Comparisons of Clinicopathologic Characteristics among Early and Late Stage of Oral Squamous Cell Carcinoma

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Abstract

Background:The past decade has seen an unprecedented increase in our understanding of the biology and etiology of oral squamous cell carcinomas (OSCC). The five year survival rate of OSCC patients has been reported approximately 50% which is not satisfactory despite new treatment modalities are required.

Aim: To compare the clinicopathologic characteristics among early and later sage of oral squamous cell carcinoma

Method: This retrospective hospital-based study evaluated the outcome of patients with early and late stage of oral squamous cell carcinoma (OSCC) with the aim of identifying factors affecting the clinical course and survival rate. We combined clinicopathologic parameters and histologic data (from both tissue types) in predicting OSCC prognosis.

Results: Tumor and adjacent non-tumor oral tissues were collected from 29 OSCC patients.

Conclusion: Our view suggest that gender, symptoms, habits, tumor size, tumor site, metastasis node, TNM staging and histological grade are high-quality biological factors that remain useful prognostic indicators in OSCC.

Keywords: Oral cancer; Oral squamous cell carcinoma; Late stage carcinoma; Prognosis

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is amongst the most prevalent form of cancer worldwide with its predominance in the Indian subcontinent due to its etiological, behavioral pattern of tobacco consumption. Late diagnosis, low therapeutic response and aggressive metastasis are the foremost confounders accountable for the poor 5 year survival rate of OSCC. As for the oral cavity OSCCs, many authors reported frequent high-risk HPV involvement by considering the over-expression of p16INK4A as equivalent to HPV infection [Alexander et al., 2016]. Risky oral habits (including smoking, alcohol drinking, and betel quid chewing) are major risk factors for OSCC development [1].

Treatment of OSCC is made challenging due to the diversity of the anatomic sites in the neck and the critical normal structures that may be near a particular tumor site. Often, the care of a patient requires a multi-disciplinary team of surgeons, radiation oncologists, medical oncologists, nutritionists, gastroenterologists, speech and swallowing therapists, amongst others. Despite the availability of aggressive treatments, the 5year survival rate for oral malignancies remains relatively poor at 65%, with only modest gains in the past few years [2].

Several clinicopathological parameters have been implicated in prognosis, recurrence and survival following oral squamous cell carcinoma. In this retrospective analysis, clinicopathological parameters of tumor size, tumor site, nodes, TNM staging and histopathological features were studied and compared to recurrence and death from tumour-related causes. The overall national 5-year survival has been reported to vary in range according to tumour size (T1/T2 commonly referred to as "low-risk tumours" and T3/T4 commonly referred to as "high-risk"). The outcome is greatly influenced by the stage of the disease (especially pathological TNM) [3]. The treatment approach to these tumors remains controversial.

Patients with advanced oral squamous cell carcinoma (OSCC) have heterogeneous outcomes that limit the implementation of tailored treatment options. Genetic markers for improved prognostic stratification are eagerly awaited. However, the prognosis of patients with advanced disease (stage III/IV) remains dismal [4]. Different prognostic factors have been identified in OSCC patients (e.g., tumor and nodal stages, tumor differentiation, tumor invasiveness, treatment modalities, and surgical margins) [5]. The aim of this retrospective study was to analyze the characteristics and outcome of early and late stage of patients with OSCC, evaluate the clinical characteristics of such tumors and investigate the prognostic factors.

MATERIALS AND METHODS

In order to analyze the clinical characteristics and prognostic factors, we retrospectively investigated 29 patients who were diagnosed with OSCC between July 2015 to January 2016. This cross-sectional study was conducted at Saveetha Dental College and ethical approval for the study was obtained from the institution ethical committee (015/10/2013/IEC/SU). The demographic and clinicopathological details of patients like age, sex, tobacco chewing, tobacco smoking, alcohol consumption, TNM stage etc., were collected from the 29 patients that were participated in this study. The details such as duration between the time a lesion or ulcer was noticed, occupation, education, address, initial treatment received were also recorded. Incisional biopsy for histopathological diagnosis were taken for the study. Before commencement of this study, approval was obtained from the Hospital and informed written consent to participate in the study was obtained from each person. The pathological diagnosis of

each OSCC case was confirmed using hematoxylin-eosin staining.

The study was conducted on a total of 29 specimens, including 29 OSCC biopsy tissues and 29 normal controls. Of 29 OSCC patients 18 were males and 11 were females. There were 18 male patients and 11 female patients. 15 patients were less than 50 years and 14 patients more than 50 years old. The average age of men was 45.38 years and for women 52.18 years. All 29 included patients were diagnosed histopathologically as oral squamous cell carcinoma. Samples from each category namely, the control group, early stage of OSCC and late stage of OSCC that passed the quality control tests on bioanalyzer were pooled and subjected to clinical analysis.

Patients with histologically confirmed primary squamous cell carcinoma and not received chemotherapy, radiotherapy and surgery were included in this study. Clinical history, positive findings and histopathology report were correlated with patient's late presentation to our hospital. Core cancer tissue from the surgically resected primary squamous cell carcinoma of the 29 patients were collected. All of the study patients were treated by surgery, radiotherapy, or combined chemoradiotherapy at the Saveetha Dental college.

Statistical analysis

The data obtained from the studies were representative of those obtained in at least five independent experiments and have been expressed as mean ± SEM. Statistical analyses were performed using one-way analysis of variance (ANOVA) followed by Newman–Keuls test for comparison between control and treatment groups using Graph Pad Prism software (version 5). Values of $p<0.05$ were considered to be statistically significant.

RESULTS

Patient characteristics

Table 1 represents the clinicopathological characteristics of OSCC patients. The survival rate among our patients in this study declined significantly with advancing stage at diagnosis. In this study, the overall survival rates were higher in patients with Stage I and II disease (100%), as compared with declining survival rates in Stage III (20%) and IV (28%) cases (Table 1).

Most common site of occurrence OSCC is the tongue. However, among the 5 patients below 40 years, three patients had carcinoma of alveolus, one in the tongue and one in the buccal mucosa. The involvement of the alveolus and buccal mucosa can be related to the pouching of tobacco between the buccal mucosa and the retromolar region.

The most overlapping habit in 25 out of 29 patients was chewing tobacco. Only 4 patients were non chewers. 11 patients had smoking habit and other 10 patients consumed alcohol. Only one patient had no habits and the ulcer which eventually turned as a carcinoma was attributed to an ill-fitting denature. 6 patients had all three smoking, alcohol and tobacco chewing habits. 11 female patients and 6 male patients had no history of smoking and alcohol. Most authors have reported higher mortality in smokers and alcohol drinkers. Betel quid chewing had also been specifically correlated with poorer prognosis. According to this study patients with chewing habit have more related systemic health problems were more likely to die as compared to non alcoholics.

This validates the fact that prolonged contact of the quid with the mucosal site is suggested as an important etiological factor in terms of high incidence at specific sites. The results showed that the sizes of the lesion ranged from less than 2 cm to 10 cm in diameter.

Table 2 represents the tumor characteristics in OSCC patients. Nodal involvement was present in 21 patients. 7 patients had nodes in the neck, 8 male patients had N1 and only 4 female patients had N2C. The other patients with primary cancer in buccal mucosa and N0 were treated with wide resection only.

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28 patients had well differentiated tumours and only one had moderately differentiated tumour. The prognosis in our study could not be related statistically with the degree of differentiation. Recurrence was mainly associated with moderately differentiated tumours. All patients were treated with surgical resection of the cancer. 23 patients also had some type of neck dissections (SOND or MRND I, II, or III) done, 11 patients were followed up with radiation and 3 patients also had chemotherapy. Reconstructive surgery may be required after the initial removal of the tumor.

Table 1: Relationship between Prognosis and Clinicopathological Features

PATIENTS	NUMBERS (%)	
Total Patients	29 (100)	
VARIABLES	SURVIVAL	MORTALITY
Gender		
Male	13 (44.82)	5 (17.24)
Female	10 (34.48)	1(3.44)
Age		
Less than 50 years	10 (34.48)	4(13.79)
50 and more than 50 years	13(44.82)	2 (6.89)
Duration of symptom		
Less than 1 month	3(10.34)	1(3.44)
1 to 3 months	10 (34.48)	0 (0.0)
More than 3 months	10 (34.48)	5 (17.24)
Habits		
Only smoking	1(3.44)	0(0.0)
Only chewing	13 (44.82)	3(10.34)
Smoking + Alcohol	1 (3.44)	1 (3.44)
Smoking + Chewing	1(3.44)	0(0.0)
Alcohol + Chewing	0 (0.0)	1(3.44)
Smoking + Alcohol + Chewing	6 (20.68)	1(3.44)
No habits	1 (3.44)	0 (0.0)

Table 2: Tumor Characteristic in Oral Squamous Cell Carcinoma

VARIABLES	SURVIVAL	MORTALITY
Tumour Site		
Buccal mucosa	7 (24.13)	2(6.89)
Tongue / FOM	7(24.13)	2(6.89)
Lower alveolus/RMT	6 (20.68)	2 (6.89)
Upper alveolus	3(10.34)	0(0.0)
Tumour Size		
T 1	4 (13.79)	0 (0.0)
T2	10 (34.48)	3 (10.34)
T3	3 (10.34)	0 (0.0)
T4	6 (20.68)	3 (10.34)
Nodes		
N 0	7 (24.13)	0 (0.0)
N1	8 (27.58)	1 (3.44)
N2a	0 (0.0)	0 (0.0)
N2b	3 (10.34)	1 (3.44)
N2c	5 (17.24)	4(13.79)
N 3	0(0.0)	0(0.0)
c TNM staging		
Stage I	1 (3.44)	0(0.0)
Stage II	5 (17.24)	0 (0.0)
Stage III	4 (	1
Stage IVa	13 (44.82)	5 (17.24)
Histopathology		
Well differentiated SCC	23 (79.31)	5 (17.24)
Moderately differentiated SCC	0 (0.0)	1(3.44)
Poorly differentiated SCC	0(0.0)	0 (0.0)
Treatment		
No neck dissection	6 (20.68)	0 (0.0)
Neck dissection done	23 (79.31)	6 (20.68)
Radiotherapy	9(31.03)	2(6.89)
Chemotherapy	2(6.89)	1(3.44)

DISCUSSION

Sensitive and reliable early diagnostic markers for oral squamous cell carcinoma (OSCC) remain unavailable. Early identification of recurrence for OSCC is also a challenge. Prognosis also depends or varies with tumour primary site, nodal involvement, tumour thickness and the status of the surgical margins. Moreover, the cumulative effects of tobacco, betel nut and alcohol decrease the survival rate. Oral cancer is known to affect more males than females with an approximate ratio of 1.5:1, respectively. Nearly a quarter of the newly diagnosed cancers in males from Sri Lanka, India, Pakistan and Bangladesh are located in the head and neck region [6].

Gender did not seem to be a significant determinant of survival for patient with OSCC. Neither for men nor women exhibited any significant clinical differences in outcome. The most commonly reported oral cancer sites include the buccal mucosa and lateral borders of the tongue. Reduction in survival is largely explained by tumour's site influence on nodal metastasis. The tumor stage was classified according to the American Joint Committee on Cancer/Union for International Cancer Control TNM staging system. Most tumors were classified as moderately and poorly differentiated tumors. The cut-off thickness of tumour varies from centre to centre. The association of tumour thickness with lymph node metastasis is believed to reflect the aggressiveness of tumour growth [7,8].

These tumors are characterised by uncertain pathogenesis, challenging etiological diagnosis and poorer prognosis compared with their primaries. Staging of OSCC is performed with the use of tumor node metastasis (TNM) classification system and its variant (PTNM), which are based on clinical and pathologic evaluation of tumor size and lymph node involvement. However, the routinely used tumor stratification based on the tumor, node, metastasis (TNM) classification together with the histological grading alone is not sufficient to predict the individual prognosis of an OSCC. Therefore, there is an urgent need to establish additional prognostic factors. Interestingly, the aggressiveness of OSCC increased with aboral localization [9].

Patients with positive neck nodes underwent removal of the lymph nodes along with neck dissections. For patients in Stages II, III and IV, some form of reconstruction were needed. Reconstruction was planned and done using forehead flap, perioral flap, PMMC or micro vascular reconstruction depending on the expected postoperative defect. Immediate post operative morbidity was more in patients who had neck dissections with or without primary reconstruction when compared to no neck incisions. The duration of hospital stay was also more for patients who underwent neck dissections and microvascular reconstruction[10].

In conclusion, in our study, the identification of the primary tumor is crucial for designing an effective treatment regimen for this group of patients, whereas imaging examinations, OSCC biomarkers evaluation and gene expression analysis are recommended.

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