European Archives of Oto-Rhino-Laryngology
https://doi.org/10.1007/s00405-018-5124-z

HEAD & NECK

Outcome of compartment resection of locally advanced oral cancers extending to infratemporal fossa: a tertiary rural hospital experience

S. M. Azeem Mohiyuddin[1] · Pooja Harsha[1] · Shreeharsha Maruvala[1] · K. R. Sumanth[1] · T. N. Suresh[2] · G. N. Manjunath[3] · A. Sagayaraj[1] · Kouser Mohammadi[1] · A. Prashanth Babu[1] · R. P. Deo[1]

Received: 21 July 2018 / Accepted: 8 September 2018

Abstract

Locally advanced oral cancers extending to infratemporal fossa (ITF) are a challenge to head and neck surgeons. These tumors are classified as T_{4b} whenever the masticator space (MS), pterygoid muscles (PM), and pterygoid plates (PP) are involved according to AJCC classification. Until recently, these tumors were considered inoperable and treated only with palliative intent. However, a few studies in the last decade showed that many of these tumors could be resected with a reasonably favorable prognosis by compartment resection of ITF, particularly when the tumor was below sigmoid notch of mandible. A few studies attempted to downstage these tumors by neo-adjuvant chemotherapy before attempting resection. Oral Squamous cell carcinoma has a high prevalence in South India. Majority of these patients are females addicted to tobacco quid chewing and present with locally advanced disease. In this retrospective analysis, we evaluated the outcome of treatment of oral squamous cell carcinoma extending to ITF and staged T_{4b} in 52 patients. All patients underwent Composite resection including compartment resection of ITF followed by adjuvant treatment. 20 patients had received neo-adjuvant chemotherapy. Pectoralis major myocutaneous flap was the mainstay of reconstruction. After mean follow-up of 2 years, 31 patients are alive and disease free. 14 patients had local recurrence in ITF and 2 patients had recurred in cervical nodes. 8 patients died due to disease and 6 are on palliative care. Neo-adjuvant chemotherapy did not benefit the outcome. Close margins of resection, extra nodal spread from lymph nodes and supra notch and involvement of posterior part of ITF were factors which predisposed to recurrence.

Keywords Oral squamous cell carcinoma (OSCC) · Infratemporal fossa · Compartment resection · Masticator space · Pterygoid plates · Sigmoid notch

✉ S. M. Azeem Mohiyuddin
azeem_hn@yahoo.co.in

Pooja Harsha
pooja021390@gmail.com

Shreeharsha Maruvala
harshamims@gmail.com

K. R. Sumanth
mails4sumanth@gmail.com

T. N. Suresh
sureshstn@rediffmail.com

G. N. Manjunath
dr.manjunathgn@gmail.com

A. Sagayaraj
Sagayaraj79@gmail.com

Kouser Mohammadi
zamahmed1999@yahoo.com

A. Prashanth Babu
drprashanthbabu@gmail.com

R. P. Deo
dr.ravideo@gmail.com

[1] Department of ENT and Head and Neck Surgery, Sri Devaraj Urs Medical College, Tamaka, Kolar 563101, India

[2] Department of Pathology, Sri Devaraj Urs Medical College, Tamaka, Kolar 563101, India

[3] Department of Radiotherapy, Sri Devaraj Urs Medical College, Tamaka, Kolar 563101, India

Published online: 17 September 2018

Introduction

Locally advanced oral cancers are a challenge to head and neck surgeons, particularly when they extend into infratemporal fossa (ITF). These tumors are classified as T_{4b} whenever the masticator space (MS), Pterygoid Muscles (PM), and Pterygoid Plates (PP) are involved according to AJCC classification. Until recently, these tumors were considered inoperable and treated only with palliative intent. The main difficulties in resecting these tumors were the difficult access, haemorrhage during surgery and possibility of positive margins in the muscles of mastication. Imaging of ITF can never give a foolproof assessment of the tumor extent. However, a few studies in the last decade showed that many of these tumors could be resected with a reasonably favorable prognosis by compartment resection of ITF, particularly when the tumor was below sigmoid notch of mandible [1–6]. A few studies attempted to downstage these tumors by neo-adjuvant chemotherapy before attempting resection [7]. Oral squamous cell carcinoma has a high prevalence in South India and is the most common malignancy in our region. Majority of these patients are females addicted to tobacco quid chewing and present with locally advanced disease. In this retrospective analysis, we evaluated the outcome of treatment in 52 patients with oral squamous cell carcinoma extending to ITF and staged T_{4b} who underwent composite resection including compartment resection of ITF followed by adjuvant radiotherapy or radiotherapy with chemotherapy.

Aims and objectives

To document the loco regional control and morbidity in patients undergoing compartment resection for locally advanced oral cancer extending to infratemporal fossa.

Materials and methods

This retrospective analysis was performed on 52 patients operated for locally advanced oral squamous cell carcinoma extending to infratemporal fossa and staged T_{4b} according to 2012 AJCC classification (7th edition). The study period was between June 2014 to June 2017, with a mean follow-up of 2 years and minimum follow-up being 1 year. Majority of these patients were females. All these patients had involvement of muscles of mastication and trismus of recent onset and were evaluated clinically as well as by contrast enhanced CT scan (Figs. 1, 2). Recurrent oral cancers, patients with past history of head and neck surgery, and patients in whom disease was extending above the lateral pterygoid muscle on CT scan, or encasing the carotids and patients with N3 neck were excluded from the study. Six patients had tumor involving upper alveolus and retromolar trigone and ITF. They underwent posterior segment mandibulectomy along with upper alveolectomy and compartment resection of ITF and reconstruction using forehead flap. Rest of the 46 patients had tumor involving buccal mucosa, lower alveolus, upper gingivo buccal sulcus, and ITF. They underwent composite resection which included hemimandibulectomy with upper

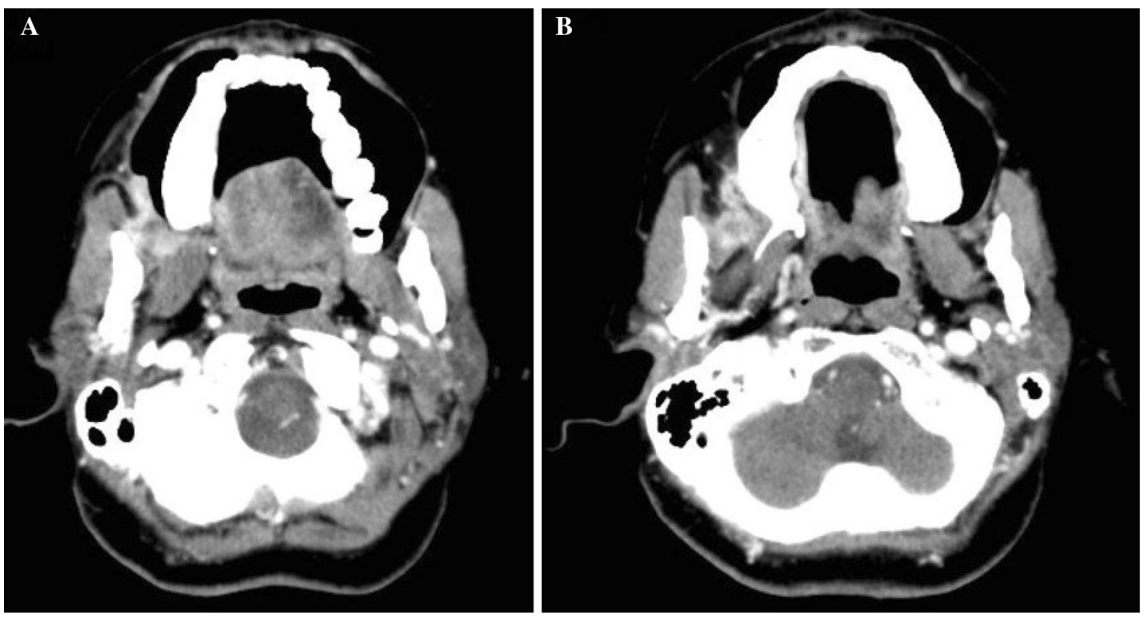

Fig. 1 CT scan axial view showing involvement of pterygoids by the tumor in infratemporal fossa

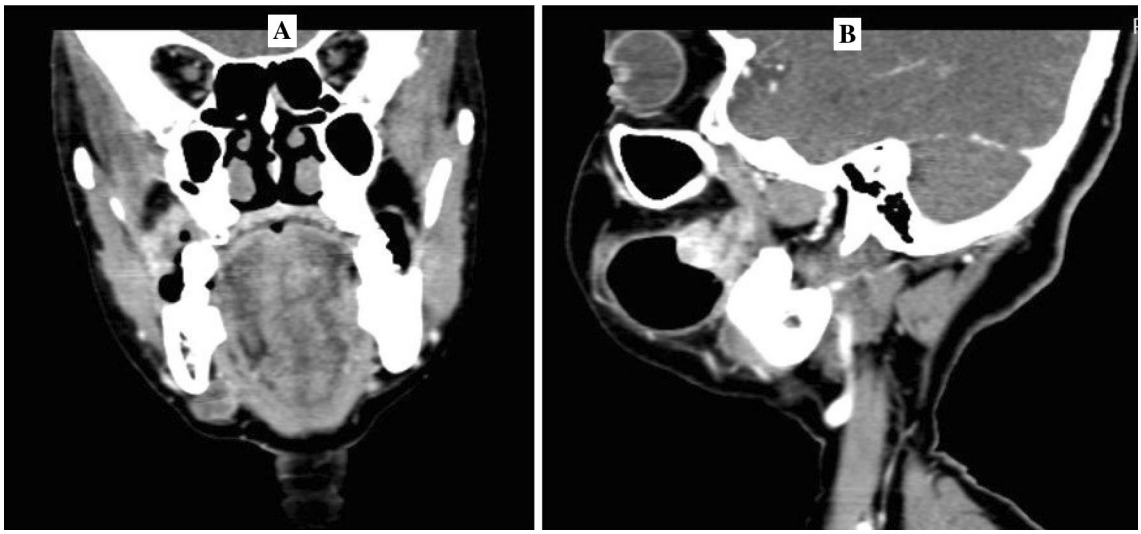

Fig. 2 CT scan showing involvement of pterygoids by the tumor

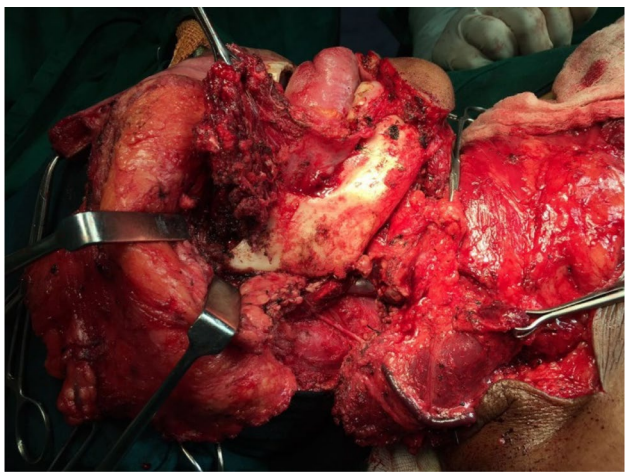

Fig. 3 Compartment resection in progress

alveolectomy and compartment resection of ITF (Fig. 3) followed by reconstruction with pectoralis major myocutaneous flap (42 patients) and anterolateral thigh flap (4 patients). All patients underwent modified radical neck dissection as part of composite resection (Fig. 4). 20 patients who had advanced disease in posterior half of ITF with severe trismus had received neo-adjuvant chemotherapy with 2 cycles of Paclitaxel and Carboplatin. 13 of these patients had partial response documented by clinical examination and CT scan, and 7 patients had no response to neo-adjuvant chemotherapy. Following informed written consent, 52 patients fulfilling the inclusion criteria were subjected to composite resection along with compartment resection of infratemporal fossa, neck dissection and reconstruction. During the surgical procedure, a modified radical neck dissection was first

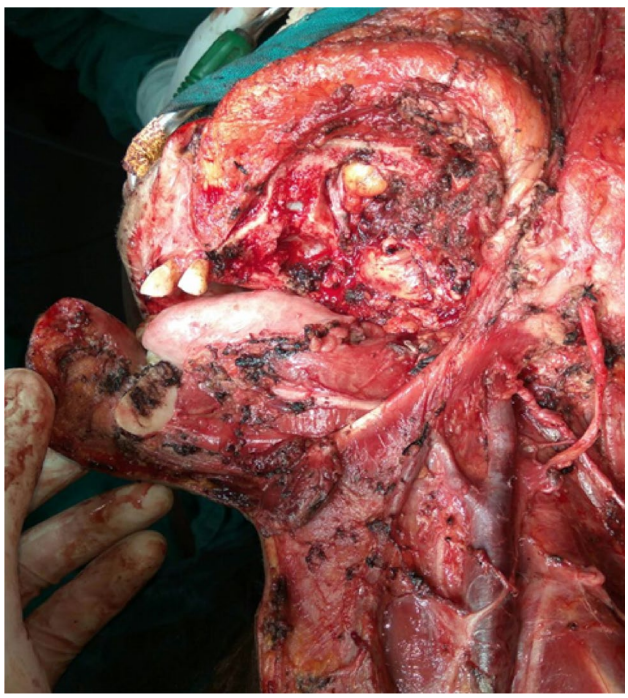

Fig. 4 Composite resection with ITF compartment resection done

performed sacrificing the sternomastoid muscle but sparing the accessory nerve and internal jugular vein, wherever they were macroscopically disease free. A lower cheek flap with a lower lip split was raised keeping a margin of at least 1 cm from the tumor. The buccal mucosa tumor was mobilized. A hemimandibulectomy was done splitting the mandible anterior to mental foramen in 46 patients and a posterior segment mandibulectomy with mandibular split

just anterior to anterior border of masseter in 6 patients who had only upper alveolus and ITF involvement. The masseter was followed superiorly until its attachment to zygoma and completely detached. The medial pterygoid was followed superiorly after cutting floor of mouth muscles and swinging the hemimandible laterally, maintaining adequate margins from the tumor. The temporalis muscle was divided 1.5 cm above the coronoid process of mandible and medial and lateral pterygoids were detached from their attachment at the skull base. Upper alveolectomy was done keeping adequate margins. The pterygoid plates were included in the resection. The inferior alveolar nerve was followed superiorly and cut close to skull base in ITF. In this way, the muscles of mastication (master, medial and lateral pterygoid, and lower part of temporalis) and inferior alveolar nerve were resected en-bloc, in continuity with the mandible and upper alveolus which can be defined as compartment resection of ITF. The extent of resection is shown in Fig. 5a, b.

All patients underwent reconstruction (42 with pectoralis major myocutaneous flap, 6 forehead flap, and 4 anterolateral thigh flap). All patients received post-operative adjuvant therapy (36—radiotherapy, 16—chemotherapy with radiotherapy). The resected specimen was evaluated histopathologically for adequacy of resected margins particularly the muscles of mastication, tumor depth, bone erosion, skin involvement, cervical lymph node metastasis, and perineural spread along inferior alveolar nerve. The patients were followed up and local and regional recurrence, metastasis if any, disease-free survival and morbidity with regard to trismus and swallowing were documented. The patients who received neo-adjuvant chemotherapy were evaluated separately to document outcome of treatment.

Results

In this retrospective analysis of 52 patients with locally advanced (T_{4b}) oral cancer with involvement of ITF who underwent composite resection which included compartment clearance of ITF, 9 patients were males and 43 were females with a male:female ratio of 1:4.7. Majority of the patients were in the age group of 50–60 years. Out of 20 patients who received 2 cycles of neo-adjuvant chemotherapy, 13 patients had partial response. The average size of the primary tumor was 7 × 5 cm. Histopathological examination of the specimen revealed close margins (< 5 mm after formalin fixation) in the ITF in 21 patients. 12 of these patients had received neo-adjuvant chemotherapy with 5 having shown no response. 31 patients were found to have clear margins of resection. 28 patients were found to have single metastatic lymph node in level Ib only. 24 patients had metastatic nodes in both level Ib and level II with 4 of them having metastatic nodes in lower neck (levels III and IV). Four of these patients were found to have extracapsular spread. The skin was found to be involved in 36 patients. 22 patients had mandibular erosion on CT scan which was confirmed by histopathology. Eight patients were found to have involvement of pterygoid plates on CT scan. Five of these patients

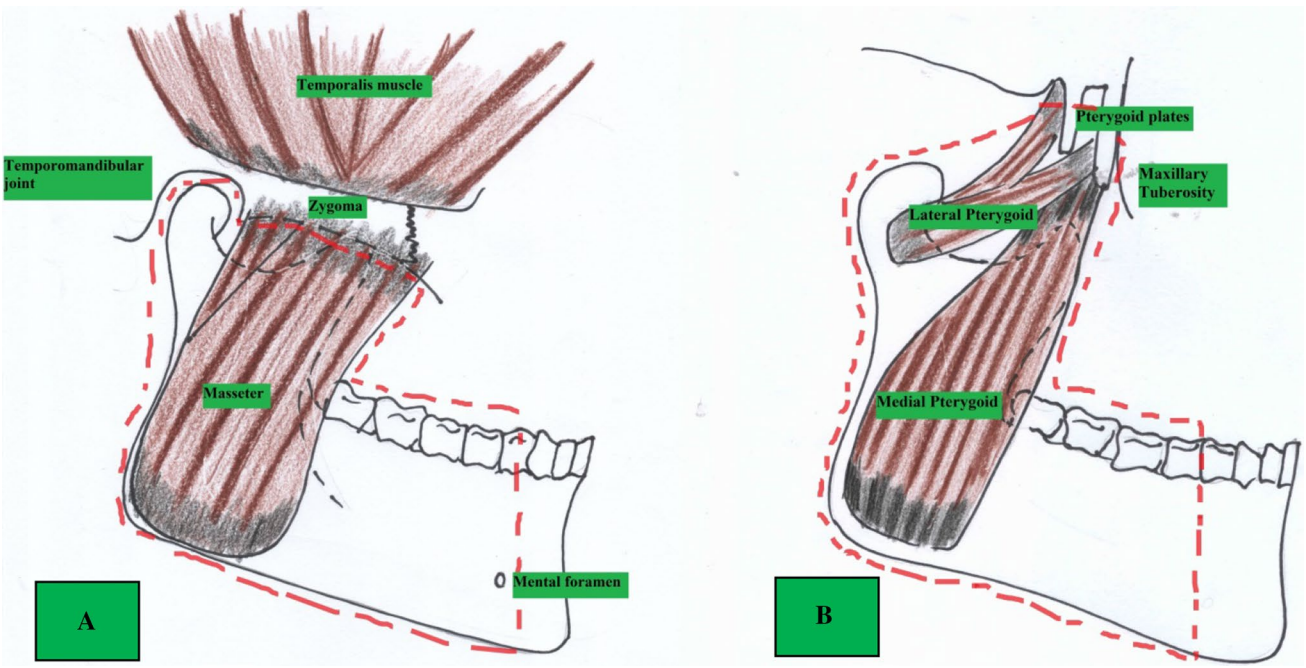

Fig. 5 **a, b** Extent of compartment resection of ITF shown by dotted red line

had involvement of pterygoid plates on histopathology. Perineural invasion along the inferior alveolar nerve was documented in two patients. All patients had tumor involving the muscles of mastication (medial pterygoid and masseter) on histopathology.

12 patients who had grade II trismus were relieved of their trismus postoperatively. However, nine patients who had grade III trismus preoperatively had worsening of the trismus after surgery. Swallowing was significantly better in three patients who had anterolateral thigh free flap reconstruction. However, they had remnants of food in oral cavity after swallowing. In majority of the patients (reconstructed by pectoralis major myocutaneous flap), swallowing was difficult due to stiffness of the cheek and mild restriction in tongue movement. These patients also had minor degrees of dysarthria. Two patients had complete flap necrosis (one anterolateral thigh flap and two bipaddle PMMC flaps) and required secondary reconstruction. 13 patients had orocutaneous fistula adjoining the upper edge of flap which healed without further intervention. Nine of the above patients had delay in adjuvant treatment until the orocutaneous fistula healed.

16 patients had post-operative chemotherapy with radiotherapy as they had close margins (< 5 mm after formalin fixation), multiple metastatic lymph nodes, perineural extension, or extra nodal spread. Rest of the 36 patients underwent post-operative radiotherapy.

After a mean follow-up of 2 years with minimum follow-up of 1 year, 31 patients are disease free. 14 patients had local recurrence in the ITF (Table 1). Three patients had recurrence in lymph nodes in level IIa. one patient died due to pulmonary metastasis 1 year after surgery. Two patients died due to other causes (one stroke and one myocardial Infarction). Two patients were lost to follow up 6 months after completing adjuvant radiotherapy. Among the 14 patients who had local recurrence, eight had received neo-adjuvant chemotherapy and had close margins of resection (Table 2). Two of them had extranodal spread of tumor and perineural extension. The three patients who had lymph node recurrence had multiple lymph nodes at the time of surgery with extra nodal spread at level II (Table 3). Two of them were salvaged by RND followed by CT + RT. 8 out of the 14 patients who had local recurrence died due to disease and 6 are alive with disease.

The recurrence and survival graphs showed about 60% overall survival. Survival among 20 patients who received NACT was 50% compared to 78% among 32 patients who did not receive NACT (Fig. 6). However, it should be noted that only patients with severe trismus and advanced posterior supranotch disease received NACT.

Table 1 Extent of tumor

Tumor	Number	Recurrence	Percentage
Infranotch	40	7	17.5
Supranotch	12	7	60
Anterior half of masticator space	31	6	19
Posterior half of masticator space	21	8	38

Table 2 Outcome of administering neo-adjuvant chemotherapy in locally advanced tumor

Tumor	Number	Recurrence	Percentage
Neo-adjuvant chemotherapy given	20	8	40
No neo-adjuvant chemotherapy	32	6	19

Discussion

Oral squamous cell carcinoma is the most common malignancy in South India and is more prevalent among women. This can be attributed to lack of awareness, illiteracy, and the addiction to tobacco quid among women. 80% of our patients present with locally advanced disease. A significant proportion of our patients present with infratemporal fossa involvement characterized by trismus of recent onset and involvement of muscles of mastication or pterygoid plates on high-resolution CT scan. These patients are staged T_{4b} according to AJCC 7th edition staging. These patients were offered only palliative care as the outcome of treatment used to be very poor due to difficult access to the tumor, difficulty in securing tumor free margins due to involvement of muscles of mastication, and proximity to skull base. However, Liao et al. demonstrated that selected T_{4b} oral cancers had outcome almost similar to T_{4a} cancers particularly when the disease was below sigmoid notch of mandible and anteriorly placed [1, 2]. Similar results were seen in few studies done in India [4, 5]. Our study included 52 patients of oral squamous cell carcinoma staged T_{4b}. However, recurrent tumors, tumors with gross involvement

Table 3 Cervical lymph node metastasis

Metastatic lymph node	Number of patients	Recurrence	Percentage
Single (Level Ib)	28	4	14
Multiple (level I, II)	20	6	30
Multiple with extranodal spread	4	4	100

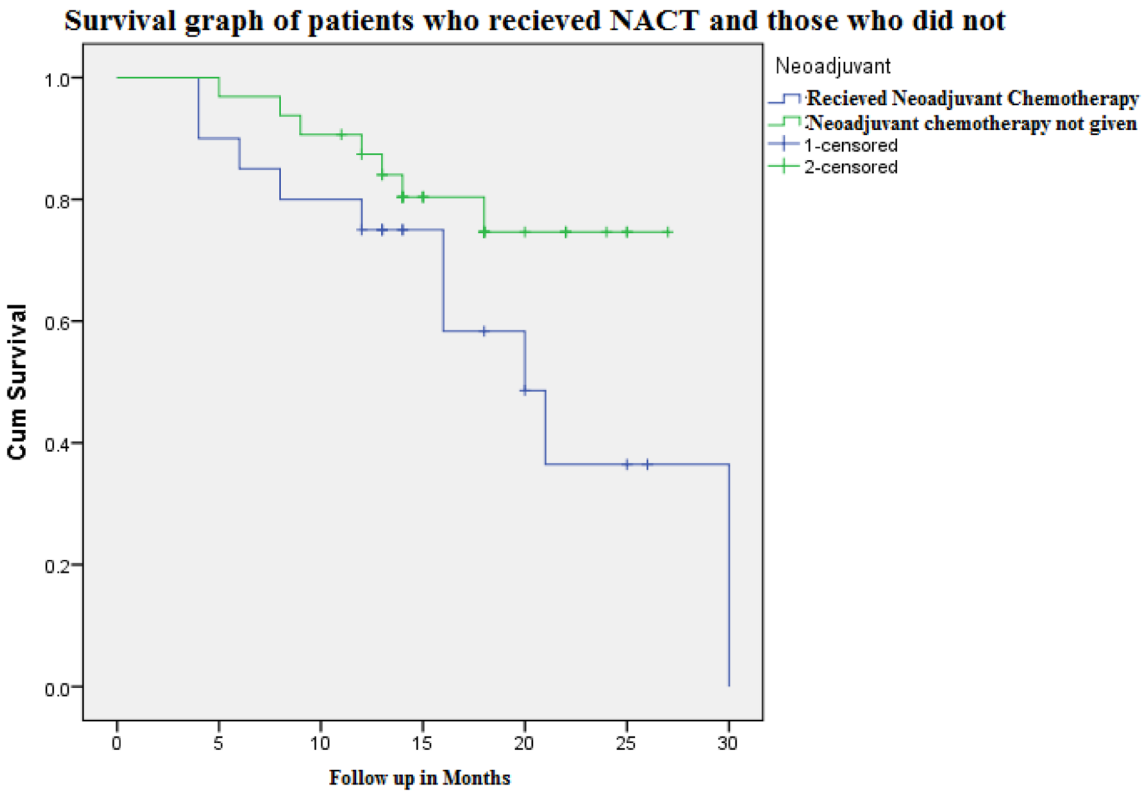

Fig. 6 Kaplan–Meier graph showing survival of patients who received neo-adjuvant chemotherapy and those who did not

of lateral pterygoid on CT scan, and patients with N_3 neck were excluded from the study. Unlike other Indian studies, we included 20 patients with T_{4b} OSCC who had undergone 2 cycles of neo-adjuvant chemotherapy for advanced disease in posterior part of ITF and had severe trismus. Unlike studies done in Taiwan and Japan, majority of our patients were elderly women. This can be attributed to the habit of chewing tobacco quid in this region. Other studies on locally advanced oral cancer in south India also showed that the disease was more prevalent among women [4, 5]. All our patients underwent compartment clearance of ITF along with composite resection of tumor, where the masseter, medial pterygoid and lateral pterygoid, and lower part of temporalis muscle were completely resected. All patients received adjuvant treatment. 21 patients had close margins (< 5 mm) on histopathology and 13 of these patients had undergone neo-adjuvant chemotherapy. This could be due to difficulty in assessing the disease during surgery and on CT scan when muscles of mastication are involved. It is all the more difficult to assess the true extent of disease after neo-adjuvant chemotherapy (diluted margins). 12 of these 21 patients who had close margins had disease involving lateral pterygoid on CT scan and posterior disease. This was similar to observations made by Liao et al and Trivedi et al. 59% of our patients had clear margins of resection (31 out of 52). This was similar to other Indian studies which showed 53–60% local control rates after compartment resection of ITF [5, 6]. It was observed that patients with grade II trismus preoperatively were relieved of trismus following surgery. However, patients who had grade III trismus preoperatively continued to have severe trismus after surgery. This can be explained by the fact that at pterygoid, spasm due to early tumor involvement was relieved after surgery; however, posterior and higher involvement of ITF by the tumor required large pectoralis major flap for reconstruction which aggravated the trismus. Nine of our patients had orocutaneous fistula as the bulky PMMC flap could not hold on high up in infratemporal fossa. This orocutaneous fistula which healed by fibrosis could have contributed to severe trismus in these patients. Similar studies by Trivedi et al. and Liao et al. had lesser incidence of orocutaneous fistula and trismus as they used micro vascular free tissue transfer for reconstruction which was more pliable and lighter. All our patients had metastatic lymph nodes. 54% of our patients had metastasis only in submandibular lymph nodes. 46% of patients had involvement of more than one lymph node with 4 patients (8%) had extracapsular spread. 36 patients (69%) had skin involvement and 22 patients (42%) had bone involvement on histopathology.

Among these 22 patients, 5 had involvement of pterygoid plates. All 5 patients who had involvement of pterygoid plates recurred locally.

After a mean follow-up of 2 years (minimum 1 year), 31 patients (59%) were alive and disease free, as shown in the overall survival graph (Fig. 7). This was similar to the disease-free survival in studies by Liao et al. and Trivedi et al. and Ota, who reported local control rates varying between 53 and 60% after compartmental resection of T_{4b} tumors. In our study, 14 patients (27%) had local recurrence in the ITF within 1 year after resection. 9 of these 14 patients had posterior disease. Eight patients had received NACT, but had close margins of resection. Two of these patients also had extracapsular spread of tumor from lymph nodes. None of the local recurrences could be salvaged as they involved the skull base. Eight of these patients died due to disease and six are on palliative care. In our study, close margins and multiple lymph node involvement were found to have poor outcome. Patients with disease involving posterior half of ramus of mandible and pterygoids had poor outcome compared to patients who had anterior disease. These findings were similar to observations made by other authors who have reported the outcome of ITF clearance [1, 3, 4, 6].

Two of our patients who had extra nodal spread of disease had recurrence in level 2. In our study, neo-adjuvant chemotherapy showed partial response in 13 out of 20 (60%) of patients. However, it did not improve the outcome. 40% of patients who received neo-adjuvant chemotherapy had positive/close margins in the muscles of mastication on resection. These findings were similar to other studies, where neo-adjuvant therapy was used in locally advanced oral cancers. In our study, skin involvement of less than 3 cm diameter did not affect the outcome. This was in contrast to Liao et al. and other Indian studies. However, Liao et al. and Trivedi et al. have not mentioned the extent of skin involvement. In our study, extension of disease into lateral pterygoid (supranotch tumors) had a worse outcome compared to infranotch tumors (7 out of 12 supranotch compared to 7 out of 40 infranotch tumors). Two of our patients died due to other causes within 6 months after surgery and two were lost to follow up. One patient died due to pulmonary metastasis. The high recurrence and poor survival among patients who received NACT in our series can be explained by the fact that only patients with advanced posterior supranotch disease received NACT. Therefore, the survival outcome between patients who received NACT and those who did not receive NACT in our series cannot be compared. Similarly, patients who received adjuvant RT and those who received adjuvant CT + RT in our series cannot be

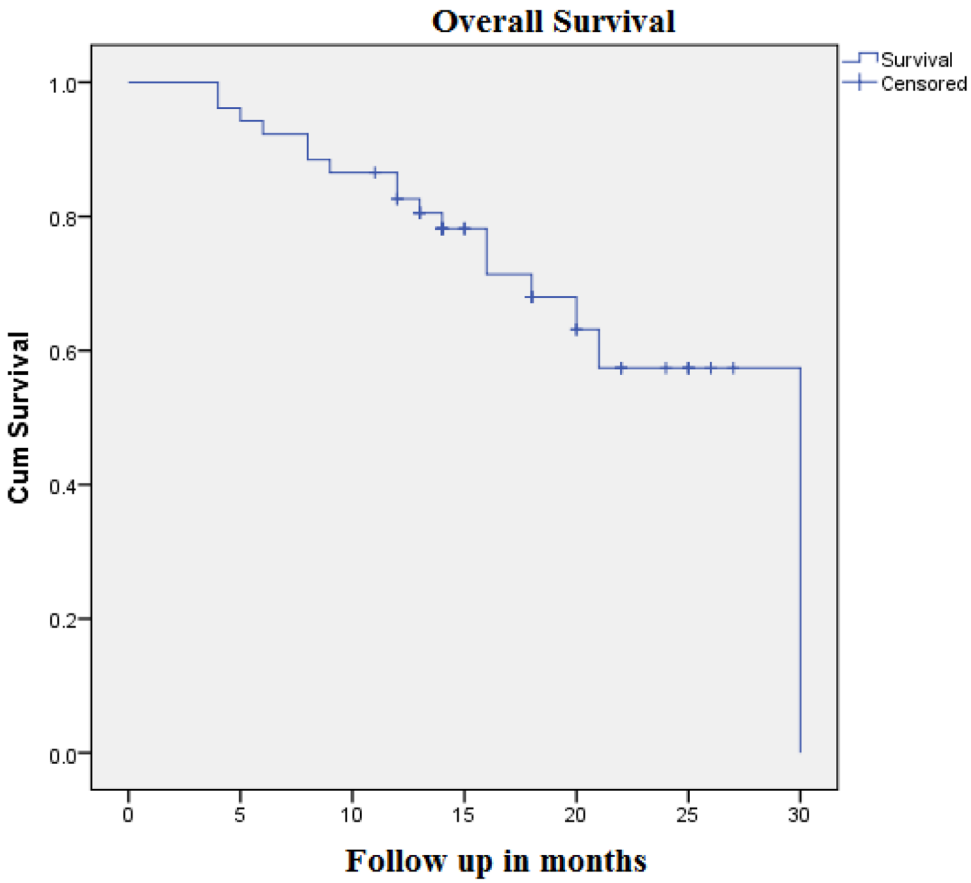

Fig. 7 Kaplan–Meier graph showing overall survival and recurrence

compared as adjuvant CT + RT was given only to patients with close margins, extra nodal spread, multiple metastatic nodes, and perineural invasion.

Conclusion

Locally advanced oral cancers with extension to infratemporal fossa are difficult to resect. However, patients with disease inferior to lateral pterygoid muscle or disease involving anterior half of masticator compartment have a reasonably good outcome with loco regional control in about 60% patients after compartment resection of ITF and aggressive adjuvant treatment. Neo-adjuvant chemotherapy does not add any advantage to the outcome. Reconstruction by microvascular free flaps reduces morbidity and improves function compared to bulky PMMC flap. Close margins of resection in the muscles of mastication, multiple metastatic lymph nodes, and extranodal spread carry poor prognosis. Compartment resection of ITF may be curative in selected patients with T_{4b} oral cancers who were only treated with palliative intent in the past.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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