Original Article

Evaluating the Clinicopathologic Parameters of Tongue Squamous Cell Carcinoma based on its Local Distribution

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Abstract

Background: Oral squamous cell carcinoma (OSCC) is one of the most common oral lesions and the tongue is one of the most common areas involved. The aim of this study was to evaluate the clinicopathologic feature of tongue SCCs based on its local distribution.

Materials and Methods: In this cross-sectional study, clinical data such as age, gender, location, and clinical appearance were extracted from the archives of the Oral Pathology Department, Isfahan Dental School, registered with a definitive diagnosis of tongue SCC during 2005-2019. Then, 34 specimens were selected for histopathological evaluation in a simple random way. The histopathologic slides were examined to determine the grade of tumor malignancy. The data were entered into SPSS23 software and analyzed by Chi-square, Fisher exact, One-way ANOVA, and Non-parametric tests. *P* value <0.05 was considered significant.

Results: Of the 275 OSCCs, 68 samples were tongue SCC. The mean age of patients was 61.7 ± 15 and 61.8% were women. The most common clinical manifestations were exophytic lesions (42.6%) and the most common site was the lateral border of the tongue (36.8%). The results did not show a significant relationship between the clinicopathologic feature including mean age (p = 0.766), gender (p = 0.338), clinical presentation (p = 0.434), grade of malignancy (p = 0.763) and location. But, among the histopathological parameters, the pattern of invasion (p = 0.047) was significantly associated with the local distribution.

Conclusion: Given that most OSCCs had moderate differentiation of malignancy, identification of clinical features is needed. Attention to the pattern of invasion and location on the tongue can be effective in determining the therapeutic approach.

Keywords: Neoplasm, oral cancer, Squamous cell carcinoma

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Submitted: 09-Jul-2021; **Revised:** 29-Apr-2022; **Accepted:** 01-May-2022; **Published:** 28-Mar-2023

Introduction

Cancers, in addition to cardiovascular disease and diabetes, are a cause of about two-third of deaths in the world. According to the World Health Organization, 8.8 million people died from cancers in 2015.[1] Oral and pharyngeal cancers are sixth among the most common cancers in the world. Squamous cell carcinoma (SCC) accounts for more than 90% of oral and pharyngeal cancers.[2] The origin of oral SCC (OSCC) is oral mucosal keratinocytes. The cause of OSCC is like any other cancer; a DNA mutation that often occurs spontaneously but is increased by chemical, physical, and microbial mutagenic agents.[3,4] Various studies have shown that the epidemiological pattern of oral and lip cancers is changing. Among them, an increase in the prevalence of SCC, especially among young people, has been shown, which is associated with higher tobacco and alcohol use among young people.[4] In some studies, the tongue has been the most common site of OSCC in young people.[5] There has also been a high prevalence of

Access this article online

Quick Response Code:

Website: www.advbiores.net

DOI: 10.4103/abr.abr_197_21

How to cite this article: Khalesi S, Abbasi A, Razavi SM. Evaluating the clinicopathologic parameters of tongue squamous cell carcinoma based on its local distribution. Adv Biomed Res 2023;12:71.

SCC among women under the age of 45 in Western societies, India, China, and Korea.[6] In the Iranian population, OSCC is recognized as the most common tongue-related malignancy.[7] Furthermore, the increased trends in HPV prevalence were observed in the tumors of the tonsil and base of the tongue, although the number of SCC at the base of the tongue and tonsils is less than in other locations.[8] So far, very few studies have been done on the clinical and pathological features of this lesion based on its location in the tongue. Given the role of the tongue in swallowing, speaking, and tasting and the significance of this lesion as a life-threatening malignant neoplasm and the increased prevalence of OSCC patients in Iran, the aim of this study was to evaluate the clinicopathologic features of tongue SCC based on its local distribution in patients referred to Isfahan Dental School.

Materials and Methods

This retrospective study is conducted on the records of the patients in the archive of the Oral and Maxillofacial Pathology Department of Isfahan Dental School. This study was supported by Isfahan University of Medical Sciences Research Grant #295121. The Ethical Committee with the number IR.MUI.RESEARCH.REC.1398.582 in Isfahan University of Medical Sciences approved the manuscript. In our study, all samples with a definitive diagnosis of tongue SCC were included. Incomplete files and samples without the required quality were excluded from the study. Demographic data including gender, age, clinical features, and location of lesions were collected. Of these, 34 tongue SCC samples prepared by excisional biopsy were selected for histopathological evaluation in a simple random way. The site of the lesion was divided into 4 areas including the posterior lateral border, anterior lateral border, the tip and ventral surface of the tongue.[9] The sections from all archived paraffin-embedded tissue specimens from 34 cases were stained with hematoxylin and eosin (H&E). A section containing the full thickness of the tumors was used for histopathological grading. The classification grading system of Anneroth *et al*.[10] was used to detect the histopathological parameters. Histopathological slides of the specimens were examined by two pathologists blindly and simultaneously under a light microscope (Olympus BX41TF, Tokyo, Japan). SPSS version 23 Statistical Software was used for analysis. The variable data were analyzed using Chi-square, Fisher exact test, One-way ANOVA, and Non-parametric tests. *P* value < 0.05 was considered significant.

Results

In the present study, of the 275 cases diagnosed with OSCC in the period of 15 years at the Isfahan Dental School, 68 tongue SCCs were collected (24.72%). According to the results of this study, the youngest person with tongue SCC was 26 years old and the oldest was 85 years old. Furthermore, the mean age of all patients was 64.2 ± 14 years. Table 1 shows the frequency distribution of tongue SCC based on gender, clinical manifestation, and location of lesions. The most common clinical manifestations were exophytic (42.6%), ulcer (35.3%), erythroplakia (8.8%), and leukoplakia (5.9%), respectively. The most common site of tongue SCC was the lateral border of the tongue (36.8%). However, this classification of the lesion is purely based on reports in the patient records.

Table 1: Frequency of tongue SCC based on clinical parameters

Clinical parameters	*n*	%
Gender		
Female	42	61.77%
Male	25	36.76%
Unknown	1	1.47%
Clinical appearance		
Exophytic	29	42.6%
Ulcer	24	35.3%
Erythroplakia	6	8.8%
Leukoplakia	4	5.9%
Unknown	5	7.4%
Location		
Lateral border	25	36.8%
Posterior-lateral border	15	22.1%
Ventral surface	10	14.7%
Anterior-lateral border	9	13.2%
Tip of tongue	7	10.3%
Dorsal surface	2	2.9%
Total	68	100

Of the 68 tongue SCC, clinicopathologic features of 34 specimens were evaluated based on their local distribution of lesions on the tongue. Table 2 shows the clinical features including mean age, gender of patients, and clinical appearance of the studied samples. According to the results of this study, despite the higher prevalence of tongue SCCs in females compared to males, the difference based on the location of the lesion on the tongue was not significant according to Fisher exact test (p-value = 0.338). However, tongue SCCs are more prevalent in males on the ventral surface of the tongue (50%).

The mean age of patients with tongue SCC based on the location of the lesion was not significantly different (p-value = 0.766) on the One-way ANOVA test. The highest mean age of patients was at the tip of the tongue (68.42 ± 7.41) and the lowest mean age was at the posterior-lateral border (60.66 ± 18.58). According to the results of the study, most of the lesions in the posterior-lateral border, ventral surface, and the tip of the tongue had an exophytic appearance (77.7%, 55.9%, 57.1%). But most of the lesions in the anterior lateral border of the tongue were ulcers (44.4%). However, the differences were not statistically significant according to Fisher's exact test (p-value = 0.434).

Table 3 shows the grade of malignancy and the histopathological parameters of tongue SCCs based on its local distribution according to Anneroth *et al*.'s[10] classification grading system. 52.9% of the lesions were moderately differentiated.

Table 2: Clinical parameters of tongue SCCs based on local distribution

Clinical parameters	Tip of tongue *n* (%)	Ventral surface *n* (%)	Posterior lateral border *n* (%)	Anterior lateral border *n* (%)	Total *n* (%)	*P*
Gender						0.238
Female	(85.7) 6	4 (44.4)	(77.8) 7	(77.8) 7	24 (70.6)	
Male	1 (14.3)	5 (55.6)	(22.2) 2	(22.2) 2	(29.4) 10	
Mean age						0.766
(mean±SD)	68.42±7.41	64.66±15	60.66±18.58	64±13.13	64.2±14	
Clinical appearance						0.434
Exophytic	4 (57.1)	5 (55.6)	(77.8) 7	3 (33.3)	19 (55.9)	
Ulcer	3 (42.9)	(22.2) 2	0 (0)	4 (44.4)	9 (26.5)	
Erythroplakia	0 (0)	1 (11.1)	1 (11.1)	1 (11.1)	3 (8.8)	
Leukoplakia	0 (0)	1 (11.1)	1 (11.1)	1 (11.1)	3 (8.8)	
Total	7 (100)	9 (100)	9 (100)	9 (100)	34 (100)	

Table 3: Histopathological parameters of tongue SCCs based on local distribution

Histopathological parameters	Tip of tongue *n* (%)	Ventral surface *n* (%)	Posterior lateral border *n* (%)	Anterior lateral border *n* (%)	Total *n* (%)	*P*
Degrees of keratinization						
Highly (>50%)	5 (71.4)	2 (22.2)	5 (55.6)	5 (55.6)	17 (50)	0.329
Moderately (20-25%)	1 (14.3)	4 (44.4)	3 (33.3)	1 (11.1)	9 (26.5)	
Minimal (5-20%)	1 (14.3)	3 (33.3)	1 (11.1)	2 (22.2)	7 (20.6)	
No keratinization (0-5%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (2.9)	
Nuclear pleomorphism						
Little (>75% mature cells)	3 (42.9)	2 (22.2)	4 (44.4)	3 (33.3)	12 (35.3)	0.934
Moderately (50-75% mature cells)	3 (42.9)	6 (66.7)	3 (33.3)	4 (44.4)	16 (47.1)	
Abundant (25-50% mature cells)	1 (14.3)	1 (11.1)	2 (22.2)	2 (22.2)	6 (17.6)	
Extreme (0-25% mature cells)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Number of mitoses (high power field)						
Few (0-1)	5 (71.4)	2 (22.2)	5 (55.6)	4 (44.4)	16 (47.1)	0.478
Moderately (2-3)	1 (14.3)	5 (55.6)	2 (22.2)	3 (33.3)	11 (32.4)	
Numerous (4-5)	1 (14.3)	2 (22.2)	0 (0.0)	1 (11.1)	4 (11.8)	
Ex numerous (>5)	0 (0.0)	0 (0.0)	2 (22.2)	1 (11.1)	3 (8.8)	
Pattern of invasion						
Pushing, well defined infiltrating border	2 (28.6)	3 (33.3)	1 (11.1)	2 (22.2)	8 (23.5)	0.047
Solid cords, bonds, strands	1 (14.3)	6 (66.7)	7 (77.8)	2 (22.2)	16 (47.1)	
Small groups or cords	2 (28.6)	0 (0.0)	1 (11.1)	4 (44.4)	7 (20.6)	
Marked cellular dissociation/single cells	2 (28.6)	0 (0.0)	0 (0.0)	1 (11.1)	3 (8.8)	
Stage of invasion						
Carcinoma in situ/questionable	2 (28.6)	0 (0.0)	1 (11.1)	0 (0.0)	3 (8.8)	0.679
Invasion into only lamina propria	3 (42.9)	4 (44.4)	4 (44.4)	4 (44.4)	15 (44.1)	
Invasion below lamina propria	2 (28.6)	5 (55.6)	4 (44.4)	5 (55.6)	16 (47.1)	
Extensive and deep invasion	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Lymphoplasmacytic infiltration						
Marked	4 (57.1)	4 (44.4)	2 (22.2)	1 (11.1)	11 (32.4)	0.552
Moderate	1 (14.3)	3 (33.3)	5 (55.6)	5 (55.6)	14 (41.2)	
Slight	0 (0.0)	2 (22.2)	2 (22.2)	2 (22.2)	6 (17.6)	
None	2 (28.6)	0 (0.0)	0 (0.0)	1 (11.1)	3 (8.8)	
Anneroth *et al*.'s grading system						
I	3 (42.9)	2 (22.2)	4 (44.4)	2 (22.2)	11 (32.4)	0.634
II	4 (57.1)	6 (66.7)	3 (33.3)	5 (55.6)	18 (52.9)	
III	0 (0.0)	1 (11.1)	2 (22.2)	2 (22.2)	5 (14.7)	
IV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Total	7 (100)	9 (100)	9 (100)	9 (100)	34 (100)	

Based on the Non-parametric test, no significant difference was found between the grade of the tumor and its local distribution (p-value = 0.634). Most of the tongue SCCs (50%) had a high degree of keratinization, moderate nuclear pleomorphism, low mitosis rate, invasion below lamina propria, solid islands, and cords pattern and moderate lymphoplasmacytic infiltration [Figure 1]. According to Non-parametric and Fisher exact tests, no significant difference was found between these histological parameters and its local distribution except for the invasion pattern, which was significantly correlated with local distribution.

Discussion

The aim of this study was to evaluate the clinicopathologic features of tongue SCC in patients referred to Isfahan Dental School. According to the results of most research in Iran such as Akbari's, Mafi's, Mir's, Razmpa's, Falaki's and Maleki's studies, the most common site of oral cancer is the tongue.[7,11-15] Also, in Falaki's study, the tongue has been reported as the most common site of SCC.[14] Studies show that 25 to 50% of all OSCCs are carcinomas of the tongue.[13,16-19] Similar to other studies, of 275 oral SCC specimens in this study, 68 (24.72%) were tongue SCC. However, in some studies, other areas of the oral cavity, including the floor of the mouth[20] and buccal mucosa[21] have been identified as the most common sites of involvement. This difference in results can be related to behavioral habits, nutrition type, and different risk factors in each geographic region. In addition to that, according to a systematic study, the tongue is the most common area involved in young patients with oral cancer. Therefore, identifying and investigating the characteristics of tongue tumors as an effective organ in the mouth has particular importance.[22]

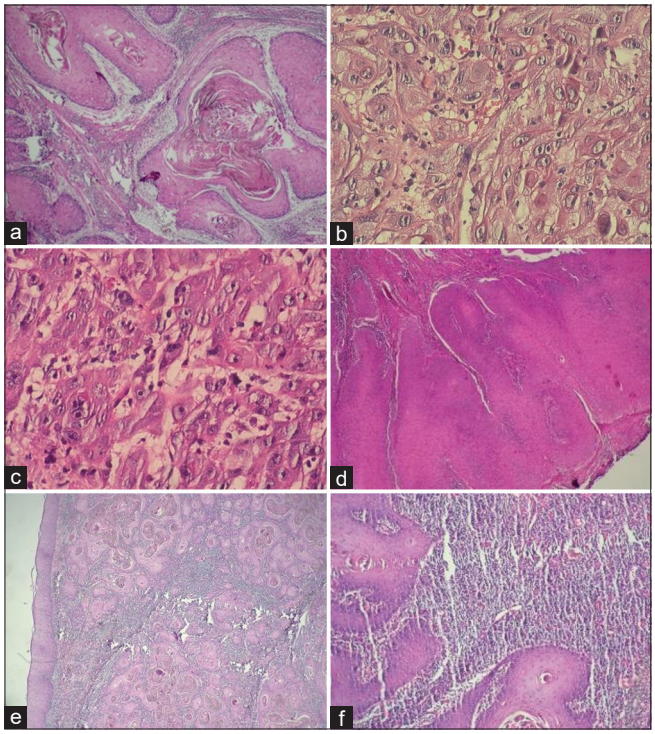

Figure 1: Photomicrographs showing: (a) Highly keratinization of tongue SCC (H&E, ×100), (b) Moderately nuclear polymorphism (×400), (c) Moderately mitosis number (×400), (d) Pattern of invasion with pushing, well- defined infiltrating borders (×100), (e) Invasion tumor cells below lamina propria (×40), (f) Marked lymphoplasmacytic infiltration (×100)

In this study, the most common areas involved in tongue were the lateral borders (36.8%), which is in line with the studies of Albuquerque,[23] Okubo,[24] Muhammad,[9] Falaki,[14] Mohideen,[22] Selvamani[25] and Aittiwarapoj.[26] On the other hand, in Muhammad's study, the posterior-lateral border, anterior-lateral border, the tip of the tongue, and the ventral surface showed the highest frequency of tongue SCC, respectively.[9] While in our study, the posterior-lateral border, ventral surface, anterior-lateral border, and the tip of the tongue were the most frequent.

In the present study, most patients with tongue SCC have been diagnosed in the sixth decade of their life. Whereas the fifth decade of life in Mir's[12] and Ciucă's studies,[27] the eighth decade in Razmpa's study,[13] and the third decade in Muhammad's study[9] had the highest frequency of tongue SCC. Although, most studies indicate a higher prevalence of tongue SCC in people over 50 years of age, different studies on the mean age of patients have had conflicting results.[13] The reasons for this result may be fewer risk factors exposure to patients with an average age of less than 50 years. Also, different sample sizes in different studies and the presence of SCC risk factors such as alcohol and tobacco use in different societies can be the cause of different results in this regard.

In this study, the frequency of tongue SCC was higher in females than men (1.68: 1), which is different from most other studies. In other studies, the frequency of tongue SCC was higher in men.[9,12-14,20,23,26] In line with our study, Razavi *et al*.,[28] who studied all SCC specimens in Isfahan Health Centers, showed a higher frequency of tongue SCC in females than males. Also in some other studies, the frequency of tongue SCC has been reported to be equal between men and women.[7,29] Given the difference in gender prevalence of tongue SCC, especially in Isfahan, the need for further research on the risk factors in females for this lesion has been clarified. In this regard, Patel's study shows an increase in tongue SCC in young, female population.[30] One of the reasons for these results may be passive smoking.[25]

In the present study, 42.6% of tongue tumors had an exophytic clinical appearance which was similar to the results of Falaki's study,[14] but it is contradictory to Mir's,[12] Razmpa's[13] and Aittiwarapoj's studies.[26] In these studies, ulcer lesions were the most common clinical manifestation of tongue SCC. Observing ulcer or exophytic lesions on the tongue can be a warning sign for the patient to visit a doctor and it is crucial in the early diagnosis of tongue tumors.

According to the results of this study, no significant relationship was found between gender, mean age, and clinical appearance

with local distribution of tongue SCC ($p < 0.05$). Given that no study has been conducted so far, it is not possible to compare the results with other studies.

In this study, the grade of malignancy of all tongue SCC specimens was (52.9%) moderately differentiated, (32.4%) highly differentiated, and (14.7%) poorly differentiated, respectively. However, there was no non-differentiated grade of malignancy. In the studies of Mohammad[9] and Rai,[31] most tongue SCCs were poorly differentiated and the least frequent were high-grade tumors. Perhaps, this is the reason for the high mortality rate of oral SCC (50-70%) in Pakistan and India.[9] However, in many studies, most tumors have been highly differentiated.[25,26,32] The use of different malignant grading systems may be a reason for different results. According to Anneroth *et al*.'s[10] classification grading systems, factors (Phrasing unclear. Please change to "systems and factors" if it is factually correct.) such as degree of keratinization, nuclear pleomorphism, the number of mitoses, pattern of invasion, stage of invasion, and rate of inflammatory cell infiltration in the histopathologic specimen determine. (Sentence incomplete. Please complete the sentence with relevant information. Or consider changing the end of the sentence to "are/were determined.") Therefore, in tumors with higher differentiation, fewer mitosis and cellular pleomorphism rates are seen than in tumors with poorer differentiation. Poorly differentiated tumors also have less keratinization.[9,10] Although, there was no significant relationship between the grade of malignancy and most of the histopathologic parameters with its local distribution over the tongue in this study ($p > 0.05$), only histopathological feature of the pattern of tumor cell invasion in different sites of tongue SCC was significant ($p < 0.05$). Our results show that the most of patterns of tumor cell invasion in the posterior-lateral border (77.8%) and ventral surface of the tongue (66.7%) tumors were solid islands and cords. Other studies have shown a significant association between lymph node involvement with tumor size, grade of tumor malignancy, and location of the primary tumor on the tongue.[33] Various studies have reported a 5-year survival rate of less than 42.6% of patients with tongue SCC, especially tumors of the posterior and anterior borders.[27] The presence of lymph node involvement and positive margins in histopathological assessment also independently predicted a poor prognosis of tongue SCC.[34] Therefore, attention to the location of the lesion in the tongue is important for early diagnosis and faster treatment to reduce lymph node involvement and increase patient survival.

Conclusion

Tongue SCC is one of the most oral malignant lesions. Given that most of the lesions in this study had moderate differentiation of malignancy, awareness and identification of clinical features is needed for early diagnosis and faster treatment. Also, attention to the histopathological features such as the pattern of invasion and location of the lesion on the tongue can be effective in determining the therapeutic approach to increase the success of treatment. Therefore, the lesions in the posterior region and ventral surface of the tongue require more attention and more aggressive treatments.

Acknowledgements

This research was supported by the Dental Materials Research Center of Isfahan University of Medical Sciences.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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