

Carcinoma Lower Lip: An Experience from a Regional Cancer Centre of North-East India

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ABSTRACT

Objective: Carcinoma of lip is a common malignant neoplasm of the oral cavity, with the lower lip more commonly involved than the upper lip. The purpose of the present study is to assess the clinicopathological features as a prognostic indicator for carcinoma lower lip.

Materials and method: 79 patients of lower lip carcinoma treated at Dr. B. Borooah Cancer Institute, a Regional Cancer Centre from 2010 to 2015 were considered. Survival analysis was estimated by Kaplan-Meier curves and log-rank test was done to examine the differences. $P < 0.05$ were regarded as statistically significant.

Results: 75.9% patients were males and 24.1% were females. Median age was 60.0 years. All the surgically operated cases were included in the study with squamous cell carcinoma (SCC) in 87.3% and 12.7% of verrucous carcinoma. 24/79 (30.4%) patients had recurrence either at the primary site, regional or distant during the follow up period. The tumor factors like positivity of lymph node (pN) and muscle involvement by the tumor were statistically significant for disease recurrence. A 5 year DFS for early and late pathological tumor stage (pT) were 62.8% and 45% respectively ($p = .205$) and tumor size (60% vs 52.4%). Overall survivals at 5-year follow-up for early and late composite stage were 79.4% and 54.7% respectively.

Conclusion: Muscle invasion and lymph node positivity are the criterion for recurrence of disease. Some biomarkers need to be investigated to assess the therapeutic effect and improve the overall prognosis of the disease.

Keywords: Carcinoma, lower lip, recurrence, survival.

INTRODUCTION

Head and neck cancers (HNC) have an incidence of approximately 14/100,000, accounting for 16% to 40% of all malignancies. Oral cancer ranks among the top three types of cancer in India. [1] Carcinoma of the lip accounts for 12% of all HNC, excluding nonmelanoma skin cancer and approximately one quarter of the oral

cancers. Lower lip is most commonly affected accounting for 95% owing to the location and exposure to sunlight and other risk factors like use of tobacco, areca nut, betel leaves, smoking, viruses, poor oral hygiene and alcohol. [2] The habit of betel nut chewing along with lime smokeless tobacco is customary habit in the north eastern part of India. Males are more

commonly affected in the sixth decade of life. 95% are squamous cell carcinoma (SCC), while basal cell carcinoma (BCC), adenoid cystic carcinoma, adenocarcinoma and muco-epidermoid carcinoma of minor salivary glands are some of the other histological variants. [3] Compared to other malignancies in the HNC sites carcinoma of lip is generally readily curable. Surgery is the mainstay of treatment for lower lip carcinoma for stage I-II; however adjuvant therapy in the form of radiotherapy (RT) and chemotherapy (CT) should be given in stage III-IV. The management involves not only control of the primary tumor by an oncologically adequate margin and reconstruction for a better oral competence, and good quality of life.

The present study aims to assess the clinicopathological tumoral factors as a prognostic factor in regard to disease recurrence and overall survival.

MATERIALS AND METHODS

A total of 209 patients were diagnosed as lip carcinoma out of which only 162 patients were lower lip carcinoma and 96 received treatment at the Institute. 79 patients underwent surgery with or without radiotherapy. This is a retrospective study based on the analysis of 79 medical records of carcinoma lower lip treated at Dr. B. Borooah Cancer Institute, a Regional Cancer Centre of North East India from January 2010 to December 2015.

Inclusion criteria

- a) Cases confined to lower lip without involvement of commissure.
- b) Histologically confirmed cases.
- c) Not treated previously.
- d) Treated with surgery with or without RT with a definitive curative intent.
- e) Complete medical records containing all the clinicopathological, demographic and follow-up information.

Exclusion criteria

- a) Imprecise and incomplete information on clinical and pathological data.

- b) Patients who underwent RT instead of surgery due to medical ailments and poor general condition.

- c) Previously treated patients.

Local recurrence, regional recurrence, or both were all defined as recurrence.

Patients were followed up by hospital revisits, home visits, phone calls, or post cards. The final date of follow-up was October 31, 2017. The study has been approved by the institutional review board.

Statistical Methods

Data was analyzed using IBM SPSS Advanced Statistics version 19.0 (SPSS Inc., Chicago, IL). The relation of overall survival status and recurrence status with clinicopathologic characteristics were analyzed using Chi-square or Fisher's exact test. The Kaplan-Meier method and log-rank test were used for survival analysis. $P < 0.05$ was regarded as statistically significant.

RESULTS

79 histologically confirmed cases of carcinoma lower lip who underwent surgery with or without radiotherapy were included in the study. Out of 79 patients, 60(75.9%) were males and 19(24.1%) were females. The patients' age ranged from 30- 82 years with a median of 60.0 years. 69/79(87.3%) patients had squamous cell carcinoma and 10 patients (12.7%) had verrucous carcinoma. The tumor size ranged from 1 - 8.5 cm and median size is 3 cm. Patients with early stage (I+ II) and late stage (III+ IV) were 59.5% and 40.5% respectively. Out of 79, 10(12.7%) patients had pathologically confirmed lymph node metastasis.

47 patients in stage I and II were treated by surgery alone. However, 32 patients in stage III and IV were treated with surgery followed by post operative radiotherapy.

Overall cases:

Out of 79 patients 18 (22.8 %) died and 61 (77.2%) were alive at the end of follow up. The 5 year overall survival rate was 68.6%. The survival time ranged from 5

to 81 months, with a median survival of 39 months. The relationship between clinicopathological characteristics and overall survival status showed that gender, age, pT stage, pN stage, tumor size and composite stage were not statistically significant ($P>0.05$) except tumors with muscle involvement ($P<0.05$) (Table 1). Kaplan Meier curves and log-rank test showed that the 5 year overall survival (OS) was lower in patients with tumor involving the muscle layer than those without it (37%

vs 79.3%) ($P=0.003$) (Fig 1). The median OS in patients with muscle involvement was 47 months and 95% CI was 32- 62 months. Further, the 5 year overall survival rates were lower among the patients with recurrence than those without (34.7% vs. 89.7%), as determined by the Kaplan Meier curve and log-rank test ($P<0.0001$) (Fig 2). The median OS in patients with recurrence was 44 months and 95% CI was 36-53 months.

Table 1: Analysis of overall and recurrence factors associated with carcinoma lower lip

| Variable | Total cases | Overall status | | P | Recurrence status | | P |
|------------------------|-------------|------------------|-----------------|-------|-----------------------|---------------------------|--------|
| | | Alive [case (%)] | Dead [case (%)] | | Recurrence [case (%)] | Non-recurrence [case (%)] | |
| Gender | | | | | | | |
| Male | 60 | 47(78.3) | 13(21.7) | 0.518 | 17(28.3) | 43(71.7) | 0.429 |
| Female | 19 | 14(73.7) | 5(26.3) | | 7(36.8) | 12(63.2) | |
| Age | | | | | | | |
| Below 60 | 37 | 31(83.7) | 6(16.3) | 0.159 | 11(29.7) | 26(70.3) | 0.608 |
| 60 and above | 42 | 30(71.4) | 12(28.6) | | 13(30.9) | 29(69.1) | |
| Tumour size | | | | | | | |
| less than 3cm | 31 | 25(80.6) | 6(19.4) | 0.211 | 9(29.0) | 22(71.0) | 0.598 |
| 3cm and above | 48 | 36(75.0) | 12(25.0) | | 15(31.2) | 33(69.8) | |
| pT stage | | | | | | | |
| T1+T2 | 49 | 41(83.7) | 8(16.3) | 0.076 | 12(24.5) | 37(74.6) | 0.205 |
| T3+T4 | 30 | 20(66.7) | 10(33.3) | | 12(40.0) | 18(60.0) | |
| pN stage | | | | | | | |
| pN0 | 69 | 56(81.2) | 13(19.8) | 0.215 | 16(23.2) | 53(76.8) | 0.001 |
| pN1+ pN2 | 10 | 5(50.0) | 5(50.0) | | 8(80.0) | 2(20.0) | |
| P stage | | | | | | | |
| Early | 47 | 39(83.0) | 8(17.0) | 0.227 | 10(21.3) | 37(78.7) | 0.066 |
| Advanced | 32 | 22(68.6) | 10(31.4) | | 14(43.8) | 18(56.2) | |
| Muscle | | | | | | | |
| Positive | 19 | 10(52.6) | 9(47.4) | 0.003 | 9(47.4) | 10(52.6) | 0.04 |
| Negative | 60 | 51(85.0) | 9(15.0) | | 15(25.0) | 45(75.0) | |
| Number of Nodes | | | | | | | |
| 0 | 68 | 56(82.4) | 12(17.6) | 0.103 | 15(22.1) | 53(77.9) | 0.0001 |
| 1 | 7 | 2(28.6) | 5(71.4) | | 7(100.0) | 0(0.0) | |
| 2 | 3 | 2(66.7) | 1(33.3) | | 2(66.7) | 1(33.3) | |
| 3 | 1 | 1(100.0) | 0(0.0) | | 0(0.0) | 1(100.0) | |

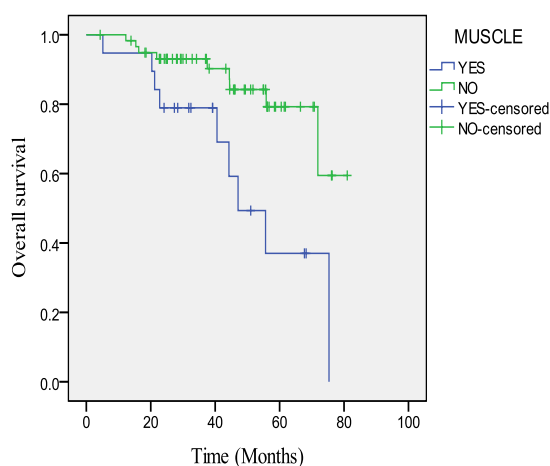


Figure 1: Overall survival of patients with muscle involvement

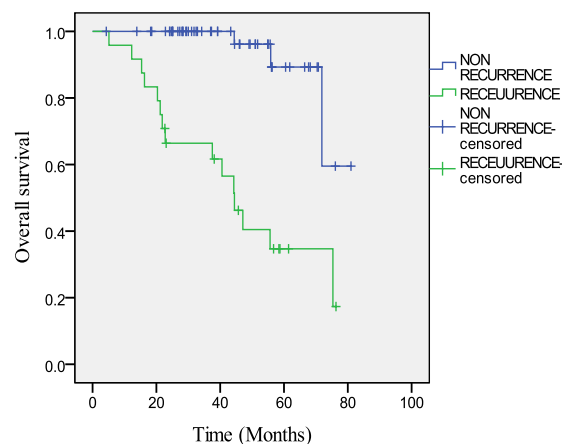


Figure 2: Overall survival of recurrence and non-recurrence patients

Recurrence cases:

Twenty four (30.4%) patients had recurrence. Recurrence time ranged from 3 to 59 months, median recurrence time was 24 month. The tumor recurred in 17 males and 7 females. Disease recurrence was observed in 11 patients at age below 60 years and in 13 patients at 60years of age and above. The relationship between patient’s clinicopathological characteristics and tumor recurrence status showed that pN stage, Muscular involvement and number of nodes were statistically significant with tumor recurrence ($P<0.05$) (Table 1).

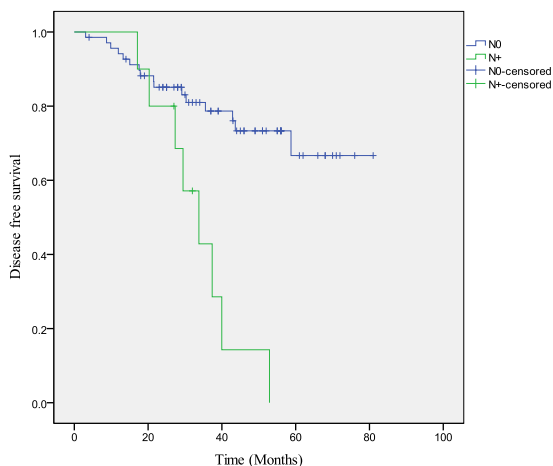


Figure 3: Disease free survival of patients with pN status

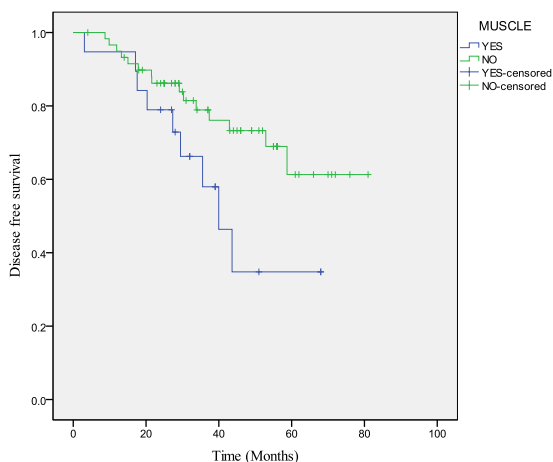


Figure 4: Disease free survival of patients with muscle involvement

Kaplan Meier method and log-rank test showed that the 5 year Disease free survival (DFS) was higher among the patients with pN0 stage (66.7%) than those

with pN+ stage ($P<0.001$) (Fig 3). The median DFS in patients with pN+ stage was 34 months and 95% confidence interval was 23- 44 months. Further, the 5 year DFS was seen lower in the patients with tumor having muscle involvement than those without it (34.85% vs. 61.3%) ($P=0.04$) (Fig 4). The median DFS in patients with muscle involvement was 40 months and 95% confidence interval was 30- 50 months.

DISCUSSION

Carcinoma of the lip accounts for 12% of all HNC, excluding non melanoma skin cancer. [1] Males are more commonly affected than females usually in the sixth decade. The same finding was observed in our study also .SCC is the most common histological variant accounting for 95%. [3] This is observed in our study as well. In the recent years factors influencing the overall survival and recurrence were studied in details. T stage and N stage were important factors affecting regional recurrence in oral SCC as stated by Ebrahimi et al. [4] However, in our study T stage was not found to be associated with recurrence; but N stage was found to be associated with recurrence. Mamelle et al stated that the number of lymph nodes indicates the risk for regional recurrence and distant metastasis and this was observed in our study as well. [5] W. Garavello et al stated that gender does not influence prognosis in patients with oral tongue cancer. [6] This was also observed in our study. Moore et al., stated that patients with tumor diameter less than 2 cm survived a DFS of 3 years was 84% as compared to 52% of patients with a tumor diameter larger than 2 cm. [7] However, in our study it was observed that the 5 year DFS was 60% for tumor with less than 3 cm diameter and 52.4% for tumor larger than 3 cm. Five year DFS was 98% for histologically superficial lesions, 44-63% for deep lesions involving muscles. [8] This was also observed in our study where the 5 year DFS for patients with muscle involvement was found to be 34.8% and 61.3% for non involved tumors. Vázquez-

Mahía et al had analysed 118 patients with oral SCC and reported a recurrence rate of 44.9%.^[9] However, in our study the recurrence rate was 30.4% which is lower; may be due to inclusion of only lower lip cases and good surgical margins.

Surgery is the treatment of choice for carcinoma of lower lip and adjuvant therapy like radiation and chemotherapy in Stage III and IV helps in reducing chances of recurrence. Lower lip cancer has the propensity for cervical lymph node especially in levels I-III. So, surgical resection with good surgical margin and selective neck dissection lowers the recurrence rate and improves the overall survival. For neck positive modified radical neck dissection should be performed. The rate of recurrence was 30.4%, and the 5-year survival rate was 68.6%, which were satisfactory results. Our study reveals that the overall 5 year survival was better in the non-recurrence group of patients than in the recurrence group which is similar to the study done by Bo Wang et al.^[10] In some recent molecular studies it was established that certain genes were reported to be closely related to the recurrence of oral SCC. Certain biomarkers like serum placental growth factor (PIGF) level could be used to assess the therapeutic effect, its recurrence and prognosis of the disease,^[11] p53 mutations, increased level of micro vessel density (MVD) were more likely to develop loco-regional recurrence. Epidermal growth factor receptor (EGFR) over expression is also associated with poor prognosis and radio resistance.^[12]

CONCLUSION

Our study shows that muscle invasion and lymph node positivity are the criteria for recurrence of disease, so it is better to have a radical dissection with good margin and lymph node clearance. Some tumors recur, in spite of offering vigorous treatment protocols. So, some biomarkers need to be investigated to assess the therapeutic effect and improve the prognosis of the disease. There are certain limitations

in our study as the sample size is small and this is a retrospective one where some information may not be adequate. But this is the only study on lower lip from NER.

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