

Original Article

Evaluation of metastasis and 5-year survival in oral squamous cell carcinoma patients in Isfahan (2001–2015)

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ABSTRACT

Background: Frequency analysis of metastasis in patients with oral squamous cell carcinoma (OSCC) helps to partly anticipate the upcoming chance of metastasis in the patients following primary diagnosis. This study was conducted to determine the evaluation of metastasis and 5-year survival in OSCC.

Materials and Methods: This was a retrospective, descriptive study. A total of 96 OSCC patients were studied. Demographic data and clinical view of lesion as well as histopathological grade of patients were recorded in previously prepared forms of pathology centers. These findings were then evaluated in relation to the 5-year survival. The obtained data were fed into SPSS and analyzed by Chi-square test, *t*-test, one-way ANOVA, and Scheffé test. A significant level of $\alpha = 0.05$ was used.

Results: The 5-year survival of patients was 41.7%. From among the patients, 44% were found to have local recurrence and 36% were reported to have distant metastasis. There was no significant association between the 5-year survival rate and primary grade ($P = 0.105$). However, it revealed a significant relationship between the 5-year survival rate and distant metastasis ($P = 0.001$).

Conclusion: This study showed that the 5-year survival is dependent on the primary site of involvement, local recurrence, regional and distant metastasis, and mean age. However, gender ($P = 0.89$), grade ($P = 0.105$), and stage ($P = 0.242$) have no effect on the 5-year survival of patients.

Key Words: Metastasis, squamous cell carcinoma, survival rate

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the sixth and fifteenth common cancer in men and women, respectively. It involves approximately 94% of all oral malignancies.^[1] The etiology of this disease is multifactorial, and no single factor has ever been considered for it.^[2] Considering its clinical view, it

is observed in the elderly with low socioeconomic status. OSCC is able to invade the underlying bone and involve the nerves.^[3] Metastatic spread of this disease greatly affects the 5-year survival of patients, and about 50% of patients with head-and-neck SCC undergo recurrence and metastasis in the first 2 years

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of their life.^[4] This metastatic spread is mostly done through lymphatics to the cervical lymph nodes of the same side of the face. Further, extracapsular extension in some patients is followed by poor prognosis, including increased risk of regional recurrence, distant metastasis, and reduced survival rate.^[5] Occasionally, metastatic spread to the lymph nodes of the corresponding side or both sides is also observed, and at least 2%–22% of patients have shown metastasis to supraclavicles during diagnosis.^[5]

The most common distant metastatic sites in OSCC include lungs, liver, and bones; however, other parts of the body may get involved too.^[6] Metastasis is not an early finding about oral carcinomas. Nevertheless, about 21% of patients have been found to have neck metastases due to delayed diagnosis.^[7] Tumors originating from more posterior areas in the oropharynx are prone to early metastasis.^[8] Oral cancer metastasis is a complex process that involves isolation of tumoral cells from each other, their proliferation and growth, escaping through the lymphatic vascular system, and positioning in different parts of the body.^[9] Tumoral cells with metastatic ability undergo certain genetic mutations in the first stage, which is in favor of the movement ability and metastasis of these cells, as these cells lose their intercellular adhesion ability and acquire the ability to pass through intercellular spaces during epithelial–mesenchymal transition process by transforming from squamous to spindle cell.^[10]

Finally, metastases of OSCC are divided into regional and distant metastases,^[11] which can be diagnosed by such methods as positron emission tomography, magnetic resonance imaging, computed tomography, ultrasound, and fine-needle aspiration.^[12] This study was aimed to determine the frequency of metastasis and survival rate in patients with OSCC during 2001–2015. The results are hoped to help to partly anticipate the chance of future metastasis after primary diagnosis, to prevent metastasis as much as possible, and to enhance the 5-year survival in patients by applying acceptable treatment methods.

MATERIALS AND METHODS

In this retrospective, descriptive study (Ethical Code:23810201942038), 96 files of patients with OSCC, from 2001 to 2015, were obtained from the Department of Oral and Maxillofacial Pathology at Isfahan University of Medical Sciences. The files contained exact data [Figure 1], including

demographic information [Table 1] and clinical, histopathologic, and radiographic findings, with at least 5 years after primary diagnosis, that is, their primary diagnosis had been made before 2011.

First, letters of introduction were obtained from Islamic Azad University of Khorasgan Branch and Isfahan University of Medical Sciences. The OSCC patients' files containing personal information, age, gender, and lesion site during 2001–2015 were extracted from the archive. The patients were called

Figure 1: Patient's data registration form

Patient's data	Patient's data
First name	Lesion site
Surname	Oncologist
Age	Radiologist
Gender	Recurrence time
Diagnosis year	Metastasis time
Grade	Metastatic site
Stage	Has the patient been alive in the past 5 years or not?

Table 1: Demographic information of patients

Variables	n (%)	5-year survival (%)	P
Gender			
Male	52 (54.2)	22 (42.3)	0.89
Female	44 (45.8)	18 (40.9)	
Subsite of involvement			
Buccal mucosa	8 (8.33)	2 (5)	0.01
Tongue mucosa	42 (43.75)	23 (57.7)	
Gingival mucosa	22 (22.91)	4 (10)	
Tongue and mouth floor mucosa	6 (6.25)	3 (7.5)	
Tongue and gingival mucosa	3 (3.12)	0	
Buccal and gingival mucosa	2 (2.08)	0	
Alveolar mucosa	1 (1.04)	0	
Palatal mucosa	2 (2.08)	2 (5)	
Lip mucosa	2 (2.08)	1 (2.5)	
Buccal mucosa	1 (1.04)	1 (2.5)	
Maxillary sinus	1 (1.04)	1 (2.5)	
Buccal mucosa and maxillary sinus	1 (1.04)	0	
Tongue and buccal mucosa	1 (1.04)	0	
Buccal mucosa and tongue	1 (1.04)	1 (2.5)	
Tongue	3 (3.12)	2 (5)	
Grade			
1	68 (70.83)	35 (51.47)	0.105
2	26 (27.08)	6 (23.07)	
3	2 (2.08)	0	
Stage			
1	45 (46.87)	34 (75.55)	242
2	2 (2.08)	0	
3	27 (28.12)	5 (18.51)	
4	22 (22.91)	2 (50)	

to get their agreement for cooperation in the study and completing the informed consent form [Figure 2]. Further, patient information (primary site, survival rate, recurrent regional or distant metastasis) until 2015 were evaluated with their records at the Oncology Center. The obtained data were then classified and statistically analyzed by Chi-square test, *t*-test, one-way ANOVA, and Scheffé test.

A significant level of $\alpha = 0.05$ was used.

RESULTS

The minimum and maximum ages of patients were 25 and 83 years, respectively. A total of 22 (42.3%) men had survived and 30 (57.6%) men had died in the past 5 years. Of women, 18 (40.9%) had survived and 26 (59.09%) had died in the past 5 years. The 5-year survival rate of patients was 41.7%. The results of Chi-square test showed no significant difference between men and women in terms of 5-year survival rate ($P = 0.89$). Among the patients, 44 (45.8%) of them had local recurrence, 44 (45.8%) had regional metastasis, and 36 (37.5%) had distant metastasis. Furthermore,

46.2 (24%) men had regional metastasis and 45.5 (20%) women had regional metastasis. Moreover, 34.6 (18%) men and 40.9 (18%) women had distant metastasis. The results of Chi-square test also indicated no significant relationship between gender and regional metastasis ($P = 0.94$) and distant metastasis ($P = 0.52$).

Moreover, the findings of Chi-square test showed no significant association between the 5-year survival rate and grade ($P = 0.242$) of disease. However, Chi-square test revealed a significant relationship between distant metastasis and 5-year survival of patients ($P = 0.001$) [Tables 1 and 2]. Furthermore, the results of Chi-square test indicated a significant relationship between the primary site of lesion and 5-year survival rate ($P = 0.01$) [Tables 1 and 2]. To find out the location of difference in terms of age, *post hoc* Scheffé test was run, which indicated a significant relationship between the patients with tongue and gingival lesions.

DISCUSSION

OSCC is one of the most prevalent cancers among women and men.^[1] The retrospective analyses done

In the name of God
Informed consent form
Study title:

Evaluation of metastasis and five-year survival in OSCC patients in Isfahan (2001-2015)

Researcher: Samaneh Shirani

I, the supervisor of the dental thesis, am performing a research entitled "Evaluation of metastasis and five-year survival in OSCC patients in Isfahan (2001-2015)". I hope the results of this study will have positive effects on epidemiology finding of oscc. However, the study will yield data that may help the nurses in identifying the problems and setting educational priorities. This questionnaires will take about 20 minutes to complete. You are free to ask any questions about the study and can call my cell phone number (09131000885) in case you have further questions.

Your participation in this study is completely voluntary. You are free to withdraw from the study anytime you wish. The obtained data will be encrypted and you will be anonymous. Your identity will be confidential in all stages of the study, including reporting or publishing. All data will be collected by the researcher and will be kept in a safe place.

I have read the informed consent form and am willing to participate in the study voluntarily.

Signature  Date 20/5/19

I have explained all the abovementioned subjects and have analyzed the participant's understanding of the informed consent form.

Signature  Date 20/5/19

Figure 2: The informed consent form.

on these patients indicate that the survival of some of them is similar to normal people and some die shortly after being affected by the disease. The present study was aimed to evaluate the 5-year survival of OSCC patients and its relationship with age, gender, stage and microscopic grade, and process of disease.

Metastasis is one of the most distinct factors that complicate the cancer process and its treatment. It is also true for oral cancer, but different areas of oral cavity are more prone to metastasis, influencing the 5-year survival rate.^[13] Before metastasis becomes evident, micrometastases occur, which, if treated in this stage, increases the survival of patients. The objective of metastasis assessment is to carry out more precise evaluations and treatments during the treatment process for areas of the mouth with greater susceptibility to metastasis.^[13,14]

In OSCC, regional metastases occur more than distant metastases.^[15-17] In the present study, 45% of regional metastases and 37% of distant metastases showed that the 5-year survival of patients was affected in all cases. In this study, all cases showed a significant relationship between regional metastases and distant metastases by the 5-year survival of patients. The metastatic sites occurring during OSCC in the study samples included lymph nodes, digestive system, pharynx, esophagus, stomach, lung, throat, jaw bone, larynx, neck vessels and skin, forehead skin, skull, brain, and temporal arteries [Table 3].

As for the primary site of lesion and distant metastasis site in the present study, no significant association was found. It is noteworthy that these results were based on few samples in any areas of lesion, and results would change dramatically even by adding or subtracting one sample.

The maximum 5-year survival in the current study was reported for the patients with SCC of the tongue ($P = 0.01$). There was a significant association between the primary site of lesion and 5-year survival of patients, which is in line with the results of Woolgar *et al.*^[14,18]

In the present study, 96 patients, 54.2 (52%) men and 45.8 (44%) women, were included, with the mean age of 59.5 years. Most of OSCCs were of well-differentiated type. The most prevalent involvement sites were tongue mucosa in 43.8 (42%) patients and gingival mucosa in 22.9 (22%) patients. However, the study of Minhans *et al.* conducted on 81 patients reported a mean age of 52 years. They

Table 2: Grade and stage of patients

Variables	n (%)	Years survival-5 (%)	P
Grade			
1	68 (70.83)	35 (51.47)	0.105
2	26 (27.08)	6 (23.07)	
3	2 (2.08)	0	
Stage			
1	45 (46.87)	34 (75.55)	242
2	2 (2.08)	0	
3	27 (28.12)	5 (18.51)	
4	22 (22.91)	2 (50)	

Table 3: Frequently distribution of patients based on metastasis site, lymph nodes, and survival in the past 5 years

Metastasis site	Survived in the past 5 years, n (%)	Not survived in the past 5 years, n (%)	Total, n (%)
Lymph nodes	0	2 (6/3)	2 (1/2)
Digestive system	0	1 (8/1)	1 (1)
Lung	1 (5/2)	3 (6/3)	4 (2/4)
Esophagus and pharynx	0	2 (6/3)	2 (1/2)
Pharynx	0	2 (6/3)	2 (2/1)
Esophagus	0	4 (1/7)	4 (2/4)
Jaw bone	2 (5)	2 (6/3)	4 (2/4)
Bone	0	7 (5/12)	7 (3/7)
Pharynx, larynx, and esophagus	0	1 (8/1)	1 (1)
Pharynx	0	2 (6/3)	2 (½)
Pharynx and neck skin	0	1 (8/1)	1 (1)
Stomach	0	1 (8/1)	1 (1)
Vessels and neck skin	0	1 (8/1)	1 (1)
Esophagus and lung	0	1 (8/1)	1 (1)
Stomach and forehead skin	1 (5/2)	0	1 (1)
Brain	0	1 (8/1)	1 (1)
Jawbone, skull, and temporal arteries	0	1 (8/1)	1 (1)
All site	4 (11.11)	32 (88.88)	36 (100)

also reported the highest number of OSCCs to be of well-differentiated type. The maximum involvement site was tongue in 55.6 (45%) patients, followed by buccal mucosa, mouth floor, retromolar area, lip, and palate, respectively.^[18]

In general, the findings of the current research showed the 5-year survival rate of 55% in men and 45% in women, with total survival rate of 41.7%. The 5-year survival rate of OSCC patients was affected by factors such as primary site of lesion, local recurrence, and regional and distant metastases. No statistically significant association was reported between the 5-year survival rate and stage and degree of disease.

These results were in contrast with those of Noguti *et al.*, as they found a relationship between survival rate and stage and degree of disease.^[13]

Yang *et al.* reported the survival rate of patients with OSCC to be 80 months, with their 5-year survival of rate factors such as age, site, stage and recurrence were found to play a role in the survival rate of patients.^[19] Similarly, the present study showed the 5-year survival of rate, and according to Yang's study, the 5-year survival of patients was influenced by tumor site and local recurrence, not stage of disease.^[19]

CONCLUSION

The findings indicated the 5-year survival of patients depending on diagnosis time, primary site of lesion, local recurrence, local and distant metastases, and metastasis site. Gender and degree and stage of disease had no effect on the 5-year survival of patients. Predictive results are hoped to be helpful in diagnosis and treatment of this disease.

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Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

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