Original Article

Factors Affecting Professional Delay in Diagnosis and Treatment of Oral Cancer in Iran

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Abstract

Background: Oral cancer is the most common malignant tumor among head and neck cancers. Delay in diagnosis affects the treatment and prognosis of oral cancer. We measured the professional delay in the diagnosis and its attributes in the Cancer Institute of Iran, the largest referral center for oral cancer patients in the country.

Methods: We interviewed oral cancer patients to measure the delay and used case-control approach to study association of various prognostic factors with professional delay and tumor stage.

Result: Out of 206 patients, 71.4% were diagnosed at the advanced stage. The median of the patient, professional and total delays were 45, 86 and 140 day, respectively. In the univariate model, prescription of medicines like analgesics (OR = 5.3, 95% CI 2.2–12.9) and history of dental procedure (OR=6.8, 95% CI 1.7–26.9) were associated with higher risk of delay compared to patient who were biopsied from the beginning. History of loose teeth increased the risk of delay 4 times (OR = 4.0, 95% CI 1.6–9.8). Patients with primary education had 70% lower risk of delay compared to the illiterate patients (OR = 0.3, 95% CI 0.1–0.7) and the risk was lower among patients who had diploma (OR = 0.04, 95% CI 0–0.7) and college education (OR = 0.1, 95% CI 0–0.4). The delayed patients were diagnosed in more advanced stage compared to the patients without delay (OR = 2.1, 95% CI 1.0–4.4).

Conclusion: Development of a national guideline for follow-up of oral lesions, training and awareness of health care professionals about oral cancer diagnosis may decrease the delay and improve the oral cancer outcome in Iran.

Keywords: Delayed diagnosis, healthcare, oral cancer, risk factor

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Introduction

Oral cancer is the most common malignant tumor among head and neck cancers.[1] According to Globocan 2012, the age standardized incidence rate (ASR) of lip and oral cavity cancer was 5.5 per 100,000 among male worldwide.[2] There are large variations in the ASR oral cancer, varying from 0.4 in Pasto region of Colombia to 22.8 in Bhbol region of India.[3] It is noteworthy that sharp increases in the incidence rates of oral/pharyngeal cancers have been reported for several countries and regions such as Denmark, France, Germany, Scotland, Central and Eastern Europe and to a lesser extent Australia, Japan, New Zealand and the USA.[3,4] Differences in incidence rate of oral cancer is related to variations in exposure to environmental risk factors including poor oral health, tobacco smoking, alcohol consumption, HPV infection, and dietary factors.[3–5] In addition, it was reported that the incidence rate of oropharyngeal squamous cell cancer has increased in men younger than 50 years who have no history of alcohol or tobacco use over the past decade in Europe and USA, indicating the importance of HPV infection in the occurrence of oral cancer in the young population.[6,7]

The 5-year survival of oral cancer was estimated to be about 56% in the US and about 30.5% in India. Survival rates are considerably low in developing countries, most likely due to delayed diagnosis and presentation of the tumor in advanced stage.[4,8–10] Despite advances in treatment of oral cancer, the 5-year survival has not improved notably.[4,11,12] Because oral cavity has a critical role in speaking, eating, chewing, swallowing and beauty, extensive operation of oral cancer leads to major structural and functional deformities in patients' head and neck. Therefore, the quality of life (QOL) of oral cancer patients is highly associated with the extent of surgery and other interventions in the head and neck area.[4,5,12]

Early diagnosis of oral cancer, when lesions are small and localized, would improve the clinical outcomes including mortality, morbidity (e.g., deformities), and the duration of treatment.[8,11,13] About 50% of oral cancer patients are diagnosed in the advanced stage and their survival is considerably poor[13] highly due to the silent nature of this cancer and the delay in diagnosis.[8,13,14] Delayed diagnosis consists of patient and professional delay.[15] Patient delay is defined as the duration from onset of signs or symptoms to the initial visit to a physician; the professional delay is the duration from initiation of investigation of cancer-related symptoms by a physician to the initiation of treatment. [15-17] Some factors have been reported to be associated with the delay in the diagnosis of oral cancer, including site of lesion, size and differentiation of tumor, involvement of regional lymph node, and presence of

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metastases, tobacco and alcohol consumption, diet and dental factors.[1,14,15]

The age standardized incidence rate (ASR) of oral cancer was reported to be 0.7, and 0.5 per 100,000 Iranian males and females, respectively.[2] The overall 5-year survival among Iranian patients was reported to be about 30%, which is greatly linked to the delay in the diagnosis and treatment of oral cancer.[4] We studied the situation of professional delays and stage on diagnosis of oral cancer among patients who were hospitalized in the cancer institute hospital, the largest referral center which treats head and neck cancer in Iran.

Material and Methods

During 2009–2010, we recruited oral cancer patients admitted to the Cancer Institute of Iran, the largest referral cancer center that admits a sizable number of head and neck cancer patients for all types of treatment modalities.

The interviewer (EB) visited the head and neck cancer ward and interviewed all patients who were diagnosed as oral cancers including cancers of tonsils, tongue, mouth, and oropharynx (ICD-10 codes C09, C10, C03-06, C01-02) and were admitted to the hospital for surgery. We only included the incident patients and excluded recurrent cancer cases. We used a questionnaire to interview the prevalent patients and collect clinical information and risk factors of the delay.

Statistical Analyses

Patient delay was defined as the interval from onset of symptoms until the first visit to a physician, while the professional delay was defined as the interval from initial investigation of cancer-related symptoms to the initiation of treatment. Sum of patient and professional delays accounted as the total delay. Using a case-control approach for analyses, we stratified the patients into two strata by the median value of the professional delay. Patients with a delay higher than the median value were included in the delay group (cases) and those with a delay less than the median were put in the control group.

We studied the association of professional delay of oral cancer with the age at diagnosis, gender, and education as well as smoking and alcohol consumption, grade, number of visits before treatment, erroneous interventions (analgesic drugs, filling the teeth or exodontia), cachexia, headache, otalgia, cervical mass, referral pain, dysphagia and experience of the loose tooth. We also analyzed data using tumor stage as the outcome and studied the association of oral cancer stage with professional delay in diagnosis, age, gender, education as well as smoking and alcohol consumption, grade, number of visits before treatment, erroneous interventions (analgesic drugs, filling the teeth or exodontia), cachexia, headache, otalgia, cervical mass, referral pain, dysphagia and experience of the loose tooth as confounding variables. We used logistic regression model to estimate odds ratio (OR) and corresponding 95% confidence interval (95% CI). Results of the crude and adjusted regression model were presented.

Factors significantly related to professional delay with *P*-values of less than or equal to 0.2 were entered to the backward stepwise multiple logistic regression model. We performed the co-linearity test between variables to control co-variability between variables and thus identify independent predictors for the delay. Although we presented the crude odds ratios for all putative risk factors, we performed the likelihood ratio test for goodness of fit of the regression model. We used STATA statistical software version 11 to perform the statistical analyses. The Regional Ethics Committee of Tehran University of Medical Sciences approved this study.

Results

In total, we studied 206 patients with a mean age of 58.3 years (SD ± 17.7). More than 69.4% of them were illiterate or had primary education. Smoking prevalence was 47% and about 24% reported ever alcohol consumption. About 60% of patients visited a doctor 3–4 times before the cancer diagnosis. At the time of diagnosis, 71.4% of patients were at the advanced stages and in 91.8%, tumor histology was squamous cell carcinoma (SCC). Almost 65% of patients visited a general physician or dentist at the beginning of their symptoms.

Totally, the median of the patient and professional delays were 45 d and 86 d, respectively and the median of the total delay reached 140 d (20 wk.) (Table 1).

Univariate analyses revealed that gender, education, age, cachexia, otalgia, smoking, erroneous intervention, number of visits before admission, cervical mass, headache, referral pain and loose teeth were significantly associated with the professional delay in oral cancer diagnosis (Table 2). However, in the multivariate logistic regression and selection of the variable based on the goodness of fit analyses, alcohol consumption, grade, otalgia, cachexia, cervical mass, referral pain, headache and dysphagia were dropped from the model. In the latter analysis, patients who were treated with different medicines like analgesics had approximately a 5-fold higher risk of professional delay compared to those who had initially undergone appropriate interventions like endoscopy or biopsy (OR = 5.3 95% CI 2.2–12.9). Likewise, patients who experienced filling their teeth or exodontias had more than 7-fold risk of professional delay compared to patients who had endoscopy or biopsy at the beginning (OR = 6.8 95% CI 1.7–26.9). In addition, patients who were visited by a doctor 3–4 times (OR = 5.2 95% CI 1.1–23.7) and those who were visited 5 times or more (OR = 8.3 95% CI 1.6–42.7) had higher risk of professional delay compared to the patients who were visited less than three time before the diagnosis. Patients who reported loose teeth had a 4-fold higher risk of professional delay compared to those who did not have loose teeth (OR = 4, 95% CI 1.6–9.8)

Education was negatively associated with the professional delay in patients. Patients with primary education had a 70% lower risk

Table 1. Distribution of delay in the diagnosis and treatment of oral cancer patients hospitalized in the Cancer Institute of Iran in 2009–2010

Variable	Mean (± SD*)	Median (d)	(min/max)
Total Delay	156.4 (74.7)	140	(36/430)
Professional delay	98.2 (48.2)	86	(28/365)
Patient Delay	57.6 (56.6)	45	(0/354)

Table 2. Crude and adjusted odds ratios (OR) and corresponding 95% confidence interval (CI) for predictors of the professional delay in oral cavity cancer patients hospitalized in the cancer institute of Iran in 2009-2010 .

Variable		Odds Ratio (95% CI)	
	Number (%)	Crude	Adjusted
Gender			
Female	87 (42.4)	Reference	Reference
Male	118 (57.6)	0.4 (0.3–0.8)	0.5(0.2-1.3)
Age group			
< 40	38 (18.6)	Reference	Reference
40–64	66 (32.4)	1.6 (0.6–3.7)	0.8 (0.2-2.7)
>64	100 (49)	4.6 (2–10.4)	0.9 (0.2-3.6)
Education			
Illiterate	65 (31.7)	Reference	Reference
Primary	77 (37.6)	0.4 (0.2–0.9)	0.3 (0.1-0.7)
Diploma	53 (53.9)	0.1 (0.1–0.3)	0.1(0-0.4)
College or higher	10 (4.9)	0.04 (0–0.4)	0.04 (0-0.7)
Smoking			
No	109 (53.2)	Reference	Reference
Yes	96 (46.8)	1.3 (0.8–2.3)	2.1 (0.9-5.1)
Alcohol			
No	156 (76.1)	Reference	—
Yes	49 (23.9)	0.7 (0.3–1.3)	—
Grade			
Low	85 (41.4)	Reference	—
Intermediate	75 (36.6)	0.8 (0.4–1.4)	—
High	45 (22)	1 (0.5–2)	—
Cachexia			—
No	97 (47.3)	Reference	—
Yes	108 (52.7)	2.2 (1.3–3.9)	—
Otalgia			—
No	180 (87.8)	Reference	—
Yes	25 (12.2)	2.9 (1.2–7.4)	—
No. of visits before admission			
1–2	29 (14.2)	Reference	Reference
3–4	119 (58)	7.7 (2.2–26.8)	5.2 (1.1–23.7)
5 or more	57 (27.8)	28 (7.3-107.7)	8.3 (1.6–42.7)
Erroneous Initial Intervention			
Endoscopy or biopsy	94 (45.9)	Reference	Reference
Only Prescription of analgesic, etc.	77 (37.6)	8.9 (4.4–18)	5.3 (2.2–12.9)
Filling or pulling teeth	34 (16.6)	17 (6.2–47.2)	6.8 (1.7–26.9)
Cervical Mass			
No	159 (77.6)	Reference	—
Yes	46 (22.4)	1.8 (0.9–3.6)	—
Referral pain			
No	78 (38)	Reference	—
Yes	126 (62)	1 (0.6–1.8)	—
Headache			—
No	148 (72.2)	Reference	—
Yes	57 (27.8)	3.2 (1.6–6.1)	—
Dysphagia			
No	160 (78)	Reference	—
Yes	45 (22)	0.9 (0.4–1.7)	—
Loose teeth			
No	116 (56.6)	Reference	Reference
Yes	89 (43.4)	5.5 (3–10.1)	4 (1.6–9.8)

Table 3. Crude and adjusted odds ratios (OR) and corresponding 95% confidence interval (CI) for predictors of stage in oral cavity cancer patients hospitalized in the cancer institute of Iran in 2009–2010.

Variable	Odds Ratio (95% CI)	
	Crude	Adjusted
Gender		
Female	Reference	Reference
Male	1 (0.6–1.6)	1 (0.5–2)
Age group		
< 40	Reference	Reference
40–64	1 (0.5–2)	3 (1.1–8.3)
>64	1 (0.6–1.9)	4.7 (1.4–16)
P-value for trend		0.01
Education		
Illiterate	Reference	Reference
Primary	1.1 (0.7–1.9)	1.4 (0.5–3.6)
Diploma	0.9 (0.5–1.7)	2 (0.6–6.8)
College or higher	0.8 (0.3–2.5)	3.3 (0.5–23.5)
Smoking		
No	Reference	—
Yes	1.2 (0.8–1.9)	—
Alcohol		
No	Reference	—
Yes	1 (0.6–1.7)	—
Delay		
No	Reference	Reference
Yes	1.8 (1–3.5)	2.1 (1–4.4)
Grade		
Low	Reference	Reference
Intermediate	4 (2.3–6.7)	3.2 (1.5–6.5)
High	105 (14.2–775.9)	47.7 (6–377.4)

of professional delay compared to the illiterate patients (OR = 0.3, 95% CI 0.1–0.7). The risk of delay decreased further by increasing the level of education (p value for trend 0.002) (Table 2).

The univariate analysis of stage showed that delay in diagnosis, grade, and number of visits before admission, erroneous initial intervention, loose teeth, age, education, smoking, and alcohol consumption were significantly associated with stage distribution among oral cavity cancer (Table 3). However, based on the multivariate model, we found that patients who were diagnosed with a delay had approximately a 3-fold higher risk of being diagnosed in advanced stage compared to patients who reported no delay (OR 2.9, 95% CI 1.03–8.3). Furthermore, the risk of advanced stage diagnosis increased with age (*P* value for trend 0.01) (Table 3).

Discussion

In this study, we showed a long patient and professional delay for oral cancer diagnosis in Iran. The main reason for the professional delay was that dentists, general practitioners, and other health professionals did not take into account the oral cancer as a differential diagnosis and prescribed analgesics or provided dental procedures on several visits. The delay in the diagnosis and treatment increased the stage of tumor at the time of diagnosis.

In our study, the professional delay was 12 weeks. In a previous report from Iran in 2009, Sargeran et al., reported that the professional delay was one month.[18] However, the professional delay in the diagnosis of oral cancer was about 7–8 weeks in China,[15] Thailand,[19] and Denmark.[16] In a study from Ontario, Canada, the delay was as high as that found in the present study (12 weeks).[17] An exceptionally low delay (i.e., 11 days) was reported by Andrea Jovanovic in the Netherlands in 1992,[20] which might be due to the difference in the definition and measurement methods for delay.

We found that prescription of different medicine, like analgesics, and dental procedures, like filling teeth or exodontias, have increased the risk of the delay compared to cases that had undergone appropriate interventions like endoscopy or biopsy. It was shown that if biopsy was adopted at first visit, it would significantly reduce the professional delay.[15,19,21] In line with Kerdpon et al.,[19] we also found that patients with loose teeth had a 4-fold higher risk of professional delay compared to patients who did not have loose teeth. We showed that the risk of delay was also associated with the number of visits before diagnosis and treatment. Our results are supported by other studies from Austria and US which showed that over one third of the patients (38%) delayed seeking professional advice for more than 3 months after first becoming aware of the lesion.[21,22] These findings emphasize that developing clear guidelines and awareness of health professionals including dentists, general practitioners, etc. about oral cancer signs and symptoms and appropriate follow-up of the patients may contribute to the timely diagnosis and management of oral malignancies. Application of valid means of diagnosis, using appropriate tools and a diagnostic approach on the first consultation, careful examination of the oral cavity during the first visits, particularly in older patients who present with loose teeth or abnormal lesions would decrease the professional delay and lead to the timely diagnosis and treatment.

Patients with primary education had a 70% lower risk of professional delay compared to the illiterate patients. The delay was decreased further by increasing the level of education. The results were supported by previous research, indicating that literacy and

low socio-economic status had a significant association with presentation of oral cancer patients in advanced stage,[23] although opposite results were also reported.[24]

As expected, we reported a significant association between the professional delay and tumor stage at diagnosis and supported the previous findings from other countries.[25,26] However, in a systematic review of 27 studies, no association was found between diagnostic delay in head and neck cancers and tumor stage disease, although the meta analysis was not restricted to the oral cancer and all head and neck cancers were included in that study.[27] In another systematic review by Gomez et al., diagnostic delay was associated with tumor stage and the pooled relative risk (RR) was 1.47 (95% CI: 1.09–1.99).[25] Therefore, the available evidence indicates that the delay in diagnosis could lead to the progression of cancer and presentation of tumor in an advanced stage.

In conclusion, we found that there is a long professional delay in diagnosis and treatment of oral cancer in Iran. We suggest development of clear guidelines for the evaluation and follow up of oral lesions in the health care system. We suggest education and awareness programs for dentists and general practitioners, emphasizing the appropriate examination of oral cavity in high risk patients, including old patients and smokers, all of which may contribute to early diagnosis of oral cancer.

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