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An evaluation on diagnosis and management patterns of patients with oral squamous cell carcinoma referred to the Cancer Institute of Tehran University of Medical Sciences during 2010-2021

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ABSTRACT

Background: Squamous cell carcinoma (SCC) is the most common malignancy of the oral cavity with multiple complications associated with the disease and its treatments and a high mortality rate. In the present study we aimed to assess the diagnosis and management of these patients referring to Imam Khomeini Hospital during 2010-2021, their survival rate and possible factors affecting mortality of the patients.

Materials and Methods: In this retrospective descriptive-analytic study, patients diagnosed with oral SCC referring to Imam Khomeini Hospital during 2010-2021 were included. Required data were gathered from the patients' records and analyzed by SPSS software last version and Microsoft Excel using the Log-rank test and Kaplan-Meier survival curves.

Results: In the specified period 146 patients with oral SCC were admitted to Imam Khomeini Hospital with a mean age of 63.4±18.1 years and a slightly higher prevalence of men. Most patients had an educational level of lower than diploma (60.2%), were living in urban areas (78.6%), were treated by a general dentist or a general practitioner (86.8%), primarily underwent surgery (78.8%) and their treatment followed the standard management for these patients (86.3%). 69.2% of the patients stayed alive until the studied period and the buccal mucosa was the most commonly involved location (51.7%). The mean survival of the patients was calculated to be 3384.3 days which was found to be affected by the educational level and compatibility of their treatment with standard guidelines.

Conclusion: The mean survival of the subjects was 9.3 years. The survival of the patients decreased from 100% to 0.4% after the 12 years period which is promising. These results indicate the effectiveness of following standard treatment protocols and early diagnosis of the patients in early stages of the disease.

Keywords: Oral squamous cell carcinoma; Survival; Kaplan-meier.

Introduction

Oropharyngeal cancers are the sixth most common cancer all around the world, 90% of which are squamous cell carcinomas (SCC). Oral cancers comprise 3% of all the cancers and are amongst the 10 causes of death worldwide [1]. Its incidence has been estimated to be 1 to 10 per 100,000 people in different

countries which increases by age in a way that 98% of oropharyngeal cancers occur in patients older than 60 years of age [2]. Ethnicity, family history, occupational factors, smoking, alcohol consumption, bacterial and viral infections, diet and alcoholic mouthwashes have been reported as risk factors for oral cancers [3,4]. Treatments of these cancers, even benign ones, are typically associated with an extended removal of orofacial tissues leading to dire complications. SCC, basically a cutaneous lesion, is highly invasive and its treatment is a difficult challenge for surgeons. Pharynx, oral cavity, oropharynx and hypopharynx are the four main locations of oral SCC. Oral cavity floor and the tongue are the most common locations affected by these cancers. SCCs most commonly metastasize to cervical lymph nodes, lungs, liver and bones [5].

Despite the vast improvements in surgery, radiotherapy and chemotherapy, 5 year survival rate of patients with oral cancer has not improved compared to the previous decades and has remained at 50 to 55% [6]. Although only 35 to 40% of oral cancers are diagnosed in early stages [7], the 5 year survival rate has been shown to increase to 85% with early diagnosis and treatment of patients [8]. In a study conducted in Iran, 59% of oropharyngeal cancers and 29% of lip cancers were reported to be diagnosed at stages III and IV [9]. This can be attributed to insufficient awareness of people about this cancer.

Early detection of precancerous lesions such as erythroplakia and leukoplakia are currently the best method for decreasing the mortality of these oral cancers [1]. However, most cases are asymptomatic in their early stages [10,11]. Based on international guidelines, all the patients over 40 should be examined for oral cancers [12] while only 13 to 20 percent of these subjects are currently being screened for this disease [13]. Treatment of oropharyngeal cancers is chosen based on the type of cells and their differentiation level, location and size of the lesion, the patients ability to speak and swallow, the psychological and physical status of the subject and the surgeons experience along with the patient's compliance. The early stages of oral SCC are treated with radical surgery. Radiotherapy and chemotherapy used in the later stages of the cancer [1,14]. In order to evaluate the diagnosis and management of patients with oral SCC, estimate their survival rate and determine the factors affecting mortalities, we aimed to assess the patients with established diagnosis of oral SCC referring to Imam Khomeini Hospital during 2002-2013.

Materials and Methods

In this retrospective descriptive-analytic study, patients diagnosed with oral SCC referring to Cancer Institute of Imam Khomeini Hospital during 2010-2021 were included. Considering the rate of appropriate diagnosis and treatment of oral SCC to be 65%, in order to identify these appropriately managed patients with an accuracy of 8% and a confidence interval of 95%, a sample size of 146 subjects would be needed. Accordingly, 146 patients were randomly selected from the archives and their records were obtained. Required data were gathered and analyzed by SPSS software last version and Microsoft Excel. Descriptive statistics were presented as mean and standard deviations for the quantitative variables and frequency and percent for the qualitative variables. The survival rate was compared between subgroups of patients using Kaplan-Meier survival curves. Since not all the subjects reached the final outcome of death during the study period, each two survival curves were compared using Log Rank test or Mantel Cox test. There was no need for using Gehan-Breslow test since the prerequisite of equal risks in the two groups applied throughout the study. Ethics Committee of Tehran University of Medical Sciences approved the methods of this study. The principles of Helsinki's Declaration were adhered to by all the authors. Data were used anonymously and were considered confidential, only accessible by the authors.

Results

A total of 146 patients with oral SCC were included in the study with a mean age of 63.4±18.1 years. The mean age at diagnosis was calculated to be 59.4±17.3 years. The youngest patient was 20 years old and the oldest subject was 92 while the minimum and maximum of age on arrival were 19 and 89 years. 67 patients (45.9%) were female and the remaining 79 (54.1%) were male. The majority of patients had an educational level of lower than diploma (60.2%), were living in urban areas (78.6%). 86.8% of patients were treated by a general dentist or a general practitioner on their first visit and 78.8% of them primarily underwent surgery. 70.5% of the subjects were only followed up on their second visit and this figure increased to 78.1% for the patients' third visit. The treatment followed the standard management for these patients in 86.3% of subjects. 69.2% of the patients stayed alive until the studied period and the buccal mucosa was the most commonly involved location (51.7%). 18.5% of the subjects had stage III and IV cancers on diagnosis while the rest were stage I and II. The perceived severity of disease by the pa-

tients was quite compatible with their actual severity. Table 1 shows the details of these descriptive characteristics. The mean survival of the patients was calculated to be 3384.3 days with a median of 3856.0. Figure 1 depicts the survival of the patients according to time passed from the diagnosis and Figure 2 shows the cumulative hazard of oral cancers. The survival curves of patients were drawn and compared between the subgroups of evaluated variables using Log Rank and Mantel-Cox tests and the results are presented in Table 2. As can be seen, although the mean survival of the 125 patients treated by a specialist was slightly lower than the subjects treated with general practitioners, the differences were not statistically significant (p=0.274). On the other hand, the mean survival of subjects with diploma or higher educational levels was significantly higher than the patients without diplomas (p<0.001). The differences in survival were not statistically significant, neither between males and females (p=0.753), nor between patients living in rural and urban areas (p=0.281). However, the patients treated according to standard guidelines were found to have a significantly higher survival compared to subjects whose treatments were not compatible with standard methods (p=0.008). Figures 3 and 4 show the survival and hazard curves developed by Kaplan-Meier analysis for compatibility with standard treatments.

Table 1. Results of descriptive analysis.

Variable		*Statistics*
Avg		*63.4±18.1*
Age at diagnosis		*59.4±17.3*
Gender	*Female*	*67 (45.9%)*
	Male	*79 (54.1%)*
Educational level	*Illiterate*	*37 (25.9%)*
	Under Diploma	*49 (34.3%)*
	Diploma	*41 (28.7%)*
	University degree	*16 (11.2%)*
Living area	*Urban*	*114 (78.6%)*
	Rural	*31 (21.4%)*
The first examiner	*General dentist*	*67 (48.2%)*
	Specialist dentist	*3 (2.1%)*
	General practitioner	*54 (38.4%)*
	General surgeon	*13 (9.2%)*
	Maxillofacial surgeon	*3 (2.1%)*
Primary intervention	*Surgery*	*115 (78.8%)*
	Radiotherapy	*24 (16.4%)*
	Follow up	*7 (4.8%)*
Secondary intervention	*Surgery*	*1 (0.7%)*
	Radiotherapy	*1 (0.7%)*
	Palliative treatment	*1 (0.7%)*
	Follow up	*114 (78.1%)*
	Other	*29 (19.9%)*
Compatibility of the treatment with standard guidelines	*Completely*	*9 (6.2%)*
	Moderately	*117 (80.1%)*
	None	*20 (13.7%)*
Status of the patient	*Alive*	*101 (69.2%)*
	Expired	*37 (25.3%)*
	Unknown	*8 (5.5%)*

Variable		Statistics
Avg		63.4±18.1
Age at diagnosis		59.4±17.3
Site of involvement	Tongue	37 (25.5%)
	Buccal mucosa	75 (51.7%)
	Minor salivary glands	6 (4.1%)
	Floor of the oral cavity	20 (13.8%)
	Mandible	7 (4.8%)
Stage of disease on diagnosis	I	29 (19.9%)
	II	90 (61.6%)
	III	20 (13.7%)
	IV	7 (4.8%)
Perceived severity of disease by the patient	Primary	39 (27.7%)
	Moderate	83 (58.9%)
	Advanced	19 (13.5%)

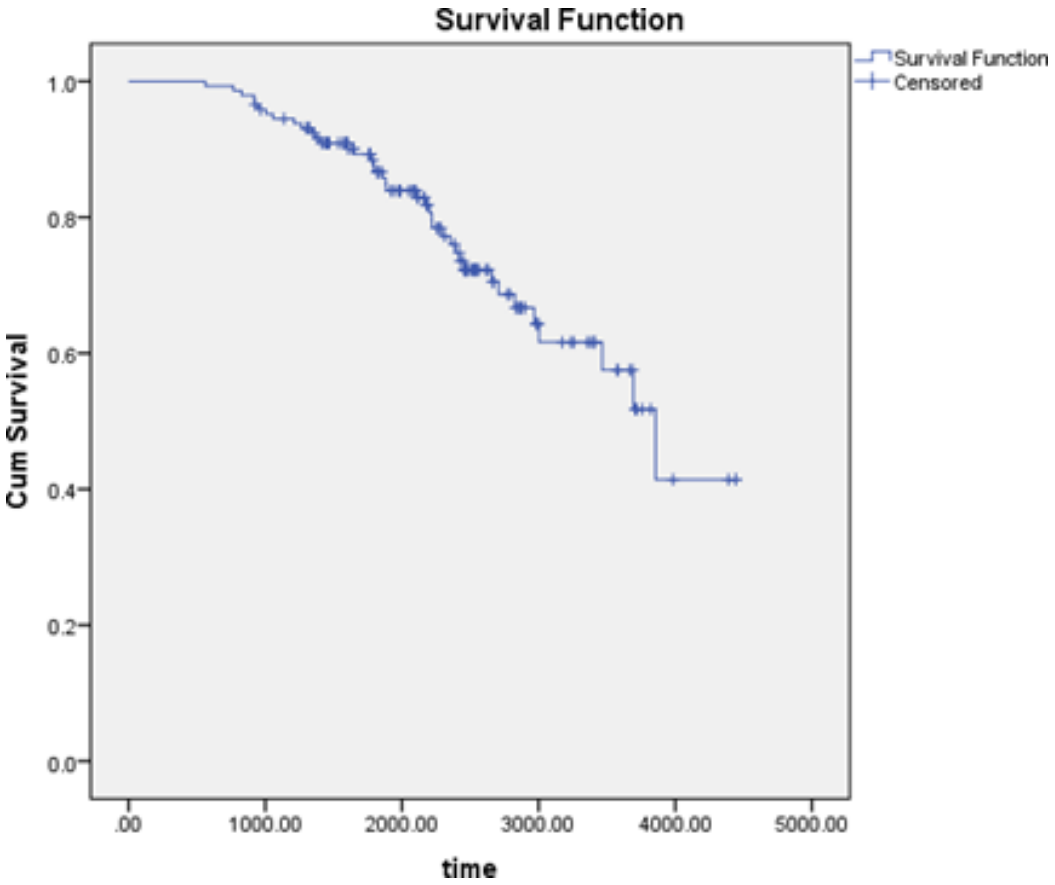

Figure 1. Kaplan-Meier analysis for survival of the patients.

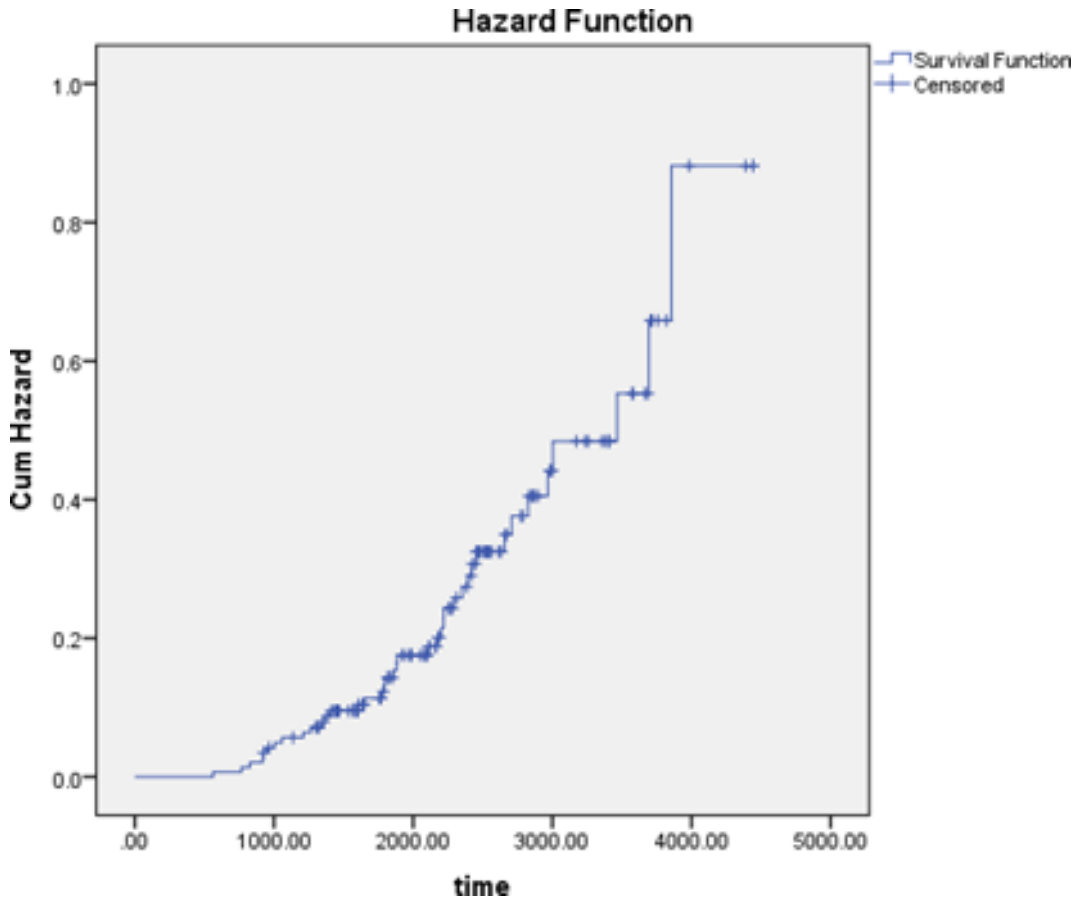

Figure 2. Kaplan-Meier analysis for hazard.

Table 2. Results of descriptive analysis.

Variable		*Number*	*Mean survival (Standard Error)*	*P vlaue*
Treated by	*Specialist*	*125*	*3350.8 (142.2)*	*0.274*
	General practitioner	*19*	*3360.8 (208.1)*	
Educational level	*Diploma and higher*	*57*	*4004.9 (181.7)*	*<0.001*
	Under Diploma	*86*	*2970.5 (174.1)*	
Living area	*Urban*	*114*	*3423.6 (151.2)*	*0.753*
	Rural	*31*	*3016.3 (189.0)*	
Gender	*Female*	*67*	*3120.7 (232.0)*	*0.281*
	Male	*79*	*3489.5 (162.8)*	
Treated according to standard guidelines	*Yes*	*126*	*3654.3 (135.9)*	*0.008*
	No	*20*	*2811.3 (277.9)*	

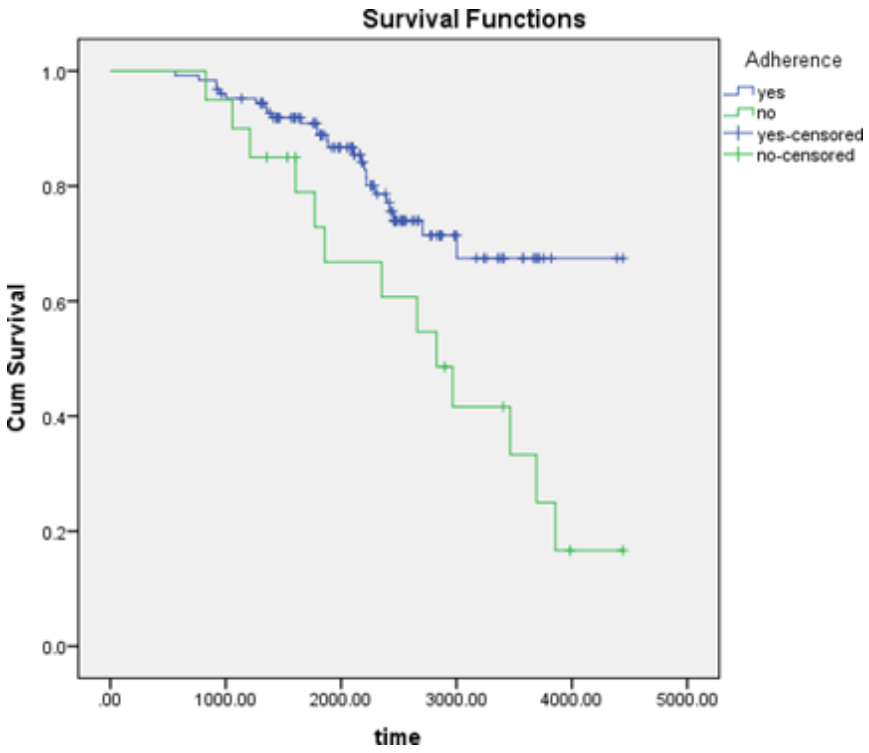

Figure 3. Kaplan-Meier analysis for survival of patients according to the compatibility of their treatment with standard guidelines.

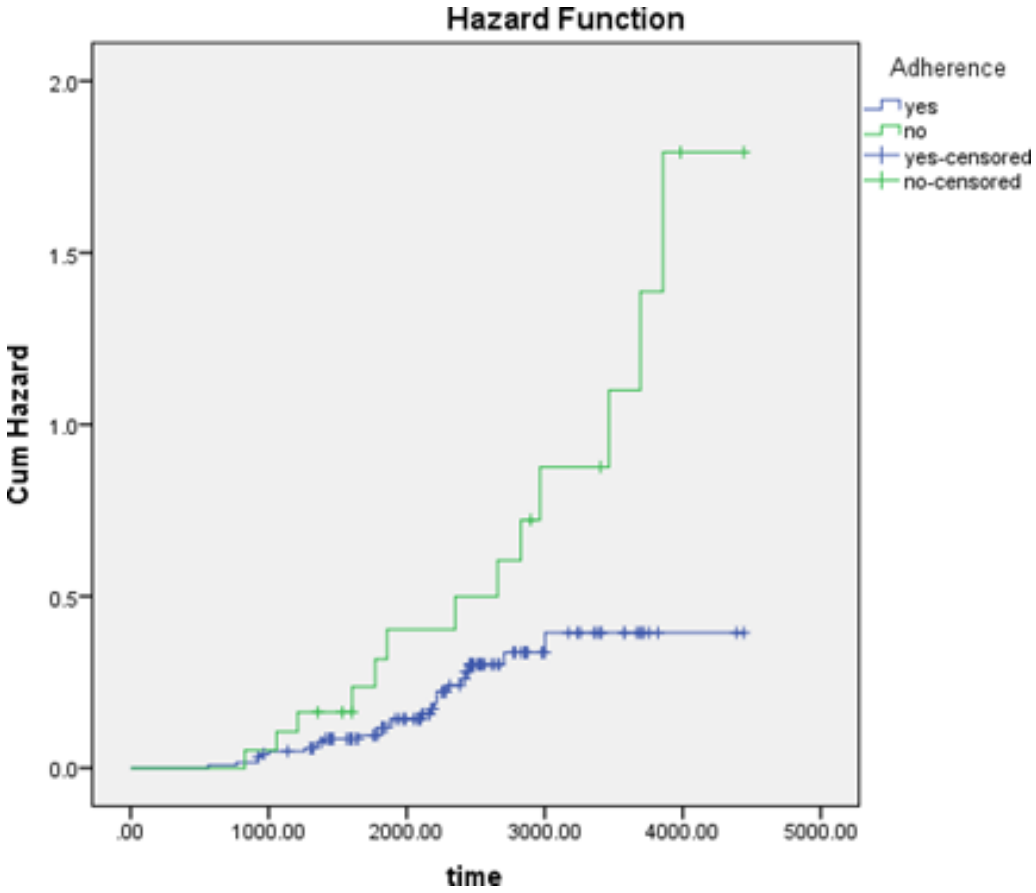

Figure 4. Kaplan-Meier analysis for hazard according to the compatibility of patients' treatments with standard guidelines.

Discussion

The present study was carried out to assess the diagnosis and management of patients with oral SCCs referring to Imam Khomeini Hospital during 2010-2021, their survival rate and possible factors affecting mortality of the patients. Based on the results yielded from assessment of 146 patients, the mean age was calculated to be 63.4±18.1 years and a slightly higher prevalence of men was observed in the included subjects. Most patients had an educational level of lower than diploma (60.2%), were living in urban areas (78.6%), were treated by a general dentist or a general practitioner (86.8%), primarily underwent surgery (78.8%) and their treatment followed the standard management for these patients (86.3%). 69.2% of the patients stayed alive until the studied period and the buccal mucosa was the most commonly involved location (51.7%). The mean survival of the patients was calculated to be 3384.3 days which was found to be affected by the educational level and compatibility of their treatment with standard guidelines. The survival of the patients decreased from 100% to 0.4% after the 12 year period which is promising.

As mentioned, the mean age of the patients was 63.4±18.1 years which is congruent with previous surveys reporting the sixth and seventh decades of life as the most common years that a person might develop the disease [15-17]. The mean age of patients with oral SCC in different studies has been reported to be 52 years [18] and 62.4 years [16]. Overall, the risk of developing SCC is higher in subjects older than 45 years but this does not mean that young people cannot be affected by the disease [19,20], as reported in the present survey the youngest patient was 19 years old. A slight male preponderance was observed in this survey which is compatible with previous studies showing higher prevalence of oral SCC in men [10]. The treatment of oral SCC depends on the clinical stage of the disease and the tumor site but primarily consists of radical surgery and in higher stages of the cancer, radiotherapy and chemotherapy are used [1]. The majority of patients admitted to Imam Khomeini Hospital (78.8%) had undergone surgery as their primary intervention and radiotherapy was done for 16.4% of the patients. Accordingly, the treatments of 86.3% of the subjects were found to be according to the standard guidelines for oral SCC treatment. The most common site of oral SCC was found to be the buccal mucosa while in other studies the tongue, lower lip, floor of the oral cavity and soft palate [1] have been reported as the most common sites.

The mean survival of patients was calculated to be 3384.3 days or 9.3 years. Considering the 12 year period of the study, this survival seems to be acceptable. The survival at the end of the study period decreased to 0.4% which is also promising. These findings can be attributed to the early diagnosis at early stages of the disease and appropriate management of patients according to current treatment guidelines. The survival of oral SCC patients was found to be affected by the educational level of the subject and the compatibility of the treatment with standard guidelines.

Patients with diplomas and higher degrees had a mean of 1034 days (2.8 years) higher survival compared to other subjects with lower educational levels. This association might be due to the fact that higher educated people are more attentive to slight changes and this can lead to early referral to physicians. These subjects also tend to have a better compliance with treatment that can also lead to better treatment outcomes [21]. Moreover, tobacco use, alcohol consumption, immunologic disorders and vitamin deficiency particularly vitamin A deficiency have been reported to be risk factors for oropharyngeal cancer, factors that are found to be associated with lower educational levels [22-24]. Appropriate treatment of the patients was also found to be an important factor in increasing the survival of patients in a way that patients treated according to standard guidelines had a mean survival of 843 days (2.3 years) higher than subjects treated inappropriately. This observation has also been reported by previous studies as well [25,26]. Other factors proposed by previous surveys that might affect the survival of oral SCC patients include early treatment, younger age, female gender, smaller size of tumor and lower stage of the cancer [26,27]. One of the most important limitations of this study was missing data in the records of the patients. In order to overcome this problem, patients with incomplete records were contacted to acquire the necessary data for the survey. In this survey we only assessed a few factors that might affect the survival of oral SCC patients while numerous variables have been proposed by other surveys. Therefore, further investigations are required to assess other probable factors in studies with larger sample populations. Prospective studies are more favorable since the problem with missing data does not apply to these surveys.

Conclusions

The mean survival of the subjects was 9.3 years which is promising considering the 12 year period of the study. These results indicate the effectiveness of fol-

lowing standard treatment protocols and early diagnosis of the patients in early stages of the disease.

Conflict of Interest

There is no conflict of interest to declare.

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