

Incidence of Distant Metastasis in Oral Squamous Cell Carcinoma on 18f FDG PET CT Scan

Distant Metastasis in Oral Squamous Cell Carcinoma

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ABSTRACT

Objective: To evaluate the incidence and pattern of distant metastasis in squamous cell carcinoma of the oral cavity

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Study was conducted in the department of oral and maxillofacial surgery/Radiology department, Jinnah Postgraduate Medical Centre, Karachi, from January, 2018 to June, 2021 for a period of six months.

Materials and Methods: A total of 416 patients were enrolled in study. Main variables of the study were area of residence, type of cancer, treatment given, recurrence rate, staging of cancer and metastasis. Data was analyzed using SPSS version 23. Mean for numerical data and frequency for categorical data was calculated. After applying test of significance p value ≤ 0.05 was taken as significant.

Results: Four hundred and sixteen squamous cell carcinoma patients were examined in our study. Mean age of the patients was 69.44 ± 18.31 years and most of the patients (49.8%) were between 46-64 years. Most patients belonged to urban areas (55.8%). Mean weight of the patients was 60.56 ± 14.89 kg and mostly (31.0%) weighed in between 51-60 kg. The most common type of cancer we found was buccal mucosa (45.7%) and tongue (43.5%). Amongst the 416 patients, 13.2% patients were diagnosed as having distant metastasis. The most common site that produced metastasis was buccal mucosa especially of the right side (34.6%). Radiotherapy and chemotherapy was given in 50.9% and 58.2% patients respectively. Recurrence was found in 45.5% patients. Most common time to occurrence was between 6-12 months observed in 40.0% patients. The most common tumor stage was observed T3 (41.8%) followed by stage IVA (38.2%) tumor stage, N0 (21.8%) was the most common nodal stage and M0 (43.6%) was the most common M stage. Lungs and mediastinum were the most common organs of distant metastasis at 25.5% and 14.5% respectively.

Conclusion: A high proportion of squamous cell carcinomas of the oral mucosa in our population developed distant metastasis with the most common primary site being the right buccal mucosa and most common metastatic site being the lungs as expected. We also found a considerable number of patients that developed extra pulmonary metastasis in liver, bones and brain which might be due to the higher stage at which patients present and possibly more aggressive characteristic of the tumors.

Key Words: Squamous cell carcinoma, oral cavity, head and neck cancer, distant metastasis.

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INTRODUCTION

Squamous cell carcinoma (SCC) is 6th most common cancer having the highest incidence rate in South Africa¹.

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Its locoregional control is 50% at 5 years and distant control is 85%². Alcohol, tobacco and lack of antioxidants in diet are the main causes of squamous cell carcinoma. In Indo-Asian population areca nut chewing is the leading cause. Less frequent causes are poor dental hygiene, human papilloma virus, irritation with sharp dentures and genetic susceptibility³. Oral cavity has many subsites including tongue, hard palate, floor of mouth, gingiva covered upper and lower alveoli, retromolar trigone, buccal mucosa, inner side and anterior boundary of lips⁴.

There are many challenges in pretreatment staging, diagnosis and evaluation of patients after treatment⁵. Clinical signs may be nonspecific depending on the site of cancer like pharynx, oral cavity, larynx, paranasal sinuses, nasal cavity, thyroid and salivary gland⁶. Sometime occult cancers were found that escaped detection by endoscopy, physical examination and

cross-sectional imaging. Many techniques like magnetic resonance imaging, contrast enhanced computed tomography and PET scans are used worldwide to diagnose the baseline extent of tumor and post treatment response⁷. PET scan is a sensitive modality for detecting distant metastasis, lymph node metastasis, residual/recurrent disease as compared to MRI and CT scan as it is functional imaging rather than anatomic imaging⁸.

Systemic metastasis in oral squamous cell carcinoma (OSCC) is associated with a dismal prognosis, systemic chemotherapy and 10 months overall median survival⁹. Mortality rate of patients from distant metastasis is 15-20%. Incidence of distant metastasis in autopsy reports is 3-4 times higher as compared to clinical evaluation¹⁰. About 90% of malignancies arise from subsites within the oral cavity. The aim of this study is to evaluate the role of imaging in diagnosis of distant metastasis and consequent management of head and neck squamous cell carcinoma.

MATERIALS AND METHODS

This retrospective study was conducted in the department of oral and maxillofacial surgery/Radiology department, Jinnah Postgraduate Medical Centre, Karachi, from January 2018 to June 2021. Study was conducted after approval from the Institutional Review board. Informed written consent was obtained from every possible patient. Non probability consecutive sampling technique was used. Sample size was calculated using an online software openepi.com with confidence interval 95% and margin of error 0.5%. Inclusion criteria was patients with biopsy proven squamous cell carcinoma of oral cavity who were undergoing staging or post treatment imaging. Patients with SCC of other sites were excluded.

Primary surgery was performed in patients with operable oral cavity cancers. Adjuvant intensity modulated radiotherapy (IMRT) was performed in some cases upto 5 fractions per week. After completion of treatment with IMRT patients were followed up with imaging every 3 months for one year. In the second year follow up was extended to every 4 months and biannually after that. Loco regional control and toxicity were assessed with endoscopy and clinical examination. SPSS version 24 was used for data analysis, mean and standard deviation was calculated for numerical data like age and frequency and percentages were calculated for categorical data like gender. Test of significance like test and chi square test were applied to see association among variables. P value less than or equal to 0.05 was considered as significant.

RESULTS

Four hundred and sixteen squamous cell carcinoma patients were examined in our study. Mean age of the patients was 69.44±18.31 years with the majority

(49.8%) of patients between 46-64 years. Most belonged to urban areas (55.8%). The mean weight of the patients was 60.56±14.89 kg and 31.0% patients were between 51-60 kg. (Table. I).

Table No.1: Demographic characteristics of patients

Variable	Mean±S.D	N (%)
Gender		
Male		351 (84.4)
Female		65 (15.6)
Age (years)	69.44±18.31	
27-45		167 (40.1)
46-64		207 (49.8)
65-83		42 (10.1)
Area of residence		
Urban		232 (55.8)
Rural		184 (44.2)
Weight (kg)	60.56±14.89	
30-50		113 (27.2)
51-60		129 (31.0)
61-70		86 (20.7)
>70		88 (21.2)

S.D: standard deviation

Table No.2: Sites of metastasis

Variable	N (%)	(95% C.I)
Tongue	181 (43.5)	(32.02-45.04)
Buccal	190 (45.7)	(30.03-48.03)
Hard plate	39 (9.4)	(6.41-12.11)
Retro molar trigone	6 (1.26)	(0.44-3.83)

Table No.3: Sites of distant metastasis and treatment

Variable	N (%)	(95% C.I)
Sites of distant metastasis		
Right buccal mucosa	19 (34.6)	(32.2-42.1)
Left buccal mucosa	13 (23.7)	(22.3-25.4)
Right retro molar trigone	3 (5.4)	(1.9-4.2)
Left retro molar trigone	3 (5.4)	(1.7-4.3)
Hard palate	4 (7.3)	(3.4-8.8)
Tongue – right border	6 (10.9)	(6.2-15.3)
Tongue – left border	5 (9.1)	(9.1-12.7)
Base of tongue	2 (3.6)	(1.3-5.5)
Radiotherapy		
Yes	28 (50.9)	(32.21-60.16)
No	27 (49.1)	
Chemotherapy		
Yes	32 (58.2)	(40.02-68.50)
No	23 (41.8)	
Recurrence		
Yes	25 (45.5)	(46.07-74.09)
No	30 (54.5)	
Time to recurrence		
6-12 months	21 (38.2)	(35.2-45.6)
13-19 months	22 (40.0)	(31.4-46.8)
19-25 months	12 (21.8)	(19.5-28.6)

Table No.4: Stages of carcinoma

Variable	N (%)	(95% C.I)
Stages		
I	7 (12.7)	(9.2-13.4)
II	8 (14.5)	(6.4-15.8)
III	10 (18.2)	(8.6-20.6)
IVA	21 (38.2)	(35.5-46.8)
IVB	9 (16.4)	(8.4-20.8)
T class		
Tx,To,T1s	8 (14.5)	(12.3-20.5)
T1	6 (10.9)	(8.5-19.7)
T2	9 (16.4)	(14.4-24.5)
T3	23 (41.8)	(30.2-40.7)
T4a	9 (16.4)	(10.6-23.6)
N class		
Nx	10 (18.2)	(14.8-24.2)
N0	12 (21.8)	(17.2-30.1)
N1	10 (18.2)	(14.3-27.4)
N2	23 (41.8)	(30.2-39.6)
M class		
Mx	15 (27.3)	(23.4-38.1)
M0	24 (43.6)	(25.7-52.6)
M1	16 (29.1)	(31.6-45.2)

Table No.5: Sites of metastases in (n=55) patients

Sites of metastases	N (%)	(95% C.I)
Skeleton	7 (12.7)	(6.1-12.9)
Cervical lymph nodes	4 (7.3)	(4.6-15.6)
Axillary lymph nodes	4 (7.3)	(3.4-12.4)
Mediastinum	8 (14.6)	(12.2-18.4)
Lungs	14 (25.5)	(16.8-32.1)
Liver	7 (12.7)	(6.5-11.5)
Brain	7 (12.7)	(8.6-13.6)
Adrenals	2 (3.6)	(2.7-6.2)
Peritoneum	2 (3.6)	(1.3-4.4)

The most common sites of carcinoma were buccal mucosa 190 (45.7%) and tongue 181 (43.5%). (Table. 2). among 416 patients 55 (13.2%) patients diagnosed with distant metastasis and most common primary site was buccal mucosa especially of the right side 19 (34.6%). Radiotherapy and chemotherapy was given in 28 (50.9%) and 32 (58.2%) patients respectively. Recurrence was found in 25 (45.5%) patients, while the most common time of occurrence was between 6-12 months observed in 22 (40.0%) patients. (Table. 3).

Among 55 patients stage IVA was the most common stage observed in 21 (38.2%) patients, T3 was the most common tumor stage observed in 23 (41.8%), N0, 12 (21.8%) was the most common nodal stage and M0 24 (43.6%) was the most common M stage. (Table. 3).

Of the 55 patients, lung and mediastinum were the most common sites of distant metastasis 14 (25.5%) and 8 (14.5%), respectively. (Table. 4).

DISCUSSION

According to current studies after the diagnosis of distant metastasis in OSCC, median time to death is 64

months. Due to lack of studies on distant metastasis in OSCC patient's data is limited.

Lungs is the most common site of distant metastasis and CT chest is considered adequate staging for newly diagnosed cases with early-stage disease. But while reading PET-CT scans of such patients it was observed that they presented with extra-pulmonary metastases in the presence of no other detectable primary. So it was decided to perform a study to see the incidence of other metastases which might be due to different demographic of our patient population.

In our group of patients all were treated with IMRT and for locally advanced SCC and concomitant cisplatin-based chemotherapy was used. About 10% of SCC patients developed distant metastasis (Table IV), these results are in line with studies by Juet al¹¹ and Arons et al¹².

Brougham et al¹³ carried out a study on frequency and metastatic stage of squamous cell carcinoma and reported median age of patients was 74 years and approximately 2.6% of patients were observed with SCC, among them common location was lip and cheek. In another study by Zbärenet al¹⁴ reported metastasis in 40% of cases, among them 15% were diagnosed in bones, 425 in liver and 705 in lungs.

In our study we observed male gender is more prone to cancers of oral cavity as compared to females. This may be due to greater exposure to carcinogenic agents like tobacco and alcohol which culturally are found more commonly amongst males in South East Asia. But a study conducted by Struhlet al¹⁵ reported that there is no difference in incidence of oral cancers between male and female genders. Both genders have equal prevalence ate of 14%. Similarly in our study most of the patients were between 46-64 years of age.

A study was conducted by Kotewallet al¹⁶ and reported that the most common site of distant metastasis is lungs followed by liver which shows that no organ is immune to squamous cell carcinoma. In this study pulmonary lesions were observed in 80% of cases. Similar findings were reported by Peltier et al¹⁷ that in human body no organ is immune to squamous cell carcinoma of head and neck and most common site of metastasis is lungs.

Some contrast studies are also available with conclusion that incidence of distant metastasis is low in squamous cell carcinoma of head and neck. In 2006 Garavello et al¹⁸ conducted a study on patients of squamous cell carcinoma and reported distant metastasis in 9.2% of patients and most of cases were observed in younger age (below 45 years). Another similar study was conducted by Gowenetal¹⁹ and reported that incidence of squamous cell carcinoma varies between 3-50% and mostly observed in immune compromised patients. Most commonly affected sites were liver, bone and lungs and metastasis which were observed in 9.3% of cases.

O'Brien et al²⁰ carried out a study on this topic and concluded that below clavicle metastasis was observed in 46.7%. Lungs and esophagus were the most common sites. Brain is also a prone site that can be affected with

metastatic lesions. Auerbach et al²¹ reported distant metastasis in 36% of patients and autopsy proved epidermoid lung cancer in major proportion of patients.

CONCLUSION

A high proportion of squamous cell cancers of oral cavity developed distant metastasis (13.2%) with the most common metastatic site being the lungs. There were also a significant proportion of patients who had metastasis to liver, bones and brain which might be related to the more aggressive characteristics and later stage of presentation in our patient population.

Author's Contribution:

Concept & Design of Study:	Raja Muhammad Daniyal
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