alcohol, which differs from other studies.[4,6,8] This can be due partly to the corresponding diagnosis of salivary gland cancer, such as mucoepidermoid carcinoma and adenoid cystic carcinoma, which has little relation to smoking or alcohol consumption.[8]

Squamous cell carcinoma was the most prevalent type of carcinoma (diagnosed in 88% of cases), as in other Brazilian studies.[8,9] Squamous cell carcinoma represents 90% of OC, followed by mucoepidermoid carcinoma and adenoid cystic carcinoma,[11] which corroborates the result obtained in the present study.

The longest interval was for the patient to seek professional care at the Stomatology clinic since the first perception of the lesion (T1), as in many similar studies.[6,7,12-15] Waiting times for patients to be treated after diagnosis, among studies conducted in Brazil, ranged from 45[7] to 71,1[8] days, mean 64, 31 days.[6-9,16] Compared to a study from Denmark,[14] where the waiting times for patients to be treated was 25 days, implying that the Brazilian health care system has to improve, and initiate the treatment earlier.

Almost half of the patients were diagnosed at an early stage (I or II) (Figure). Scott et al.[11] concluded that there may be no association between delayed

Table 2. Data of the time gap (in days) between the first symptom of the lesions, diagnosis and treatment of patients.

Variable	T1				T2				T3				T4			
	Mean	Median	SD	n	Mean	Median	SD	n	Mean	Median	SD	n	Mean	Median	SD	n
Private	275	105	526.6	174	13	9.5	8.4	172	19	10	23.7	11	36	30	33.6	11
Public									33	20	30	74	63	60	46.8	70

T1 the time gap in days between the first sign/symptom and the first appointment at the stomatology clinic; T2 the time gap in days between the first appointment and the result of the biopsy; T3 the time gap in days between the result of the biopsy and the first appointment at the oncological clinic; T4 the time gap in days between the first appointment at the treatment center and the start of treatment.

diagnosis and the stage of the disease as in their study, 27% of patients were diagnosed at the first appearance of signs and symptoms, but with an advanced stage of disease; and 19% of patients with late head and neck cancer diagnosis had early stages of the disease.[15] This may be because some people in the early stages of head and neck cancer may be asymptomatic.[1] In this study, 18% of patients were asymptomatic at the time of diagnosis.

Regarding the delay related to professionals (T2), the interval for diagnosis in this study was 13 days, with the same result as the study by Lyhne et al.[14] and represents the best time for diagnosis compared to all other studies. As for the delay in the health system (T3 + T4), the largest interval was that of the present study, similar to the result of Le Campion et al.[8] carried out in Alagoas, Brazil.

Although 20 years passed between the Costa and Migliorati[6] study, in a similar study conducted in our institution, and the present study, there was an increase of approximately 10 days for the patient to start the treatment after diagnosis. This time is related to the procedures that the patient goes through in the oncological clinic before starting the treatment itself, such as redoing the histological and immunohistochemical analysis, imaging tests, and laboratory tests for treatment planning. To improve this delay, it would be necessary to have an integration between the diagnosis and treatment centers, as already explained in another study,[7] there is no need to redo the histological analysis, immunohistochemistry, and imaging tests already done at the diagnostic center, hence, reducing the time in the pre-treatment.

There was a big difference in the interval between diagnosis and first appointment at the treatment site (T3) and first appointment until treatment commencement (T4) between patients treated by private-sector health care and public health care. The results of patients treated by private-sector health care correspond to approximately half the time of patients treated by public health care. That indicates the need to improve organization and infrastructure in public cancer care facilities to reduce the diagnosis and treatment delay and, by that, the mortality.

Additionally, the present study demonstrates that the interval between diagnosis and treatment does not fit the 60-day law, established in 2012.[10] The interval corresponded to a mean of 96 days for patients to be attended in public health care.

With the delayed start of treatment, carcinoma may progress, increasing its stage, affecting treatment, and worsening prognosis.[6,7,13] According to Kowalski and Carvalho,[15] for an advanced case with stage III or IV to become a case where treatment is not possible, the time taken was from 1 to 23 months with a median of 3 months, and for these cases to progress to death, the time taken was from 1 to 21 months with a median of 4 months. Thus, both early diagnosis and access to treatment are important. Measures must be taken to decrease the interval between diagnosis and treatment commencement for these patients, thereby reducing morbidity and mortality due to OC.

It is a consensus that early diagnosis of cancer has a better prognosis, compared to cases of late diagnosis. Nevertheless, some studies have not shown better survival rates, even with early diagnosis.[17,18] The difference between the results of the studies can be justified by several factors, including the study design and memory bias.[19,20] A study showed that even the memory of recent events has limited reliability.[21] Therefore, memory bias is an important bias to be considered, especially in studies retrospectively evaluating patients who have undergone treatments. To mitigate memory bias, a combination of data collection methods, combining prospective and retrospective data is a feasible alternative.[18] In this study, to reduce memory bias, we retrieved retrospective information from the patients' medical records, combined with prospective information through the questionnaire. In the phone interview, we also asked patients to answer the questions, with all their medical data in their hands, such as exams and appointments.

There is also a need to train the health team to identify these lesions, using strategies to motivate and involve the patient in the detection process[22] and even develop oncology education in undergraduate health courses.

With the training of the health team to diagnose these lesions, and the integration of the diagnosis and treatment center, the time for diagnosis and

treatment of these patients may decrease, improving their prognosis.

The present study has some limitations. First, as previously stated, besides all the effort to avoid memory bias, it is still an important source of bias, as the phone interview was a key source of data. Another limitation might be the low response rate, as we were able to contact only 94 patients from a total of 184. This may be due mostly to the death of these patients, thus being a source of survivorship bias, affecting our results regarding survivability of OC.

Conclusion

The interval between the first sign and symptom of the disease and the first appointment at the Stomatology clinic was excessively long. Those who were treated in public health care took twice as long to start treatment when compared to patients treated in private-sector health care, which shows the inequality of access to health care in Brazil. There was an improvement in early diagnosis at the School of Dentistry of the University of São Paulo.

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