

ORIGINAL RESEARCH**Outcome Analysis of Operated Cases of Squamous Cell Carcinoma of Oral Cavity at a Tertiary Care Centre in North-East India****¹Nitin Sharma, ²Neha Mahajan, ³Nabajyoti Saikia, ⁴Debojit Sarma**¹Assistant Professor, Department of ENT, Government Doon Medical College and Hospital, Dehradun, India²Assistant Professor, Department of General Surgery, Government Doon Medical College and Hospital, Dehradun, India³Associate Professor, Department of ENT, Jorhat Medical College and Hospital, Jorhat, Assam, India⁴Assistant Professor, Department of ENT, Assam Medical College and Hospital, Dibrugarh, Assam, India**Corresponding Author:**Debojit Sarma

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Abstract

Introduction: Carcinoma of the oral cavity and pharynx is the sixth most common cancer in the world, grouped together. The principal modalities of therapy remains surgery and radiotherapy, often in combination. Other modalities, including chemotherapy have been tried not only as palliative treatment but also as induction therapy or as an adjunct to surgery or radiotherapy with curative intent. The aim of this study was to analyse our experience with surgical management of squamous cell carcinoma of oral cavity; prognostic factors and factors affecting the outcome.

Materials and method: A retrospective study of prospectively maintained data of patients was conducted of all cases of squamous cell carcinoma of oral cavity treated surgically Between June'2015 to June'2017 at a tertiary teaching centre in North - East India.

Results: The results were evaluated in the form of tables and figures wherever required and assessed depending on the aims and objective of the study.

Conclusion: The stage of disease, tumour size, nodal status, margin status, final histopathological report and habit of tobacco chewing strongly influence the overall outcome. This emphasizes on the importance of prevention, early diagnosis, and proper follow up after completion of treatment of oral cavity carcinoma.

Keywords: Bone Resection, Disease free survival, Oral cancer, Neck Dissection, Tobacco.

Introduction

Among all the cancers in the world, oral and pharyngeal cancer, grouped together, is the sixth most common cancer [1, 2,3,4]. Cancers of the oral cavity are known to be associated with high mortality and morbidity [1]. A significant variation in the site of occurrence of cancer in the oral cavity has been seen which can be attributed to the habit of tobacco consumption in its various forms [1,5,6]. In the Western developed countries, it is commonly seen that smoking tobacco leads to involvement of the tongue, floor of mouth and hypopharynx, while, chewable tobacco shows occurrence of cancer more frequently in the retromolar trigone (RMT) and the buccal mucosa region [1]. The consumption of alcohol has a combination of local toxic effects on the mucosa and systemic effects from the associated dietary deficiency, hepatic damage and possible alteration in patient's immunity. This has been linked to the

development of cancer[7]. In India, the most common site involved in oral cavity carcinoma is buccal mucosa[1,5,6,7]. The vast majority (>85%) are primary squamous cell carcinoma followed by minor salivary gland neoplasms as the next most common[3,4]. The remainder are lymphomas, malignant melanomas, sarcomas, secondary tumours, etc. [3]. Treatment is directed at the elimination of the primary tumour and any neck node metastasis, with minimum morbidity to the patient[3]. The principal modalities of therapy are surgery and radiotherapy, often used in combination. Other modalities, including chemotherapy have been tried not only as palliative treatment but also as induction therapy or as an adjunct to surgery or radiotherapy with curative intent[3]. Although there has been progress in various treatment modalities over the past 50 years, the survival rates have not improved drastically [1]. These results show us that there is a need of more studies that put more insight on “site specific” studies of oral cancer in the Indian population. Although the treatment of carcinoma of oral cavity remains well established, reviews of institutional experiences are of prime importance[1]. The aim of this study was to analyse our experience with surgical management of squamous cell carcinoma of oral cavity; prognostic factors and factors affecting the outcome.

Material and Methods

Study design and settings

The study was a retrospective analysis of the prospectively maintained data of all the cases of squamous cell carcinoma of oral cavity that were treated surgically between June’2015 to June’2017 at a tertiary teaching centre in North-East region of India.

Study population

All the patients who underwent surgical management for oral cavity carcinoma between June’2015 to June’2017. The case records of the patients were reviewed. The details of clinical presentation, preoperative therapy, operative procedure, histopathological examination, postoperative complications and outcome were retrieved from the case records.

Inclusion criteria

1. Patients with histologically confirmed primary squamous cell carcinoma (SCC) of oral cavity including verrucous carcinoma.
2. Only patients who underwent surgery as primary modality of treatment were included.

Exclusion criteria

1. Patients presenting with recurrences or previously treated disease.
2. Patients with distant metastasis.

Statistics

Data was analyzed and necessary tables and graphs were plotted. Results of continuous measurement were presented as Mean \pm SD. Kaplan-Meier methods were used for analyzing Disease free Survival (DFS).

A total of nineteen cases were included in the study. Staging was done as TNM criteria (T- tumour size, N- lymph node involvement, M- distant metastasis)[8]. The period of follow-up was calculated as duration between the date of surgery to the date of last contact or death of patient.

Patient status at the time of last contact was categorized as:

- Alive without disease (Disease free survival, DFS)
- Alive with disease.
- Dead due to disease;

- Dead due to other causes;

Local recurrence was defined as the presence of a lesion at the site of, or adjacent to the primary tumour in the oral cavity[7]. Regional recurrence was defined as occurrence of positive palpable lymph node in the ipsilateral or contralateral side; post-treatment. Recurrence also included those cases who presented with distant metastasis[7]. In regard to the site of oral carcinoma, we adhered to TNM classification: AJCC[8]; which recognizes oral cavity, includes mucosal lip, buccal mucosa, floor of the mouth, hard palate, upper and lower alveolar ridge, anterior two third of the tongue and retromolar trigone. Patients were subjected to wide local excision of the tumour with 1-1.5cm from the palpable margins of the tumour with reconstruction. Neck dissection was performed in all stage 4 disease patients (8 patients; 42.10%) and one patient (5.26%) in stage 3 with positive neck node confirmed by USG guided FNAC.

Results

The mean age of the patients was 51.15 ± 9.6 yrs (age range from 31 yrs to 70 yrs) (Table 1). The highest frequency of patients was seen in the age group between 41 to 50 yrs (6 patients). The male to female ratio was found to be 3.75:1 (Table 2)

Table 1: Age distribution of patients

| Age group(in yrs) | No. of patients |
|--------------------------------|-----------------|
| 31-40 | 4 (21.05%) |
| 41-50 | 6 (31.57%) |
| 51-60 | 4 (21.05%) |
| 61-70 | 5 (26.31%) |
| Mean age : 51.15 ± 9.6 yrs | |

Table 2: Sex distribution of the patients

| Sex | No. of patients |
|-----------------------|-----------------|
| Male | 15 (78.94%) |
| Female | 4 (21.05%) |
| Total | 19 |
| Ratio(Male to Female) | 3.75:1 |

Out of 19 patients, 12 belonged to rural areas (63.15%). All the patients had a history of consumption of tobacco in some form. However, sixteen patients (84.21%) gave a history of chronic use of one or more forms of tobacco use for more than 10 years. Thirteen patients (68.42%) of the patients admitted to frequent alcohol consumption. Gingivo-buccalsulcus was involved in seven patients (36.84%) followed by involvement of the buccal mucosa in six patients (31.57%). Lip involvement was seen in three patients (15.78%), tongue was involved in two patients (10.52%) and floor of the mouth was involved in one patient (5.26%). (Fig 1)

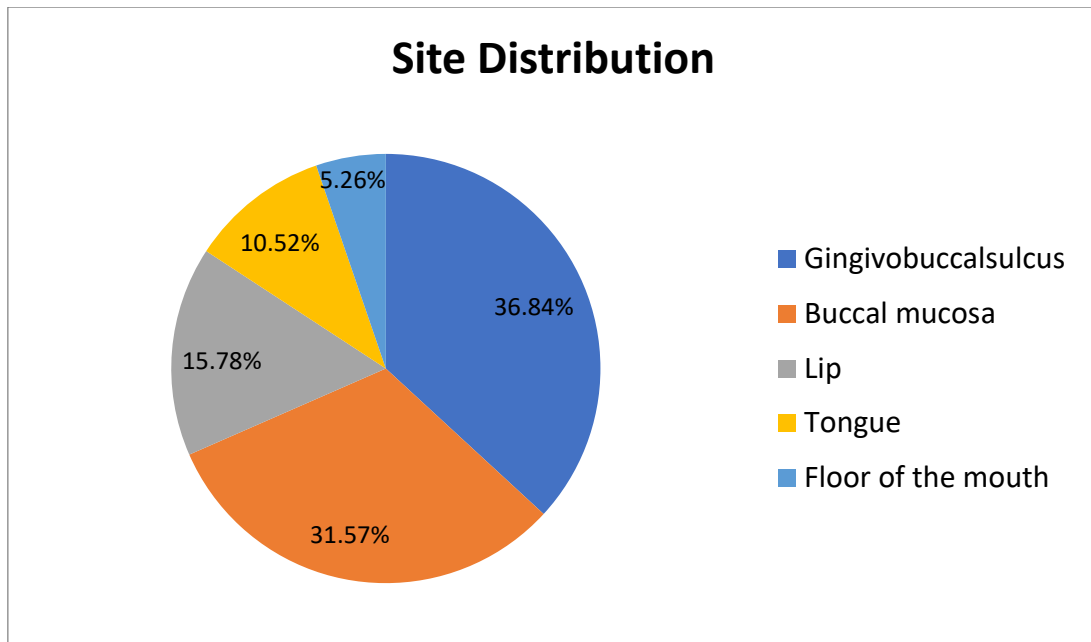


Fig 1:Site specific distribution of oral cavity carcinoma in operated patients

The patients were divided on the basis of stage of the disease. Eight patients (42.10%) belonged to stage 4. Distribution of patients according to TNM classification and stage is given in table 3 and 4 respectively.

Table 3: Distribution of patients according to TNM Classification[8]

| STAGE | No. of patients |
|--|-----------------|
| T ₁ N ₀ M ₀ | 1(5.26%) |
| T ₂ N ₀ M ₀ | 7 (36.84%) |
| T ₂ N ₁ M ₀ | 1 (5.26) |
| T ₃ N ₀ M ₀ | 2 (10.52%) |
| T ₄ N ₀ M ₀ | 4 (21.05%) |
| T ₄ N ₁ M ₀ | 1 (5.26%) |
| T ₄ N ₂ M ₀ | 3 (15.78 %) |

Table 4: Distribution of patients according to stage

| Stage | No. of patients |
|-------|-----------------|
| 1 | 1 (5.26%) |
| 2 | 7 (36.84%) |
| 3 | 3 (15.78%) |
| 4 | 8 (42.10%) |

Nodal metastasis was present in 5 patients(26.31%) confirmed by USG guided FNAC. Patients were subjected to wide local excision of the tumour with 1-1.5cm from palpable margins of the tumour. Frozen sectioning was not done as it was not available. Neck dissection was performed in all stage 4 disease patients (8 patients; 42.10%) and one patient in stage 3 who had a positive neck node confirmed by USG guided FNAC(Table 5).

Table 5: No. of patients who underwent neck dissection (9 patients)

| Neck dissection | No. Of patients |
|----------------------------------|-----------------|
| Supra omohyoid neck dissection | 4 (44.44%) |
| Modified radical neck dissection | 5 (55.55%) |

Bone resection was done in 6 patients (31.57%). Segmental mandibulectomy was done in 3 patients (50%), marginal mandibulectomy in 2 patients (33.33%) and hemi-mandibulectomy in 1 patient (16.66%). (Table 6)

Table 6: Distribution of patients who underwent bone resection (6 patients)

| Bone Resection | No. Of Patients |
|--------------------------|-----------------|
| Segmental mandibulectomy | 3 (50%) |
| Marginal mandibulectomy | 2 (33.33%) |
| Hemi-mandibulectomy | 1 (16.66%) |

Repair was done with primary closure where defect was small and reconstruction was done with flaps wherever necessary (11 patients) (57.89%) (Table 7)

Table 7: No. of patients who underwent flap surgery (11 patients)

| Flaps used | No. of patients |
|------------------------------------|-----------------|
| Submental flap | 2 (18.18%) |
| Deltpectoral flap | 2 (18.18%) |
| Forehead flap | 3 (27.27%) |
| Pectoralis major myocutaneous flap | 4 (36.36%) |

The complications related to surgery are discussed in Table 8

Table 8: Complications related to surgery

| Complication | Number of patients |
|--------------|--------------------|
| Infection | 3 |
| Flap failure | 1 |

The final histology of all the patients showed the presence of Squamous cell carcinoma. The follow up period ranged from 1-36 months. Out of 19 patients, 5 patients (26.31%) were lost to follow up. Follow up patients were categorized as alive without disease, alive with disease, dead due to disease, dead due to other causes as shown in Table 9. One patient (5.26%) died due to disease within one year of getting operated.

Table 9: Patients distribution on follow up

| Patient/ Stage | At 6 month | At 12 month | At 18 month | At 24 month | At 30 month | At 36 month |
|----------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Pt.1(STG 1) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.2(STG 4) | Alive without disease | Dead Due to Disease | | | | |
| Pt.3(STG 4) | Alive without disease | Alive without disease | Lost to follow up | | | |
| Pt.4(STG 2) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Lost to follow up | |
| Pt.4(STG 2) | Alive without disease | Alive without disease | Lost to follow up | | | |

| | | | | | | |
|---------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Pt.6(STG 3) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.7(STG 3) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.8(STG 2) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.9 (STG 4) | Alive without disease | Alive without disease | Lost to follow up | | | |
| Pt.10(STG 4) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.11(STG 4) | Alive without disease | Alive with Disease | Alive with Disease | Alive with Disease | Alive with Disease | Alive with Disease |
| Pt. 12(STG 2) | Alive without disease | Alive without disease | Alive without disease | Lost to follow up | | |
| Pt.13(STG 4) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.14(STG 3) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.15(STG 2) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.16(STG 4) | Alive without disease | Alive without disease | Alive with disease | Alive with Disease | Alive with Disease | Alive with Disease |
| Pt.17(STG 4) | Alive without disease | Alive without disease | Alive with disease | Alive with Disease | Alive with Disease | Alive with Disease |
| Pt.18(STG 2) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |
| Pt.19(STG 2) | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease | Alive without disease |

Post operative radiotherapy was given in 4 patients(21%) where margins were found to be positive. Recurrences were seen in 4 patients(21%) and were treated with radiotherapy and chemotherapy. All the patients with recurrence belonged to stage 4 disease. Two patients presented with local recurrence (10.52%), one patient (5.26%) presented with regional recurrence and one patient presented with distant metastasis (5.26 %) [Table 10]

Table 10.Outcome after treatment

| | |
|---------------------------------------|------------|
| Post-op radiotherapy and chemotherapy | 4 (21%) |
| Local recurrences | 2 (10.52%) |
| Regional recurrence | 1 (5.26%) |
| Distant metastasis | 1 (5.26%) |

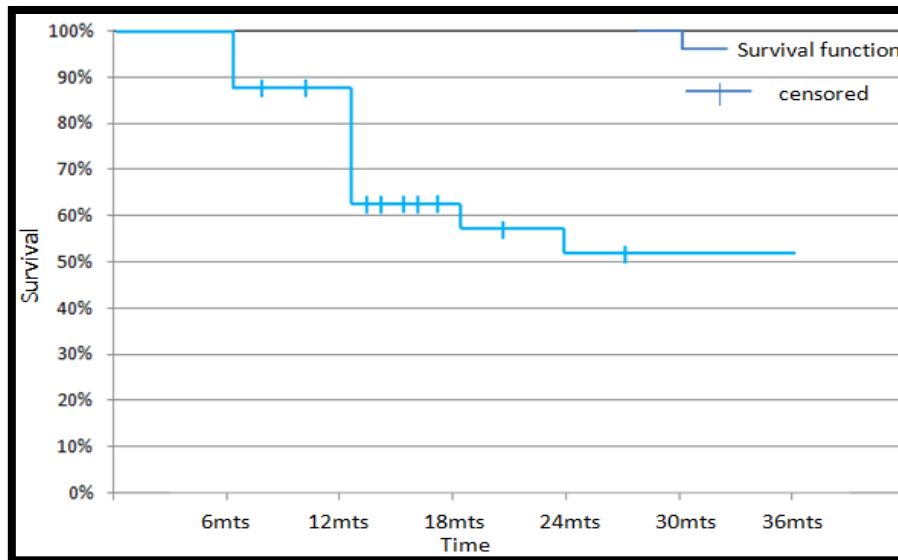
The disease free survival rate was calculated using Kaplan-Meir analysis.(Table 11, Fig 2)

Table 11: Kaplan-Meier Survival Probability Estimates

| Time Period | At Risk | Became unavailable(Censored) | Died/recurrence | Survival Probability Estimate | 0.95 Confidence Interval | |
|-------------|---------|------------------------------|-----------------|-------------------------------|--------------------------|-------------|
| | | | | | Lower Limit | Upper Limit |
| At 6 month | 19 | 0 | 0 | 1 | 0.790795 | 1 |
| At 12 month | 19 | 0 | 2 | 0.894737 | 0.654618 | 0.981555 |
| At 18 month | 17 | 3 | 2 | 0.789474 | 0.539021 | 0.930293 |
| At 24 month | 12 | 1 | 0 | 0.789474 | 0.539021 | 0.930293 |
| At 30 month | 11 | 1 | 0 | 0.789474 | 0.539021 | 0.930293 |
| At 36 month | 10 | 0 | 0 | 0.789474 | 0.539021 | 0.930293 |

Number of subjects enrolled at beginning of study= 19 Patients

Fig 2.Overall disease free survival



Discussion

A retrospective analysis of the prospectively maintained data of all the cases of squamous cell carcinoma of oral cavity was done in the Department of ENT, Assam medical college, Dibrugarh to analyse the outcomes of squamous cell carcinoma of oral cavity treated surgically. Known risk factors for oral cavity cancer include tobacco consumption and alcohol apart from genetic predisposition and low socioeconomic status[4].Tobacco chewing, smoking and paan chewing are however more commonly seen in Indian population [9]. Our study showed that out of 19 patients included in the study, all the patients had a history of tobacco consumption with 84.21% having a history of consumption of tobacco for long duration, for more than 10 years. Also, 68.42% gave a history of frequent alcohol consumption. Out of the total of 19 patients included in the study, 15(78.94%) were male and 4(21.05%) were females, showing a male predominance. These correlates with the study by Singhania etal where 87% were males and 13% were females [1].

Pathak[10] in their study reported that oral cancer shows a prevalence of 75-89% among males in Asian countries. The male preponderance in the study group suggested the association of common habit of tobacco consumption among males and thus a high incidence of carcinoma of the oral cavity. The age range of the patients included in the study varied from 31 to 70 years with mean age of 51.15 yrs. This suggested that contact with tobacco is an important etiological factor associated with oral cavity carcinoma in terms of prolonged habit of consumption among older individuals. This correlates with the study conducted by Varshney et al[7] who found average age among study group to be 50 yrs. and all patients(50 patients) had a history of use of tobacco in some form. The goal of surgery is complete resection of the tumour with treatment of lymphatics and staging of the disease. The primary tumour should be resected with negative margins[11]. Local regional spread is improved with margins of 0.5cm or greater[11]. Liao et al found 0.7cm to be ideal distance for resection in oral cavity carcinoma[12]. In our study, resection of primary tumour was done with 1-1.5 cm from palpable margins of tumour. In the N0 neck, there are variable factors which are associated with occult metastasis, depth of tumour invasion being the best predictor for regional metastasis[13]. Huang et al described that Elective neck dissection (END), should be done in tumors with a depth of 4 mm from the mucosal surface, with a NPV of 95.5%[13]. Increased risk of occult metastasis and late recurrences are associated in tumors with depth of greater than 4 mm[13]. For floor of the mouth tumors, 33 % occult regional metastasis was seen in tumors with depth of invasion greater than 1.5 mm[14]. Depth has not been extensively studied for buccal carcinomas, tumors of the maxillary alveolar ridge, and hard palate tumors, although occult metastases are rare occurring in 9% of patients, most often associated with T4 tumors[15]. Therefore, END is not indicated with N0 Neck node for early-stage buccal, maxillary alveolar ridge, or hard palate cancers[15]. There are other factors which are associated with metastasis like growth type, mitosis, lympho-vascular invasion, and poor differentiation and infiltrative growth patterns. But no clear consensus exists regarding which risk factors necessitate END[16,17]. However, when the decision is made to proceed with END, the literature supports dissection of at least the supraomohyoid neck, including levels I to III[15]. But the exception to this is cancer of the oral tongue, because of the occasional identification of skip metastases, which are difficult to salvage, extension to remove level IV can be considered[15]. In our study, Neck dissection was performed in all stage 4 disease patients (8 patients;42.10%) and one patient(5.26 %) in stage 3 who had a positive neck node confirmed by USG guided FNAC. Segmental mandibulectomy is indicated if there is bone invasion, tooth loss with low mandibular bone height[18]. When both mandibulotomy and marginal mandibulectomy are performed, the risk of post-irradiation osteoradionecrosis is unacceptably high at 71% and should be avoided [19]. Segmental mandibulectomy with osteocutaneous free-flap reconstruction is preferred instead [19]. In our study, bone resection was done in 6 patients, out of which segmental mandibulectomy in 3 patients, marginal mandibulectomy in 2 patients and hemi-mandibulectomy done in 1 patient. Recurrence was found in 21%(4 cases) of the cases which correlates with the study conducted by Singhanian et al[1] where the recurrence rate was found to be 26%. The majority of patients belonged to stage 4 disease. This can be attributed to the low economic status, lack of public awareness and poor health facilities amongst rural population as most of the patient in this group(stage 4) were from rural background. Out of 19 patients in the study group, 10 patients were alive without disease(52.63%) on follow up, 3 were alive with disease(15.78%), 1 was dead due to disease(5.26%) and 5 cases(26.31%) were lost to follow up.

Limitations

There were some limitations of the study. Firstly, it included patients who were operated surgically; hence the results could not be analyzed with patients who underwent radiotherapy and chemotherapy as a primary modality of treatment. Secondly, five patients (26%) among study group were lost to follow up. This suggested towards improvising the system for proper long term follow up of the patients in our country.

Conclusion

Oral cavity carcinoma is a commonly occurring cancer in India. Most patients present late and respond poorly to treatment. Stage of presentation, tumour size, extension, nodal involvement, histopathology and distant metastasis, are important factors affecting the final outcome of treatment of the patients. Late diagnosis and lost to follow adversely affect overall prognosis. The patients should be encouraged for follow up after treatment. Public awareness regarding the risk factors, proper screening of population, continued education, better health facility in rural areas and training of health care professional are important for early diagnosis and better management of oral cavity carcinoma.

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