RESEARCH COMMUNICATION

Oral Cancer Survival among Malay Patients in Hospital Universiti Sains Malaysia, Kelantan

Asmani Abdul Razak[1], Norkhafizah Saddki[2]*, Nyi Nyi Naing[3], Nizam Abdullah[2]

Abstract

Aims: This study was performed to determine oral cancer survival among Malay patients in Hospital Universiti Sains Malaysia (HUSM), Kelantan. Methods: The medical records of 118 Malay patients with oral cancer admitted in HUSM from 1st January 1986 to 31st December 2005 were reviewed. Data collected include socio-demographic background, high-risk habits practiced, clinical and histological characteristics, and treatment profile of the patients. Survival status and duration were determined by active validation until 31st December 2006. Data entry and analysis were accomplished using SPSS version 12.0. The Kaplan-Meier method was used to perform survival estimates while the log-rank test and the Cox proportional hazards regression model were employed to perform univariate analysis and multivariable analysis of the variables, respectively. Results:The overall five-year survival rate of Malay patients with oral cancer was 18.0%, with a median survival time of 9 months. Significant factors that influenced survival of the patients were age, sex, tumour site, TNM stage, histological type, and treatment received. Conclusion: Survival of oral cancer patients in HUSM was very low. Being elderly, male, presenting with an advanced stage at diagnosis, and not having treatment all contributed to poor survival.

Key Words: Oral cancer - survival - Malay

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Introduction

Oral cancer is one of the most devastating and disfiguring malignancies. The survival rate for oral cancer has been low despite advances in its treatment modalities. The five-year survival rate of oral cancer ranged from 30% to 80% (Yeole et al., 2003; Carvalho et al., 2005; Chandu et al., 2005; Oliveira et al., 2008; Sargeran et al., 2008). Marked racial differences in survival have been reported (Arbes et al., 1999; Chen et al., 2007; Kolker et al., 2007). These variations were attributed to the genetic predisposition and socio-cultural risk factors such as lifestyle and dietary habits (Zain, 2001; Chen et al., 2007). Other factors like age at diagnosis, sex, anatomic site of tumour, size, clinical spread, lymph node involvement, histological type, and treatment given may also influence patient survival (Yeole et al., 2003; Chen et al., 2004; Vallecillo-Capilla et al., 2007). More importantly, oral cancer prognosis relies greatly upon tumor stage at the time of diagnosis (Chandu et al., 2005; Choi et al., 2006; Vallecillo-Capilla et al., 2007).

Late diagnosis of oral cancer has been repeatedly shown to be associated with poor survival rate. The overall survival was longer in patients with tumour diagnosed in stage I or II compared with those in stage III or IV (Chandu et al., 2005; Vallecillo-Capilla et al., 2007; Sargeran et al., 2008). This problem of late diagnosis is partly due to the fact that oral cancer is relatively painless during the early development such that patients tend to postpone seeking help (Scott et al., 2006). Although in most instances oral cancer is preceded with visible mucosal tissue changes, these may be oblivious to the patients who considered their symptoms to be minor and transient. It is thus an irony that despite being in the most accessible site, oral cancer often went unnoticed in its early stages. Most oral cancer cases are detected at advanced stages such that they require complex and costly treatments that are not associated with favourable outcomes (Mignogna et al., 2002).

In Malaysia, the prevalence of oral cancer was 0.04% (Zain et al., 1997). A study done in Kelantan reported an overall crude incidence rate of 0.74 per 100,000 population (Ghazali et al., 2006). Although the prevalence of oral cancer was relatively low and accounted for only less than 1% of the total incidence of all malignancies, the impact and burden of the disease to the individual, community and the country is tremendous. The morbidity is high, and more than half of the patients die of it within five-years after diagnosis. In this study, the five-year survival rates of oral cancer in Malay patients who form the major constituent of oral cancer patients in Kelantan were investigated.

Materials and Methods

The medical records of 118 Malay patients diagnosed

*[1]Department of Community Medicine, [3]Biostatistics and Research Methodology Unit, School of Medical Sciences, [2]School of Dental Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia *For Correspondence: fizah@kb.usm.my*

with oral cancer from 1st January 1986 to 31st December 2005 in HUSM were reviewed. The definition of oral cancer in this study follows the International Classification of Diseases (ICD), which is the international standard diagnostic classification used to classify diseases and other health problems. Both the ninth edition of the ICD (ICD-9:140-145) and the tenth edition (ICD-10: C00-C08) were used for oral cancer cases diagnosed before year 2000 and from year 2000 onwards, respectively. Ethical approval was obtained from the Research and Ethics Committee, Universiti Sains Malaysia (USM) prior to conduct the study.

Details of the patients and the tumour at the time of diagnosis were obtained. The collected data were as follows: age, sex, marital status, high-risk habits practiced, characteristics of the tumour such as site, Tumour-Node-Metastasis (TNM) stage, and histological type, time lapse from the onset of symptoms until initial visit, and treatment received. Active follow-up and validation was done until 31st December 2006 to determine the survival status and survival duration of the patients.

Data entries and analyses of results were done using the SPSS for Windows (version 12.0, SPSS Inc., Chicago) and Intercooled Stata (version 7.0, StataCorp, Texas) statistical software packages. Cumulative survival was determined by Kaplan-Meier methods assessing overall survival. Univariate analyses of the variables were performed using log-rank test, and multivariable analyses were done using Cox Proportional Hazards Regression Model.

Results

During the follow-up study period, a total of 91 patients (77.1%) died from oral cancer. The median survival time was 9 months. The overall five-year survival rate was 18.0%. The survival probability curve for Malay patients with oral cancer is presented in Figure 1.

Univariate analysis of factors associated with oral cancer and five-year survival rates are presented in Table 1. Being in the older age group of 60 years and above had less five-year survival rate compared to the younger group (p=0.034). Male patients also had significantly lower five-year survival rate compared to female patients (p=0.035).

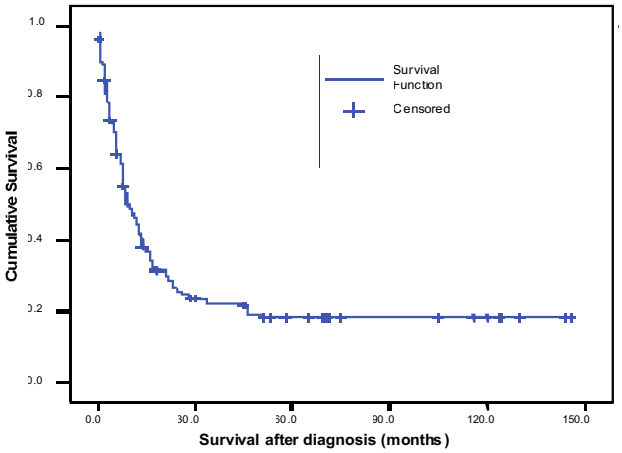

Figure 1. Kaplan-Meier Curve for Oral Cancer Survival among Malay patients in HUSM, Kelantan

Table 1. Five-year Survival Rates for Malay Patients with Oral Cancer in HUSM, Kelantan (n=118)

Variables	N	Survival	95% CI	χ2 (d.f.)	p-value[a]
Age (years)					
< 60	57	20.4	9.8, 33.7	4.50 (1)	0.034
≥ 60	61	14.8	4.5, 24.8		
Sex					
Male	76	11.8	5.6, 20.4	4.46 (1)	0.035
Female	42	31.6	17.0, 47.3		
Marital status					
Single	19	36.8	15.4, 58.5	1.51 (1)	0.220
Married	99	14.9	8.3, 23.2		
Smoking					
Ever	69	15.0	7.6, 24.7	0.46 (1)	0.499
Never	46	22.3	10.5, 36.8		
Betel quid chewing					
Ever	27	23.5	4.7, 30.5	0.10 (1)	0.751
Never	88	76.5	10.5, 28.1		
TNM stage					
Stage I	3	100	-		
Stage II	12	53.5	21.2, 77.7	13.8 (3)	0.003
Stage III	12	18.8	3.0, 45.1		
Stage IV	91	10.0	4.5, 18.2		
Anatomic site					
Lip	7	100	-	36.6 (5)	<0.001
Tongue	44	2.3	0.2, 10.4		
Salivary gl	10	0.0	-		
Gingiva	8	12.5	0.7, 42.3		
Mouth Floor	8	0.0	-		
Unspecified	41	22.0	10.3, 36.5		
Histological type					
SCC	89	10.9	5.4, 18.5	13.7 (1)	<0.001
Other	29	43.1	21.4, 63.2		
Treatment					
None	39	0.0	-	34.9 (4)	<0.001
Surgery	26	38.5	0.2, 0.6		
Radiotherapy	11	0.0	-		
Surg+ radio	28	30.6	0.1, 0.5		
Chemo+	14	0.0	-		
Duration of symptoms (months)					
< 3	20	12.4	2.2, 32.3	5.88 (3)	0.118
3 to <6	42	13.1	4.5, 26.3		
6 to <12	21	14.3	3.6, 32.1		
≥ 12	34	26.0	11.6, 43.1		

[a]log-rank test; SCC, squamous cell carcinoma

Table 2. Significant Prognostic Factors for Oral Cancer in Malay Patients using the Cox Proportional Hazards Regression Model

Variables	b Coefficient	Adjusted HR	95% CI	LR statistic	p value[a]
Dysphagia					
No		1.00			
Yes	0.61	1.79	1.18, 2.72	2.75	0.006
Cancer stage					
Stages I & II		1.00			
Stages III & IV	1.24	3.79	1.62, 8.87	3.07	0.002
Treatment					
No		1.00			
Yes	-1.07	0.32	0.21, 0.50	-5.13	<0.001

[a]p value for LR statistics

Marital status was not associated with survival. Similarly, smoking and betel quid chewing habits practiced by the patients did not affect survival, as well as time lapse from the onset of symptoms until initial visit

Oral cancer survival was significantly reduced with advanced TNM stage. All patients diagnosed at stage I survived for five years, compared with 53.5% for stage II, 18.8% for stage III and 10.0% for stage IV (p=0.002). Oral cancer survival was also significantly affected by the anatomical site, histological type of tumour, and treatment received (p <0.001). Multivariable analysis using Cox Proportional Hazards Regression Model identified three significant prognostic factors of oral cancer among Malay patients in HUSM. The significant independent variables were presence of dysphagia, TNM stage of oral cancer and treatment as shown in Table 2.

Discussion

This study analysed the survival and factors that influenced five-year survival rate of oral cancer among Malay patients in HUSM. The results demonstrated a high mortality due to oral cancer. Most oral cancer deaths in this study occurred within the first two years after diagnosis. The five-year survival rate was only 18.0%, very much lower compared with other studies using the Kaplan Meier analysis. Chandu et al. (2005) in a study done in Victoria, Australia reported an overall survival of 83.3%, Chen et al. (2004) in Taiwan reported a 55.6% survival rate for oropharyngeal carcinoma, in India the observed survival rate for oral cancer was 30.5% (Yeole et al., 2003), and in Sao Paulo, Brazil the survival rate was 28.6% (Oliveira et al., 2008). It is most probable that our much lower survival was due to the fact that besides having more patients diagnosed in stage III and IV compared to stage I and II, the prevalence of those diagnosed in the advanced stages was also higher than that reported by others (Chandu et al., 2005; Sargeran et al., 2008; Doobaree et al., 2009). Besides, the majority of patients in this study presented with squamous cell carcinoma, the most common malignant neoplasm of the oral cavity. It is also one of the most difficult malignancies to control and has been associated with poor prognosis that may be explained by frequent lymph node metastases and local invasion characteristic (Arduino et al., 2008).

The survival rate of oral cancer among Malay patients in this study declined significantly with advancing stage at diagnosis. None of the patients presented in stage I died due to oral cancer within five years of diagnosis compared to 81.2% and 90.0% deaths among those diagnosed in stage III and IV respectively. These findings add to the growing body of evidence that advanced stages of oral cancer at the time of diagnosis are associated with shorter survival (Yeole et al., 2003; Vallecillo-Capilla et al., 2007; Sargeran et al., 2008). These, in turn, further highlight the importance of oral cancer and precancer screening for early detection and prevention of the disease. Nevertheless, differences in duration of time from the onset of symptoms until initial visit for help did not significantly influence survival of patients in this study. This is probably due to incorrect estimation of the time lapse due to poor knowledge and awareness regarding the early symptoms that may easily go unnoticed (West et al., 2006).

Age was an important factor affecting survival for oral cancer in this study. Patients aged 60 years and above, whom constituted more than half of the oral cancer patients, had significantly shorter survival as compared with those diagnosed below the age of 60. These results are in accordance with previous studies (Yeole et al., 2003; Choi et al., 2006; Chen et al., 2007; Oliveira et al., 2008). Further, there is a general agreement that the lower survival rates in older patients may be related to the higher prevalence of debilitating illnesses associated with aging (Ribeiro et al., 2003). Some authors, though, did not find any association between age of diagnosis and oral cancer survival (Lo et al., 2003; Chandu et al., 2005; Sargeran et al., 2008). The lack of consensus for the age ranges that define the periods of life may attribute to the discrepancies in the influence of age on survival (Oliveira et al., 2008).

The association between sex and oral cancer survival also seems controversial. Some authors reported no difference in survival between male and female patients (Lo et al., 2003; Chandu et al., 2005; Sargeran et al., 2008), whereas some others reported that males had poorer survival rate (Yeole et al., 2003; Chen et al., 2004; Choi et al., 2006). In this study, the five-year survival rate for male patients was significantly lower than for females. Although the effect of sex on survival rates for oral cancer remains unclear, it is believed that more males are affected by oral cancer because of their exposure to carcinogenic factors associated with lifestyle and dietary habits such as tobacco and alcohol use as well as betel quid chewing (Johnson, 2001; Chung et al., 2005; Ide et al., 2008).

Tobacco and alcohol consumption are the established risk factors for oral cancer which may act either separately or synergistically (Warnakulasuriya, 2008). In this study, cigarette smoking had no significant influence on the survival of oral cancer patients. This is in agreement with some earlier studies (Chen et al., 1999; Lo et al., 2003; Vallecillo-Capilla et al., 2007; Oliveira et al., 2008), but in contrast to others (Leite and Koifman, 1998; Molina et al., 2008). Therefore it seems that although cigarette smoking has been implicated as a causal factor in oral cancer, its influence on patient survival is still unclear. However, it is noted that in studies on oral cancer survival done thus far the patients were classified solely based on their smoking status. No attempt has been made to capture differences in the duration and amount of exposure when the influence of tobacco use on oral cancer survival may be dose related. Besides, the risk of developing oral cancer was also found to be modulated by the amount and duration of smoking habit (Yen et al., 2008; Muwonge et al., 2008). A significant decrease in risk was also reported in patients who gave up smoking (Znaor et al., 2003).

Another causative factor for oral cancer associated with lifestyle habit, particularly in the South Asia, Southeast Asia and Pacific Islands countries, is betel quid chewing. Betel quid chewing may act alone or in combination with tobacco and alcohol use (Jacob et al., 2004; Chung et al., 2005; Yang et al., 2005; Chen et al., 2008). Studies done in Taiwan where the habit is popular

among the population demonstrated that betel quid chewing, consumed alone or in combination with smoking and/or alcohol increased the likelihood of death due to oral cancer (Chen et al., 1999; Lo et al., 2003). The prognostic effect of betel quid chewing was also suggested to be dose- and time- dependent (Lee et al., 2005). On the other hand, while the synergistic effects of betel quid and smoking and/or alcohol consumption were apparent in the Taiwan studies, the independent effects of smoking and alcohol were not seen (Chen et al., 1999; Lo et al., 2003). This lack of association, again, may be due to differences in the duration and amount of tobacco and alcohol use among the samples. Besides, it is also possible that the biological effects of betel quid chewing on oral cancer development are stronger and more aggressive such that the influence of tobacco and alcohol use on oral cancer survival was obscured (Lee et al., 2005). In this study, while the effect of alcohol on survival was not investigated because none of the Malay patients in this study ever consumed alcohol, the effect of betel quid chewing on oral cancer survival was not apparent. Perhaps this is due to the disproportionate number of samples where only 27 patients chew betel quid while another 88 did not.

The site of primary tumour has an important influence on patient survival for reasons including ease of early diagnosis and accessibility for surgical removal with sufficient margin (Vallecillo-Capilla et al., 2007). In addition, the vascular and lymphatic networks which vary between different sites may influence the metastatic capacity and hence the prognosis (Oliveira et al., 2008). Different opinions exist in the literature with regard to influence of oral cancer sites on patient survival. However, most studies agreed that lip cancer was associated with the best survival rates while tongue had the worst (Yeole et al., 2003; Chen et al., 2004; Chen et al., 2007; Oliveira et al., 2008). Likewise, in this study, cancers on the lip have the highest survival time and tongue cancer has very low survival rate. However, the fact that tumours in the floor of mouth and major salivary glands have the lowest survival rates were in contrast with findings from Leite and Koifman (1998) where it was reported that salivary glands had the highest five-year survival time of 47.5 months, even better than tongue which was 44.6 months. These disparities are perhaps due to misclassification of the original tumour site owing to the complex anatomical structures in the oral cavity. Besides, tumours that arise from adjacent sites may both spread and become overlap easily. It is thus quite common for a certain level of uncertainties in determining the intraoral sub-sites of tumour origin to occur, particularly in advanced stages (Yeole et al., 2003).

The effect of treatment on the survival of oral cancer patients was apparent in this study. Of 118 patients, 66.9% were treated. Surgery, either alone or in combination with radiotherapy, was the most common treatment modality in this study, as observed by Chen et al. (2004) and Arduino et al. (2008). Patients treated with surgery showed the highest survival rate, followed by surgery plus radiotherapy. However, all untreated patients died, and none of the patients treated with radiotherapy alone or chemotherapy survived for five years. Similar outcomes were reported by other authors (Leite and Koifman, 1998; Chen et al., 2004; Sargeran et al., 2008). Whether a patient has surgery alone, surgery and radiotherapy, radiotherapy alone, and chemotherapy, is dependent on the stage of cancer as well as other clinical parameters such as tumour size, distant metastasis, histological type, and lymph node involvement (Chen et al., 2004). Surgery may be recommended for patients at earlier stages while treatment with radiotherapy alone or chemotherapy indicated that patients were at advanced stages, which might explain for the poor survival (Zheng et al., 2008).

This study provides a greater understanding of factors that influence survival of Malay patients with oral cancer. It is hoped that this valuable information would aid clinicians in making informed decisions that would optimize treatment planning with the aims to maximize patient survival. The results of this study also highlighted the importance of oral precancer and oral cancer screening for early detection. Strategies to improve public awareness of oral cancer and continuing education for oral health professionals about early detection and diagnosis must be in place. However, primary preventive measures to curb risk habits associated with oral cancer should be the main agenda to reduce its incidence in view of the low survival rates.

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