OUTCOME OF SURGICAL RESECTION IN LOCALLY ADVANCED ORAL MALIGNANCY EXTENDING TO INFRATEMPORAL FOSSA

By

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In partial fulfilment of the requirements for the degree of

MASTER OF SURGERY IN OTORHINOLARYNGOLOGY

Under the guidance of

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DEPARTMENT OF OTORHINOLARYNGOLOGY

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LIST OF ABBREVIATIONS

ABBREVIATION	
BM	Buccal mucosa
RMT	Retromolar trigone
GBS	Gingivobuccal sulcus
AJCC	American Joint Committee against Cancer
OSCC	Oral squamous cell carcinoma
ITF	Infratemporal fossa
Ca	Carcinoma
CIS	Carcinoma in situ
HPV	Human papilloma virus
VEGF	Vascular endothelial growth factor
EGFR	Epidermal growth factor receptor
SCC	Squamous cell carcinoma
CECT	Contrast enhanced computerized tomography scan
MRI	Magnetic resonance imaging scan

USG	Ultrasonography scan
FNAC	Fine needle aspiration cytology
NACT	Neoadjuvant chemotherapy
RT	Radiotherapy
CT	Chemotherapy
HPE	Histopathological examination

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Background:

Head & neck malignancies constitute 30%-35% of all malignancies in India. Oral cancer accounts for 30%-45% of these malignancies. Around 60-80% of these patients present with advanced disease. Majority of these patients present with locally advanced disease : T3 and T4 in this hospital.

A significant proportion of these patients present with extension to retromolar trigone (RMT) and infratemporal fossa (ITF) with associated trismus.

Earlier these patients were only given palliative treatment. However recently, few studies have shown that these patients can be offered surgery followed by adjuvant therapy.

Locally advanced OSCC which does not extend above the sigmoid notch of the mandible have been classified as resectable in the recent past. The functional outcome following these surgeries has been found to be acceptable.

The advances in better understanding of anatomy, better approaches to ITF, better surgical instruments & aids, better reconstructive techniques, etc. have facilitated these surgeries

Objectives:

1> To perform a composite resection in locally advanced oral malignancy extending to infratemporal fossa.

2> To study the adequacy of resection by histopathological examination of resected margins and lymph nodes.

3> To study the locoregional control and morbidity post operatively

Methods:

After having taken an informed written consent and performing investigations for fitness for surgery, a composite resection of the tumor (including neck dissection) with infratemporal fossa clearance and reconstruction of the defect was performed. The resected specimen was evaluated by histopathological examination to look for adequacy of surgical margins in infratemporal fossa and muscles of mastication. Based on the histopathology patients received adjuvant treatment.

Post operatively patients were assessed for locoregional control & functional outcome and the findings were documented at each follow up.

Results:

25 patients were included in the study. All were confirmed as OSCC extending to ITF with the help of histopathology and radiological scans. 18 out of 25 patients had carcinoma of buccal mucosa. All surgical margins were free from tumour. 12 out of 25 patients had near margins (</= 4mm after formalin fixation). 12 patients had T4a tumours and 13 had T4b tumours. After completion of treatment the patients who had presented with grade II trismus had statistically significant improvement in their trismus. Majority of the patients had no problems with mastication and speech after treatment. There was no statistically significant difference in the functional outcome between patients with T4a and T4b tumours. There were 3 cases with local recurrence, all 3 had near surgical margins. 2 out of these 3 died due to disease and 3 other patients died due to other causes.

Conclusion:

Patients presenting with locally advanced OSCC (T4a and T4b) were previously considered inoperable and were offered only palliative treatment. However with better understanding of anatomy and better surgical techniques, patients presenting with locally advanced OSCC extending into ITF upto sigmoid notch of mandible can be treated with surgery followed by adjuvant treatment. This gives better locoregional control with acceptable functional outcome in majority of the patients.

Keywords: locally advanced oral cancer, infratemporal fossa, composite resection

INTRODUCTION

INTRODUCTION

Oral cancer is the sixth most common cancer worldwide. In India head & neck cancer accounts for about 30-40% of all malignancies compared to 2-4% in western countries [1] . Oral cancer accounts for 30- 45% of these malignancies and 60-80% of these are advanced cancers [1.]

In India, buccal mucosa (bm) and lower alveolus complex, quite often extending to retromolar trigone (rmt) are common sites of primary tumour . This is due to the habit of betel nut and tobacco chewing. The use of quid, which comprises of betel leaf (piper betle), areca nut (areca catechu) & slaked lime (calcium hydroxide) predominantly causes malignancy in the gingivobuccal sulcus (gbs)[2].

The usual age of presentation is between the 3rd – 7th decade [3.]

According to American Joint Committee Against Cancer (ajcc) 2002 staging system , advanced / t4 oral cavity squamous cell carcinomas (oscc) are divided into two groups: t4a (resectable) and t4b (unresectable)[4] .

T4a: tumor invades cortical bone, extrinsic muscles of tongue, maxillary sinus or skin of face.

T4b: tumor involves masticator space, pterygoid plates, skull base or encasement of internal carotid artery.

Due to the proximity to vital structures and difficult surgical access to these areas mainly infratemporal fossa (itf), most of the patients presenting with t4b tumors were considered inoperable and were offered only palliative treatment.

Now with a better understanding of anatomy and better surgical access and techniques some studies have shown compartmental resection of infratemporal fossa appears to be feasible which can provide these select patients with better locoregional control.

The functional deficit following the surgery may include trismus, difficulty in mastication, speech or cosmetic deformity.

In this study we aim to assess the surgical outcome of advanced oral cavity squamous cell carcinoma extending to infratemporal fossa in patients who presented to the Department of Otorhinolaryngology and Head and Neck Surgery, R L Jalappa Hospital and Research Centre, Tamaka, Kolar.

AIMS & OBJECTIVES

AIM OF THE STUDY

To study the outcome of surgical resection of oral cavity squamous cell carcinoma extending to infratemporal fossa with regards to adequacy of resection, post operative morbidity and locoregional control.

OBJECTIVES

1.To perform a composite resection on advanced oral cavity cancers (T4a and T4b tumors) extending to infratemporal fossa.

2.To assess the adequacy of resection by histopathological examination.

3.To document post operative morbidity and locoregional control.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY OF CANCER:

The oldest description of human cancer dates back to 3000-1500 BC. Hippocrates (400 BC) named "cancer" as "karldnoma" (Greek for "crab") because a tumour looked like a crab with a central body (tumour) and the legs of the crab (tumour extension).

Roudolf Virchow, the "founder of cellular pathology" provided the pathologic basis for study of cancer. This gave a better understanding of the damage cancer could cause to the patient & laid the foundation for the development of cancer surgery. The excised specimen could be examined & a precise diagnosis made. More importantly, the pathologist could report regarding the completeness of tumour excision.

A famous Scottish surgeon, John Hunter (1728-1793) suggested that if a tumour has not involved surrounding tissues & was "moveable", such tumors could be cured by surgery[5]. He thus laid the foundation of surgical oncology.

Three surgeons made substantial contributions to cancer surgery. Namely ; Billroth from Germany, Hadley from London & Halsted from Baltimore. Their work led to removal of entire tumour along with regional lymph nodes.

Oral cavity cancer surgery was based on Halsted's principles i.e in which the tumour and its lymphatic drainage was removed.

Later it was expanded to remove all this tissue en bloc along with intervening tissue. Marchetta et al showed that even the mandible was to be removed when there was direct tumour involvement. Mandibulectomy was also done for adequate exposure and to get sufficient margins around the tumour.

The term composite resection (previously known as COMMANDO operation) has been credited to Hayes Martin. It is a surgical procedure wherein the primary tumour in oral cavity/ oropharynx is removed in continuity with a segment of mandible along with a neck dissection[6].

Fairbanks – Barbosa was the first to report infratemporal fossa surgery for advanced maxillary sinus tumours.

ETIOLOGY OF CANCER:

Gene mutations:

Gene alterations mainly occur in various mechanisms involving :

- Cytochrome p450 members
- Glutathione – S- transferases
- Alcohol and ethanol dehydrogenase
- DNA damage repair
- Alteration in tumour suppressor genes (silencing, overexpression of proto-oncogenes)
- Nucleotide excision repair enzymes
- Inflammation / angiogenesis
- Apoptosis
- Cell cycle

Molecular pathways altered in head and neck squamous cell carcinoma (Ca):

- Loss of 9p21 → inactivation of p16 gene (most common)

  This is found in dysplasia, carcinoma in situ (CIS) and invasive tumours

- Deletion of 17p13 chromosomal region on p53 along with point mutation → critical step in tumour progression.

  Carcinogens in tobacco and alcohol cause p53 mutations.

  Epigenetic alterations have been brought about by tobacco, alcohol, Human papilloma virus (HPV).

  Viral oncoprotein E6 promotes accelerated degradation of p53. This is seen mainly with HPV 16 & 18.

- Amplification of 11q13 on cyclin D1.
- Mutation of PI3- K signaling pathway.
- Up regulation of HIF- 1a → increases invasive capacity
- Increased expression of vascular endothelial growth factor (VEGF) →increases tumour angiogenesis.
- Down regulation of E- cadherin → diminished cell to cell adhesion.
- Overexpression of Laminin 5 → invasion, increases cell survival and proliferation.
- Up- regulation of epidermal growth factor receptor (EGFR) → leads to dysplasia → carcinoma[7,8].

  Trigger factors:

  - Alcohol
  - Tobacco (in beedis, cigarettes and smokeless tobacco)
  - Betel nut
  - spices
  - Viruses
  - Sharp teeth

- Chronic irritation

Alcohol consumption in combination with smoking greatly increases the risk of oral cancer.

Cigar / pipe smoking, smokeless tobacco also causes cancer of the oral cavity. In India and neighbouring areas beedi's are a popular mode of smoking. Beedi smoking consist of a small amount of tobacco wrapped in Temburni leaf & tied with a string[9].

CARCINOGENS IN CIGARETTE SMOKE:

Polycyclic aromatic hydrocarbons

Heterocyclic compounds

N- nitrosamines

Aromatic amines

Heterocyclic aromatic amines

Aldehydes

Phenolic compounds

Volatile hydrocarbons

Nitrohydrocarbons

Metals [10]

The main carcinogens responsible for oral cavity cancers [11,12]:

Polycyclic aromatic hydrocarbons

4- (methylnitrosoamino) -1- (3-pyridyl) -1- butanone

N' nitrosonornicotine

Tobacco carcinogenesis :

Smoking initiation:

1> Carcinogens bind to receptors, activate Akt & PKA which leads to decreased apoptosis, increase in angiogenesis and transformation → cancer

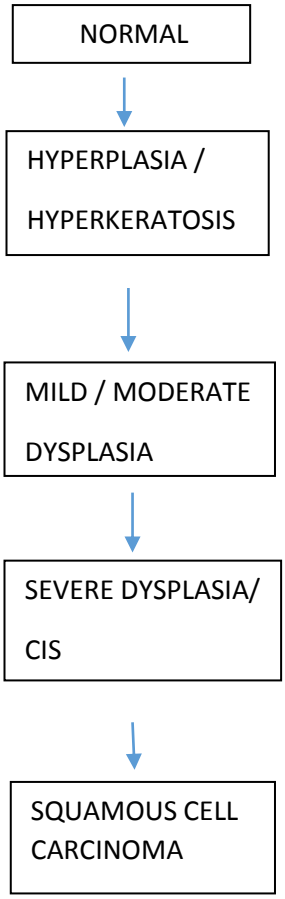
2> Carcinogens cause metabolic activation which leads to mutation in RAS, Tp53 and other genes. These cause a loss of normal growth control → cancer.

3> Tumor suppressor gene inactivation, enhanced carcinogenicity → cancer [13,14].

CARCINOGENESIS:

Development of squamous cell carcinoma (SCC) is a multistep process. It involves activation of oncogenes and inactivation of tumour suppressor genes.

The first change that occurs is loss of chromosomal regions of 3p & 9p21. Hypermethylation causes inactivation of p16 gene. This causes transition from normal to hyperplasia / hyperkeratosis.Subsequent mutation of p53 gene is associated with progress to dysplasia. Invasion is brought about by overexpression of Cyclin D1[15].


NORMAL
HYPERPLASIA / HYPERKERATOSIS
MILD / MODERATE DYSPLASIA
SEVERE DYSPLASIA/ CIS
SQUAMOUS CELL CARCINOMA

ANATOMY OF ORAL CAVITY:

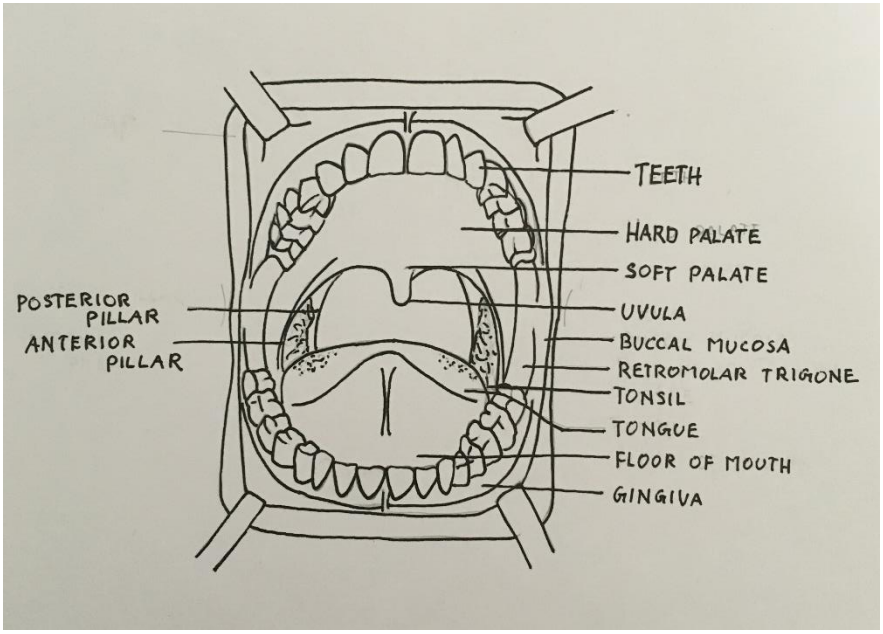


Fig.1 anatomy of oral cavity

Oral cavity extends from the vermilion border of lips anteriorly to the oropharyngeal isthmus posteriorly.

This comprises the circumvallate papillae on the dorsum of the tongue, anterior pillars on either side and superiorly to the junction of hard and soft palate[16].

ANATOMY OF RETROMOLAR TRIGONE:

Triangular area over the ascending ramus of mandible.

Base is behind the lower 3rd molar,

Apex is directed posteriorly behind maxillary tuberosity,

Medially bounded by anterior pillar

& laterally bounded by buccal mucosa.

It borders buccal, masticator & parapharyngeal spaces.

ANATOMY OF INFRATEMPORAL FOSSA :

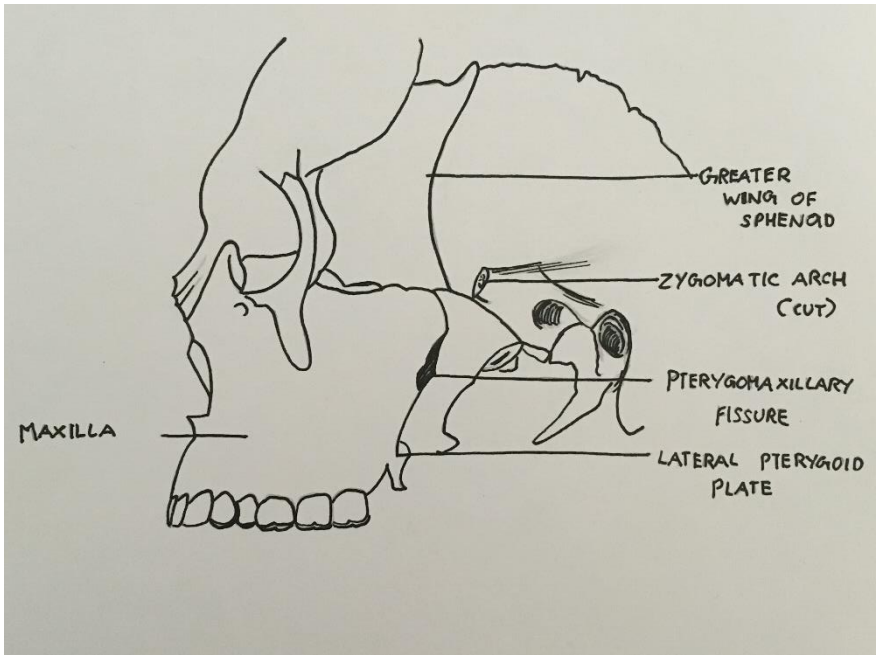


Fig.2 anatomy of infratemporal fossa

Boundaries:

Roof : Greater wing of sphenoid & squamous temporal bone.

Anterior: Posterior wall of maxilla with pterygomaxillary and inferior orbital fissures.

Posterior: Carotid sheath and styloid apparatus.

Medial: Medial pterygoid muscle and interpterygoid fascia.

Lateral : Mandible.

Floor : No anatomical floor.

CONTENTS:

Medial and lateral pterygoids

Maxillary artery and its branches

Pterygoid venous plexus

Maxillary veins

Mandibular nerve[17].

Pterygoid plates:

1> Lateral pterygoid plate:

Part of sphenoid bone.

Broad , thin and everted.

Lateral surface forms medial wall of ITF and gives attachment to lateral pterygoid muscle.

Medial surface forms part of pterygoid fossa and gives attachment to medial pterygoid muscle.

Posterior edge has a sharp spinous process – pterygospinous process.

2> Medial pterygoid plate:

Part of sphenoid bone.

Horseshoe shaped process.

Narrow and long process with a hook-like process i.e the pterygoid Hamulus.

Tensor veli palatini muscle glides around the Hamulus.

Lateral surface of the process is part of pterygoid fossa.

Medial surface forms the lateral boundary of choana.

The pharyngeal aponeurosis is attached to entire length of posterior edge of the plate.

Superior constrictor muscle takes origin from its lower third.

Anteriorly it articulates with the palatine bone[18].

LYMPH NODES IN THE NECK:

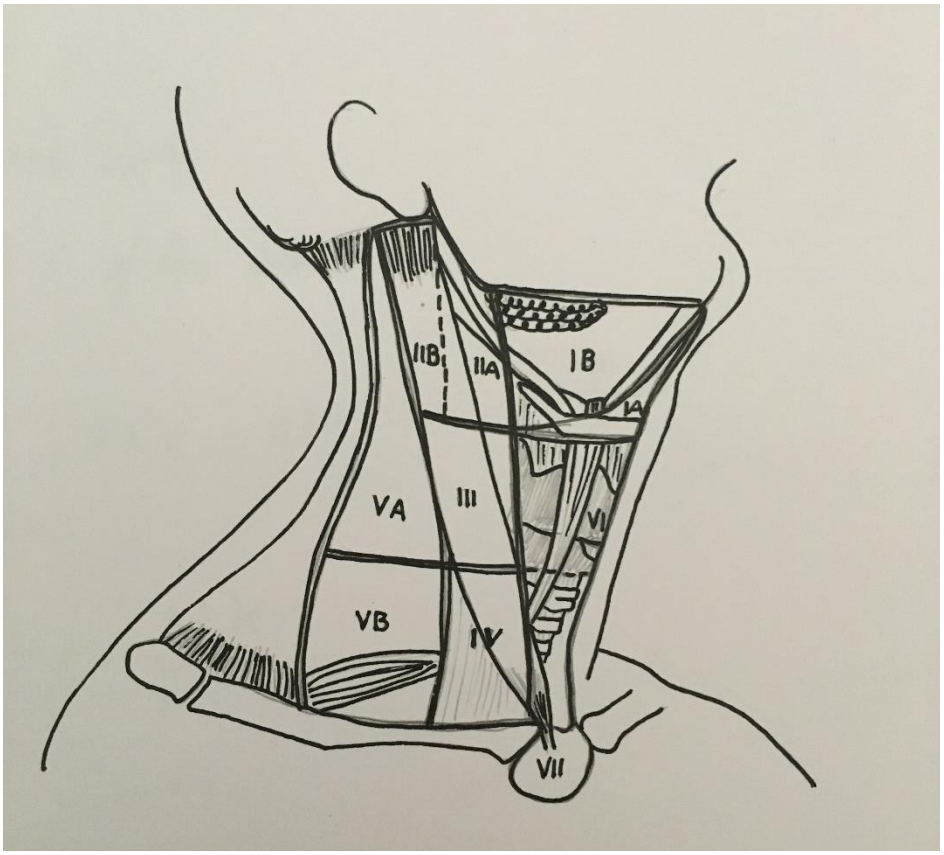


Fig.3 lymph node levels in the neck

LEVEL 1:

Submental and submandibular groups:

The submental lymph nodes (level 1A) refer to the nodes lying within the submental triangle. The submandibular lymph nodes (level 1B) are defined as those contained within the submandibular triangle.

LEVEL 2:

Upper jugular nodes:

The level 2 lymph nodes are located around the upper third of neck, extending from carotid bifurcation (surgical landmark) or hyoid bone (clinical landmark) to the skull base, laterally bounded by posterior border of sternocleidomastoid , medially by lateral border of posterior belly of digastric muscle, anteriorly by posterior border of ramus and angle of mandible and a line joining angle of mandible to greater horn of hyoid.

Level 2 is further divided into two zones by the spinal accessory nerve. Level 2a is located anterioinferior to the nerve and level 2b is located posterosuperior to the nerve.

LEVEL 3:

Mid jugular nodes:

Level 3 nodes are located around middle third of internal jugular vein.

Boundaries:

Superiorly- carotid bifurcation/ hyoid bone

Inferiorly – omohyoid muscle

Laterally- posterior border of sternocleidomastoid

Medially- lateral border of sternohyoid muscle

LEVEL 4:

Lower jugular nodes:

Located around lower third of neck.

Boundaries:

Superiorly- omohyoid muscle/ cricoid cartilage

Inferiorly- clavicle

Laterally- posterior border of sternocleidomastoid muscle

Medially- lateral border of sternohyoid muscle.

It can be further divided into:

4a :lymph nodes located beneath sternal head of sternocleidomastoid

4b: lymph nodes located beneath clavicular head of sternocleidomastoid

Level 5:

Posterior triangle lymph nodes:

Lymph nodes located along lower half of spinal accessory nerve and transverse cervical artery.

Divided into:

5a: lymph nodes located above inferior belly of omohyoid muscle

5b: lymph nodes located below inferior belly of omohyoid muscle.

Level 6 :

anterior compartment lymph nodes

boundaries:

superiorly – hyoid bone

inferiorly – suprasternal notch / innominate artery

laterally- bounded by carotid artery on either side

Level 7:

upper anterior mediastinal lymph nodes[19].

DISTANT METASTASIS:

Risk of distant metastasis is related more to neck stage & location of the involved nodes than primary stage. Risk is <10 % for N0 or N1 disease & increases to 30% for N3 as well as N1 & N2 nodes with disease below the level of thyroid notch. Lung is the most common site of distant metastasis[20,21].

TNM CLASSIFICATION:

PRIMARY TUMOR (T)

T_X Primary tumour cannot be assessed

T0 no evidence of primary tumour

Tis carcinoma in situ

T1 tumour 2cms or less in greatest dimension

T2 tumour more than 2cms but not more tan 4cms in greatest dimension

T3 tumour more than 4cms in greatest dimension

T4a tumour invades adjacent structures (cortical bone, deep extrinsic muscles of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), maxillary sinus, skin of face.

T4b tumour invades masticator space, pterygoid plates, skull base &/or encases internal carotid artery.

REGIONAL LYMPH NODES:

Nx regional lymph nodes could not be assessed

N0 no regional lymph node metastasis

N1 metastasis in single ipsilateral lymph node more than 3 cms but none more than 6cms in greatest dimension

N2a metastasis in single ipsilateral lymph node more than 3cms but not more than 6cms in greatest dimension

N2b metastasis in multiple ipsilateral lymph nodes, none more than 6cms in greatest dimension

N2c metastasis in bilateral or contralateral lymph nodes, none more than 6cms in greatest dimension

N3 metastasis in a lymph node more than 6cms in greatest dimension

DISTANT METASTSASIS:

Mx distant metastasis could not be assessed

M0 no distant metastasis

M1 distant metastasis[22]

STAGE GROUPING:

Stage 0	T0	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IV A	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IV B	Any T	N3	M0
	T4b	Any N	M0
Stage IV C	Any T	Any N	M1

QUALITY OF LIFE:

Various quality of life scales are used to assess functional status in cancer patients. They are:

1> Karnofsky performance scale

2> The University of Washington Quality of Life Scale

3> The Sickness Impact Profile

4> The Head & Neck Cancer Specific Quality of Life Instrument

Karnofsky Perofrmance Scale:

100 - normal; no complaints; no evidence of disease

90 - able to carry on normal activity; minor signs or symptoms of disease

80 - able to carry on normal activity with effort; some signs or symptoms of disease

70 - cares for self; unable to carry on normal activity or do active work

60 - requires occasional assistance but able to care for most of own needs.

50 - requires considerable assistance and frequent medical care

40 - disabled; requires special care and assistance[23] .

NATURAL HISTORY OF SQUAMOUS CELL CARCINOMA:

PATTERNS OF SPREAD

Primary lesion:

SCC can begin as surface lesions or from ducts of minor salivary glands. The early lesions may show erythema, elevated or roughened mucosa.

Spread of the tumour is governed by the local anatomy & therefore varies according to each anatomical site. Muscular invasion is common & the tumour can spread to distant sites along muscle or fascial planes.

In the early stages tumour gets attached to periosteum or perichondrium. Bone & cartilage usually act as barriers to spread of tumour. Therefore, the tumour gets diverted & spreads along pathways of least resistance.

SCC can have perineural spread. This causes a poorer rate of control when managed by surgery & chances of recurrence are increased. The tumour can travel along the nerve to reach the skull base or central nervous system.

Vascular space invasion has an increased risk for regional & distant metastasis[24].

Pathways of spread of tumours of RMT cancers:

- Laterally buccal mucosa
- Inferiorly mandibular alveolus
- Superiorly maxillary alveolus
- Medially floor of mouth / tongue
- Posteromedially to tonsil along pterygomandibular raphe
- Posteriorly to pterygopalatine fossa, masticator space and infratemporal fossa.
- Skull base involvement either through direct spread or via perineural spread[25].

Lymphatic spread:

Lymphatic spread depends on:

> Size of primary lesion

> Tumour differentiation

> vascular space invasion

> density of capillary lymphatics

Patients who have clinically positive large / multiple ipsilateral lymph nodes are at a risk for contralateral disease. Surgery & radiation therapy cause obstruction to lymphatics causing shunting of lymphatic flow to opposite neck[26].

Distant spread:

Stage for stage, the risk of distant metastasis is the same for those treated by surgery alone or radiation therapy alone. The risk for distant metastasis depends more on the location & staging of neck nodes. The lung is the most common site for distant metastasis.

CLINICAL PRESENTATION:

Non healing ulcer in the oral cavity

Pain

Loose teeth

Ill fitting dentures

Inappropriate dental extraction

White patch / leukoplakia in the oral cavity

Paresthesia of lower lip, tongue

Trismus

Referred pain to the ear.

Signs and symptoms which herald infratemporal fossa involvement are:

- Ulcer/ mass in RMT, GBS
- Trismus
- Swelling of face extending upto zygoma
- Hemifacial pain
- Frontoparietal headache
- Paraesthesia / hypoaesthesia of infraorbital area, zygoma, nasal ala and upper lip[27].

DIAGNOSTIC EVALUATION:

General medical evaluation

Thorough head & neck examination

- location of primary tumour

- clinically positive cervical lymph nodes

> Contrast enhanced computerized tomography scan (CECT)/ Magnetic resonance imaging scan (MRI) : skull base to T4

> ultrasonography scan (USG) of neck and abdomen

> Biopsy of tumour

> Fine needle aspiration cytology (FNAC) of lymph node

> Chest X-ray (metastasis, synchronous primary lung tumour)

> Positron emission tomography in selected cases

RADIOLOGICAL EVALUATION:

RMT requires special attention during radiological examination as SCC at this site are usually diagnosed late, prone to bone invasion & have poor prognosis.

The pterygomandibular raphe has been implicated in the spread of SCC from RMT.

55- 73 % RMT carcinomas present with stage III / IV disease.

26 – 56 % have positive nodes at presentation[28].

Imaging of OSCC:

Tumour size

Tumour thickness

Bone invasion

Cervical lymphadenopathy

Extracapsular spread (ECS) in pathological nodes

Perineural spread

Presence of second primary tumours

Distant metastasis

Radiological investigations for imaging infratemporal fossa:

1> CECT :

For gingivobuccal and RMT cancers – “puffed cheek” technique is used.

Best modality for assessing bone erosion i.e pterygoid plates, sigmoid notch / mandible & skull base.

Perineural spread causing widening of foramen ovale can also be appreciated on CECT.

CT performs comparably to MRI for soft tissue assesement.

2> MRI:

Helps to assess soft tissue involvement.

Perineural spread causing thickening of the nerve is better appreciated on MRI. This can be seen as excessive enhancement within foraminae or loss of normal fat density.

GENERAL PRINCIPLES FOR SELECTION OF TREATMENT:

2 forms of curative treatment of head & neck squamous cell carcinoma:

- Surgery
- Radiation

However advanced tumours require multimodality treatment i.e

1> Neoadjuvant chemotherapy (NACT) → surgery → radiotherapy (RT) / chemotherapy (CT) + RT

2> Surgery → RT / CT + RT

T4 SCC's are further divided into:

T4a (resectable) & T4b (unresectable) by AJCC 2002.

AJCC 7th edition has reclassified T4a as moderately advanced local disease and T4b as very advanced local disease.

Studies have shown that not all T4b tumours are unresectable and that some of these patients can be offered surgery as the primary treatment rather than just palliation.

Those tumours involving skull base or with encasement of carotid artery are excluded.

Better reconstruction options in recent times have allowed to reduce the morbidity associated with such radical surgeries.

Advantages of surgery compared to radiation therapy offering similar cure rates:

1> Limited amount of time exposed to treatment

2> Treatment time is shorter

3> Risk of immediate & late radiation sequelae are avoided

4> Irradiation is reserved for subsequent head & neck primary tumour which may not be suitable for surgery

Surgical management of retromolar trigone squamous cell carcinoma:

Retromolar trigone malignancy can spread to :

- Adjacent buccal mucosa, anterior tonsillar pillar, maxilla , early in the disease
- Posteriorly it can spread to pterygomandibular cone & medial pterygoid muscle
- Posterolaterally it can spread into buccinators muscle & fat pad
- First echelon lymphatics: level I & II nodes

  Incidence of clinically positive nodes at presentation is about 30 %.

Selection of treatment modality:

Retromolar trigone:

- Advanced carcinomas → surgery + post operative radiation / chemoradiation.

Surgical management of retromolar trigone :

Tumour should be resected with atleast 1 cm margin all around and atleast one plane away in all dimensions possible. Incidence of positive margins in retromolar tumours is higher than other oral cavity subsites.

Posteriorly located tumours with extension to adjacent sites require a visor flap, lip splitting incision with a mandibulotomy for access.

Extensive tumours require a cervicofacial incision, +/- zygomatic osteotomy or maxillectomy.

There should be a high index of suspicion regarding resection of bone in these tumours. A posterior marginal mandibulectomy, segmental mandibulectomy, hemimandibulectomy (HM) or posterior maxillectomy should be performed depending on the extent of cortical bone involvement[29].

Reconstruction:

Larger tumours require reconstruction to prevent trismus.

The available options are:

Pedicled myocutaneous flaps such as pectoralis major myocutaneous flap (PMMC).

Free flaps: radial forearm free flap, anterolateral thigh flap

Reconstruction of bone : by fibula, scapula, DCIA flap

Neck dissection:

An elective modified radical neck dissection is most commonly performed for any tumour bigger than T1. Levels I- IV is removed[30]. Neck dissection also helps for reconstruction purpose, to make place for a pedicled flap or where access to vessels is required for anastomosis.

Adjuvant treatment:

Almost all patients post operatively require multimodality treatment. Most of these patients are those who present with advanced malignancies.

A study conducted in Memorial Hospital Linkou Medical Center, Taoyuan in Taiwan by Liao C T, Chang J T and Wang HM et al; showed that those patients with T4b OSCC whose tumors were found to be resectable who underwent radical surgery with adjuvant therapy had outcomes similar to patients with T4a OSCC. It was the lymph node status that was a prognostic factor for local control and survival[31].

A similar study conducted in France showed that by performing surgery first for locally advanced oral cavity cancers they were able to achieve negative margins in 96% of the cases & a 5 year local control in > 70% of their cases[32].

However there are some studies which state that neoadjuvant chemotherapy has a beneficial role in locally advanced oral cavity cancers in terms of locoregional control and disease free survival[33].

MATERIALS & METHODS

MATERIALS AND METHODS

This study to evaluate the surgical outcome of locally advanced squamous cell carcinoma of oral cavity extending to infratemporal fossa was undertaken at R.L.Jalappa Hospital attached to Sri Devaraj Urs Medical College, Kolar.

After the confirmation of diagnosis and extent by CECT and biopsy the patients underwent composite resection with neck dissection with compartment clearance of infratemporal fossa. followed by radiotherapy / chemoradiation based on the histopathology.

Post operatively patients were assessed for locoregional control. Their morbidity profile was also assessed with regards to trismus, mastication & speech. The patients were followed up for a minimum period of 6 months.

SOURCE OF DATA

All patients with locally advanced carcinoma of oral cavity with infratemporal fossa extension (diagnosed clinically and with the help of contrast enhanced computed tomography scans) admitted under Otorhinolaryngology and Head and Neck Surgery ward of R L JALAPPA HOSPITAL AND RESEARCH CENTRE attached to SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR between December 2014 – April 2016.

INCLUSION CRITERIA

All patients with biopsy proven locally advanced oral squamous cell carcinoma (stage T4a and T4b) with extension to ITF, not extending above lateral pterygoid muscle on computed

tomography scan and willing to undergo composite resection of tumor with neck dissection and reconstruction followed by radiotherapy/ chemoradiotherapy.

EXCLUSION CRITERIA

1)Patients with grade 4 trismus where assessment of tumor may not be possible.

2)Patients who have received previous radiotherapy or anti-cancer chemotherapy or surgery.

3)Patients found unfit for major surgery.

METHOD OF COLLECTING DATA:

After having taken an informed written consent and performing investigations for fitness for surgery, a composite compartment clearance of ITF with neck dissection and reconstruction of the defect was performed. The resected specimen was evaluated by histopathological examination to look for adequacy of surgical margins in infratemporal fossa and muscles of mastication. The patients also received post-operative radiotherapy/ chemoradiation. The patient was followed up for a minimum period of six months by periodic clinical examination to look for locoregional control (absence of any recurrence at the primary site/ neck), and the morbidity like trismus, difficulty in speech and mastication, external deformity etc. The results were documented on each follow-up and the overall outcome of surgical resection was also documented.

STATISTICAL ANALYSIS:

The data was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test and Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data.

P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

OBSERVATION AND RESULTS

Table 1: Age distribution of subjects in the study

		Number of patients (N)	%
Age	<40 years	5	20.0%
	41 to 50 years	8	32.0%
	51 to 60 years	5	20.0%
	>60 years	7	28.0%
	Total	25	100.0%

Mean age of the patients was 52.76 ± 13.85 years. Majority of patients were in the age group of 41 to 50 years, followed by >60 years.

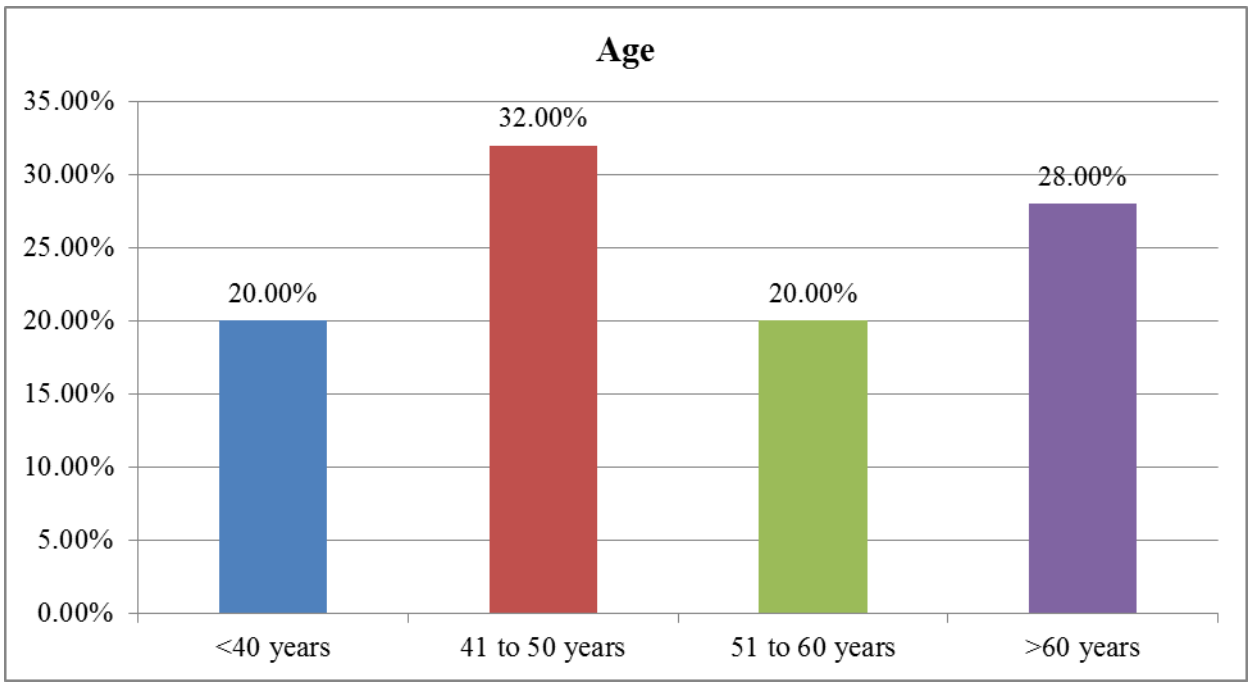


Figure 1: Bar diagram showing Age distribution of patients in the study

Table 2: Sex distribution of patients

		Number of patients	%
Sex	Female	18	72.0%
	Male	7	28.0%
	Total	25	100.0%

72% of the patients were Female and 28% were males.

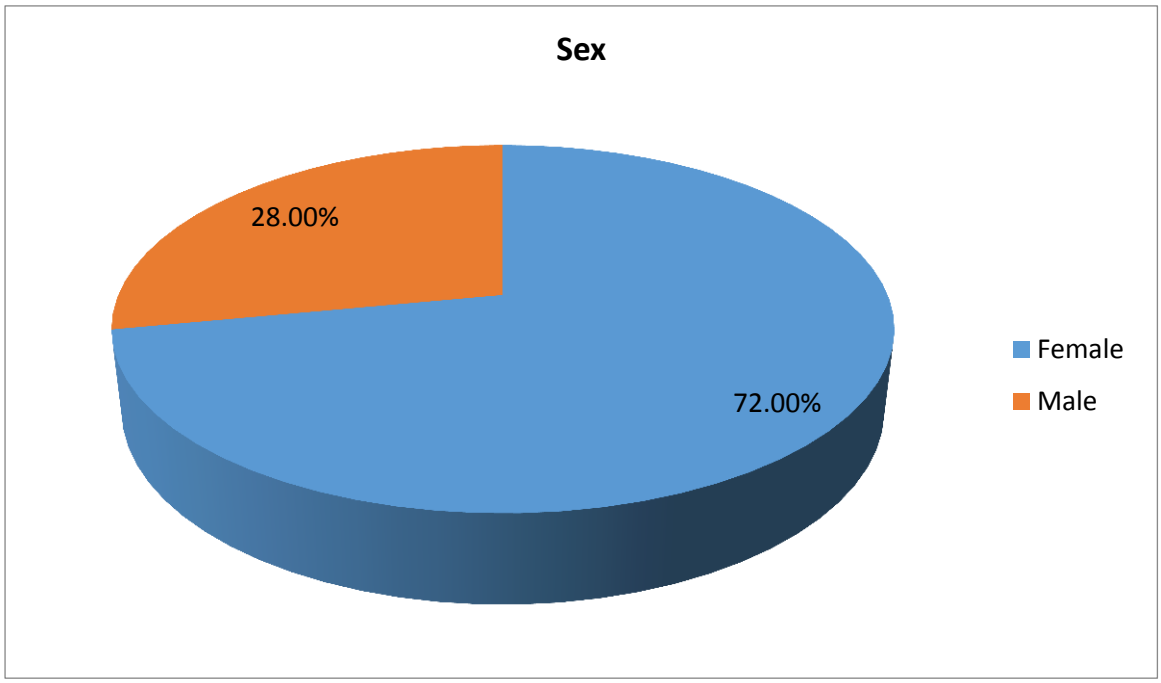


Figure 2: Pie diagram showing Sex distribution of patients

Table 3: Distribution of patients based on site of tumor

		No. of Patients	%
Site	Buccal mucosa	18	72.0%
	Lower alveolus	5	20.0%
	Upper alveolus	1	4.0%
	Retro molar trigone	1	4.0%

72% of lesions were located on buccal mucosa, 20% were located on lower alveolus and 4% were located on upper alveolus and retro molar trigone respectively.

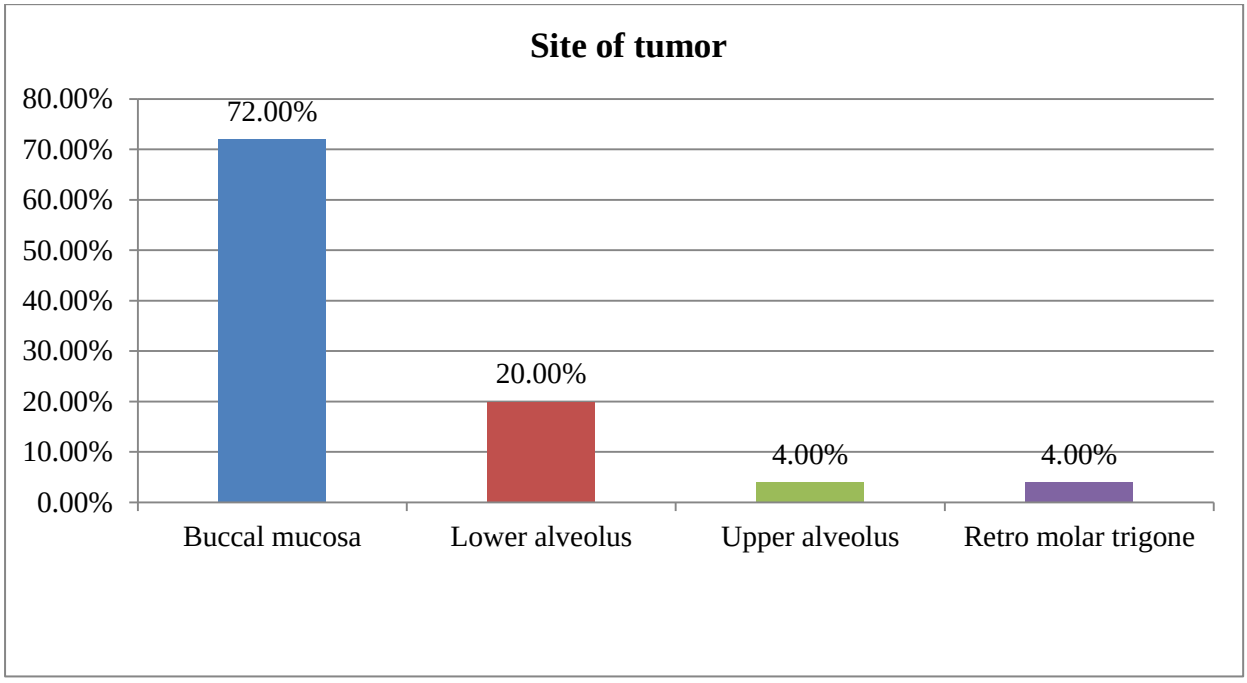


Figure 1: Bar diagram showing Distribution of patients based on site of tumor

Table 4: TNM staging of tumor in the patients

		No of Patients	%
T staging	T4a	12	48.0%
	T4b	13	52.0%

In this study 48% of the patients were in T4a stage, 52% were in stage T4b.

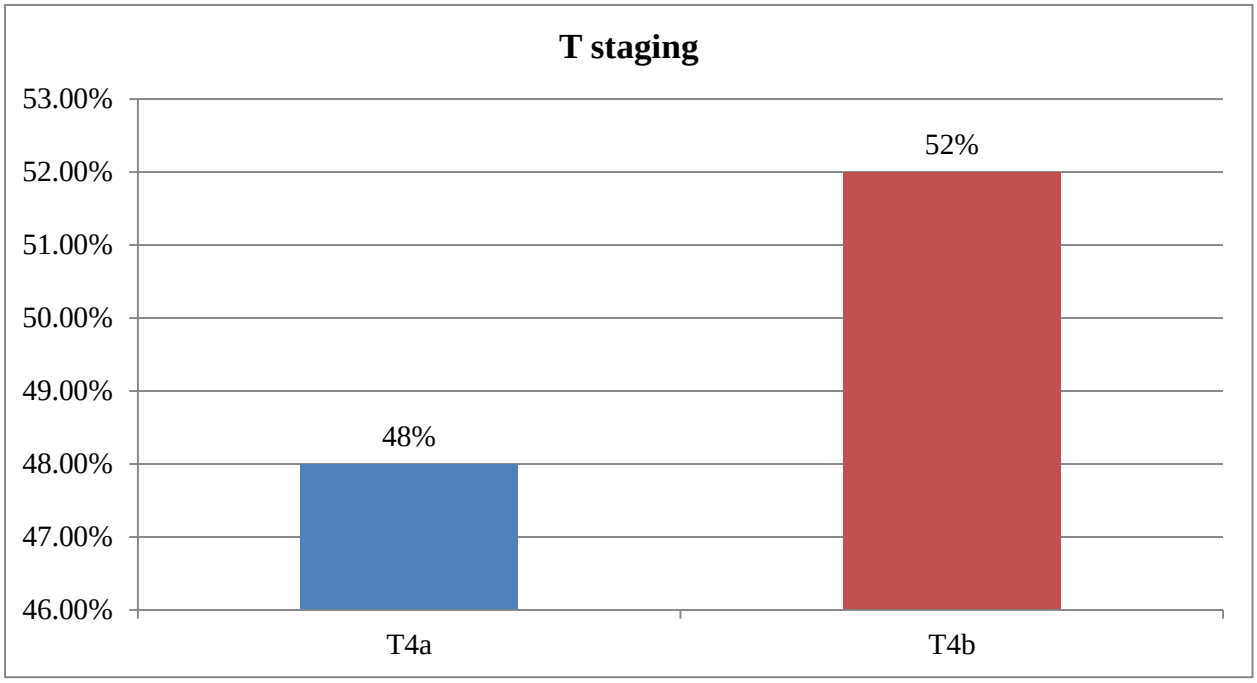


Figure 2: Bar diagram showing T staging of tumor in the patients

Table 5: T & N staging of patients

		N staging									
		N0		N1		N2a		N2b		N2c	
		No of Patients	%	No of Patients	%	No of Patients	%	No of Patients	%	No of Patients	%
T staging	T4a	3	25.0%	4	33.3%	3	25.0%	2	16.7%	0	0.0%
	T4b	1	7.7%	2	15.4%	6	46.2%	3	23.1%	1	7.7%

$\chi 2 = 3.833$, df = 4, p = 0.429

25% of the patients were in T4aN0 stage, 33.3% were in T4aN1 stage, 25% were in T4aN2a stage and 16.7% were in T4aN2b stage.

7.7% of the patients were in T4bN0 stage, 15.4% were in T4bN1 stage, 46.2% were in T4bN2a stage, 23.1% were in T4bN2b stage and 7.7% were in T4bN2c staging.

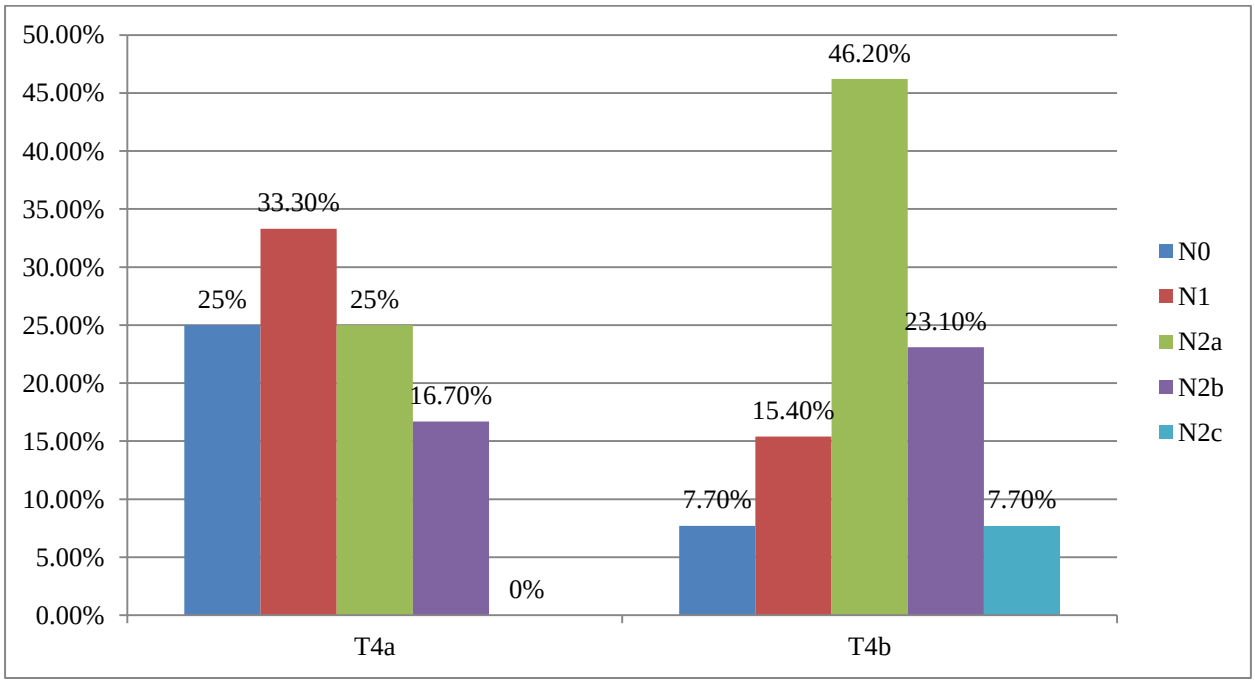


Figure 3: Bar diagram showing T & N staging of patients

Table 6: Preoperative and Post operative grade of Trismus

		Pre Operative		Post Operative	
		No of Patients	%	No of Patients	%
Grading of Trismus	No trismus	1	4.0%	7	28.0%
	I	17	68.0%	7	28.0%
	II	5	20.0%	9	36.0%
	III	2	8.0%	2	8.0%

χ 2 = 36.092, df = 9, p <0.001*

Preoperatively 4% of the patients had no trismus, 68% had Grade I, 20% had Grade II and 8% had Grade III Trismus. In postoperative period, 28% of the patients had no trismus and Grade I respectively, 36% had Grade II and 8% had Grade III Trismus. This improvement in post-operative period was statistically significant.

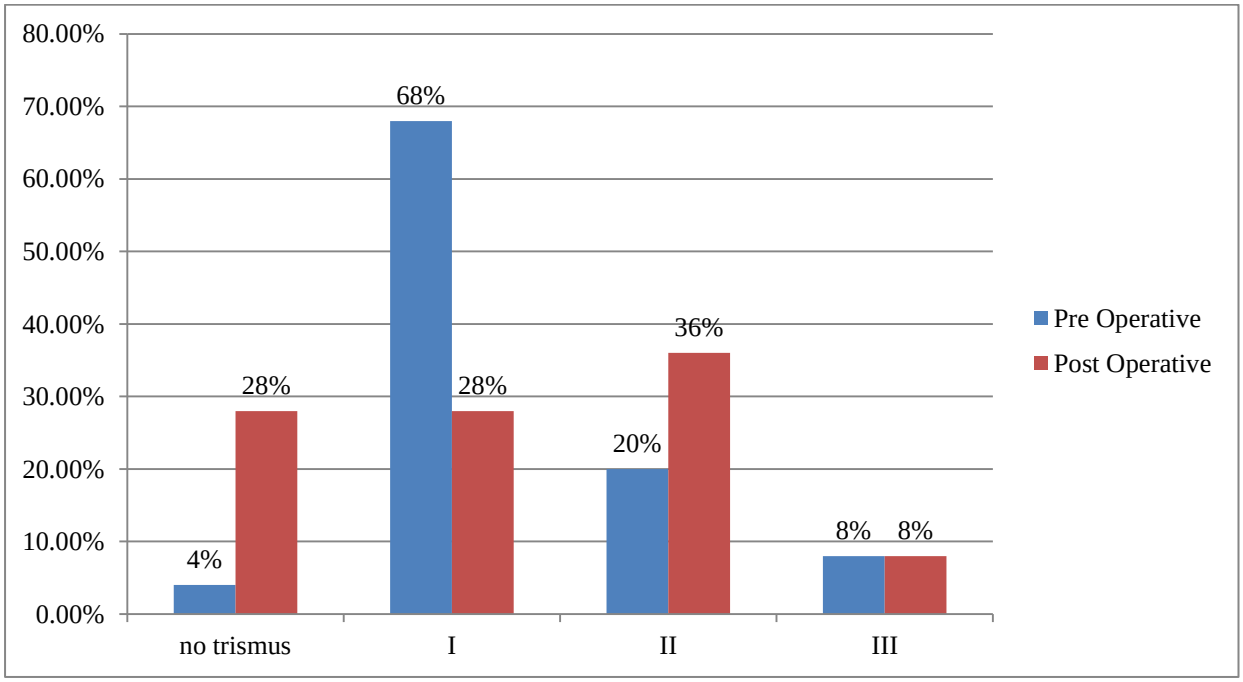


Figure 4: Bar diagram showing Preoperative and Post operative grade of Trismus

Table 7: HPE findings among patients

		No of Patients	%
HPE	Well differentiated SCC	17	68.0%
	Moderately Differentiated SCC	6	24.0%
	Poorly differentiated SCC	1	4.0%
	Verrucous Carcinoma	1	4.0%
	Total	25	100.0%

On HPE, 68% of the patients were found to have well differentiated SCC, 24% were moderately differentiated SCC, 4% were poorly differentiated and Verrucous Ca.

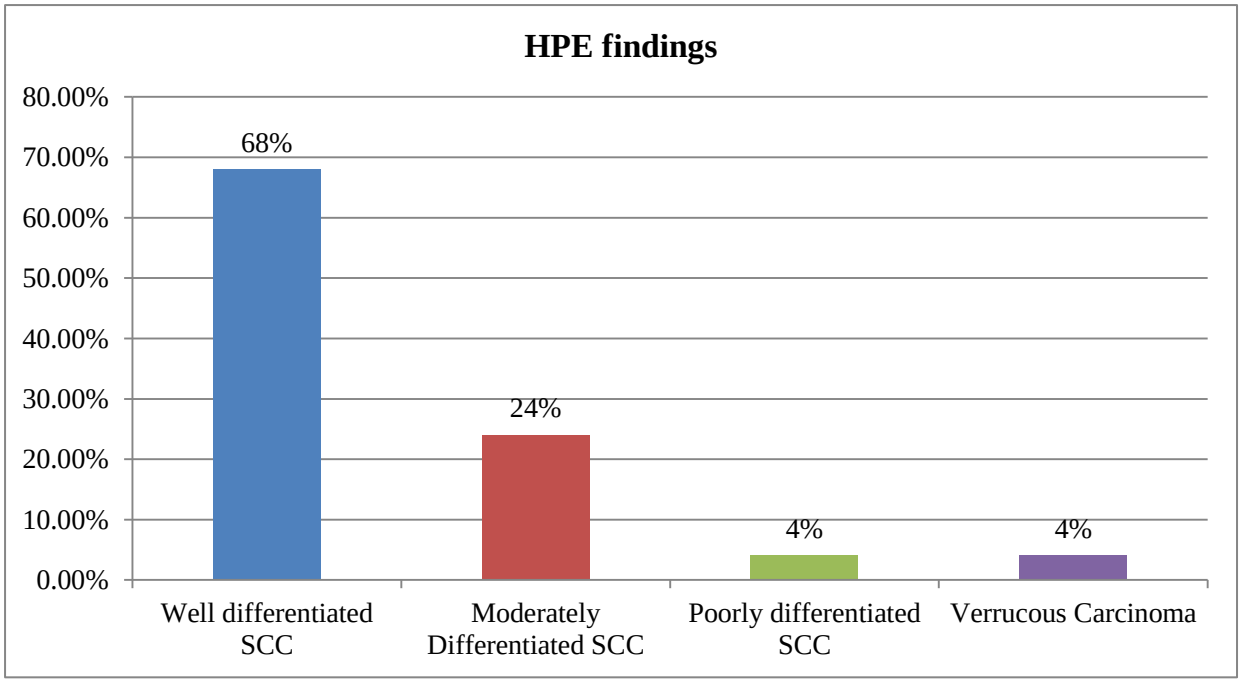


Figure 5: Bar diagram showing HPE findings among the patients

Table 9: surgical margins (after formalin fixation) among patients

		No of Patients	%
Surgical Margins (N=25)	< 4 mm Margin (after formalin fixation)	12	48.0%
	> 4 mm Margin (after formalin fixation)	13	52.0%

Surgical margin is the outermost visible limit of tumour. All 25 patients had negative surgical margins. 48% of them had near margin <4 mm (after formalin fixation) and 52% >4 mm (after formalin fixation)respectively.

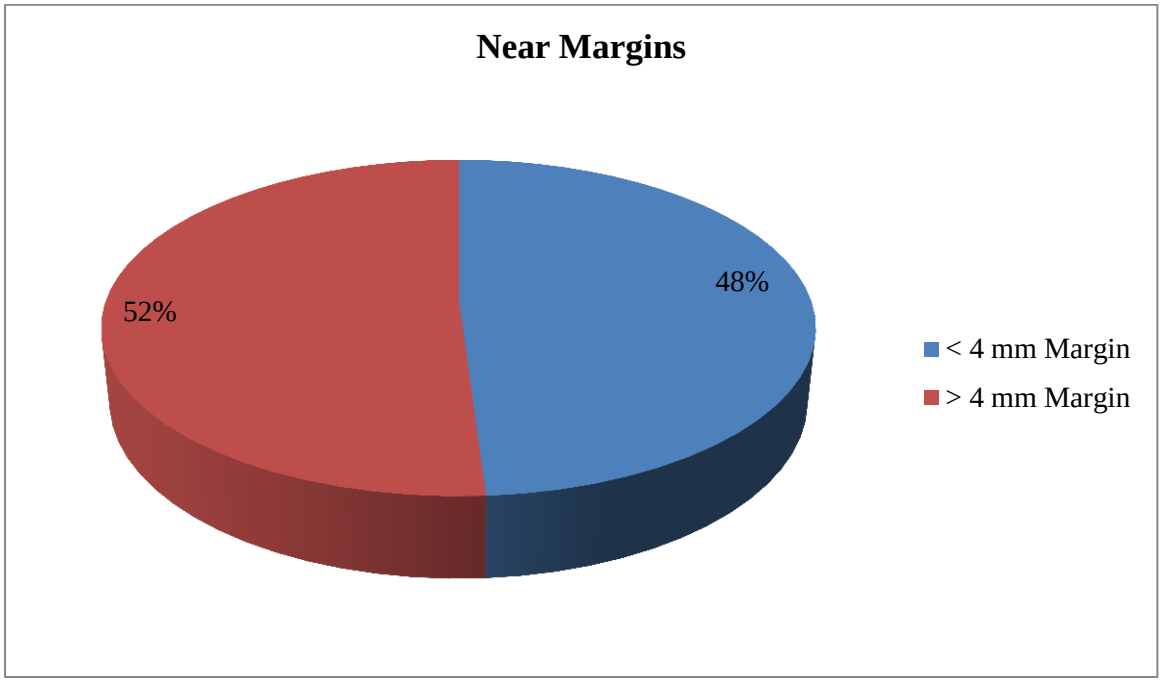


Figure 6: Pie diagram showing Near margins among patients

Table 10: Comparison of Near Margin (< / = 4mm) sites after formalin fixation

		< / = 4 mm Margin	
		No. of patients	%
Margins (after formalin fixation)	Inferior	2	16.67%
	Posterior	3	25.0%
	Superior	7	58.33%

The HPE of patients with near margins < / = 4mm margins were analysed.

In 2 patients inferior margin was < / = 4mm

In 3 patients posterior margin was < / = 4mm

In 7 patients superior margin was < / = 4mm

After formalin fixation

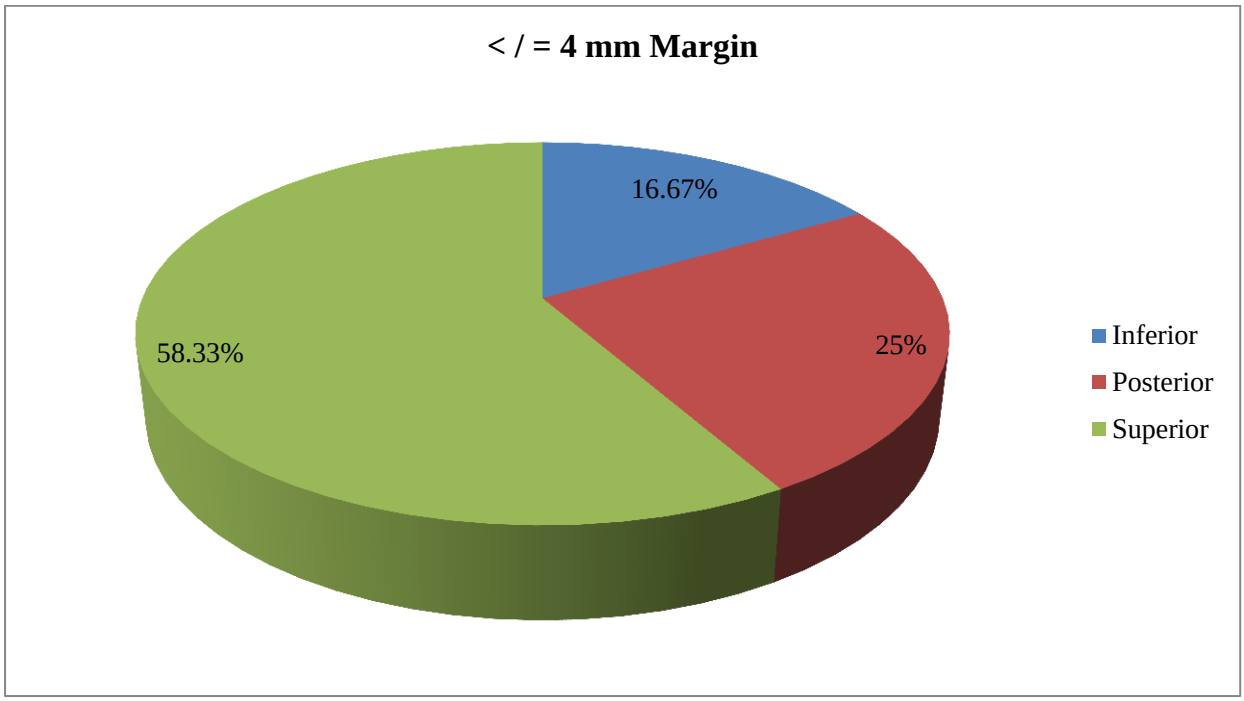


Figure 7: Pie diagram showing Comparison of Near Margin (< / = 4mm)

Table 11: Bone erosion among patients

		No of Patients	%
Bone erosion	Bone erosion Present	5	20.0%
	Bone erosion Absent	20	80.0%

20% of patients showed bone erosion and 80% had no erosion.

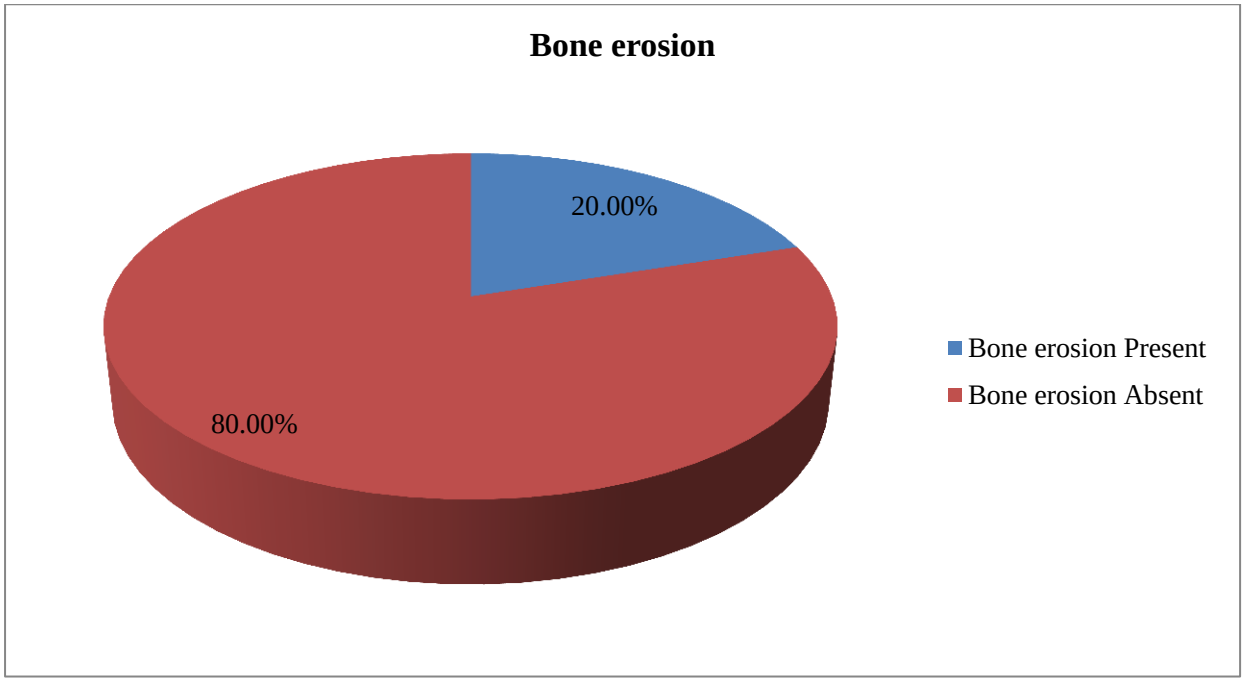


Figure 8: Pie diagram showing Bone or invasion among patients

Table 12: Lympho vascular invasion among patients

		No of Patients	%
Lympho vascular	Lympho vascular invasion Present	1	4.0%
	Lympho vascular invasion Absent	24	96%

In this study 4% of the patients had lympho vascular invasion.

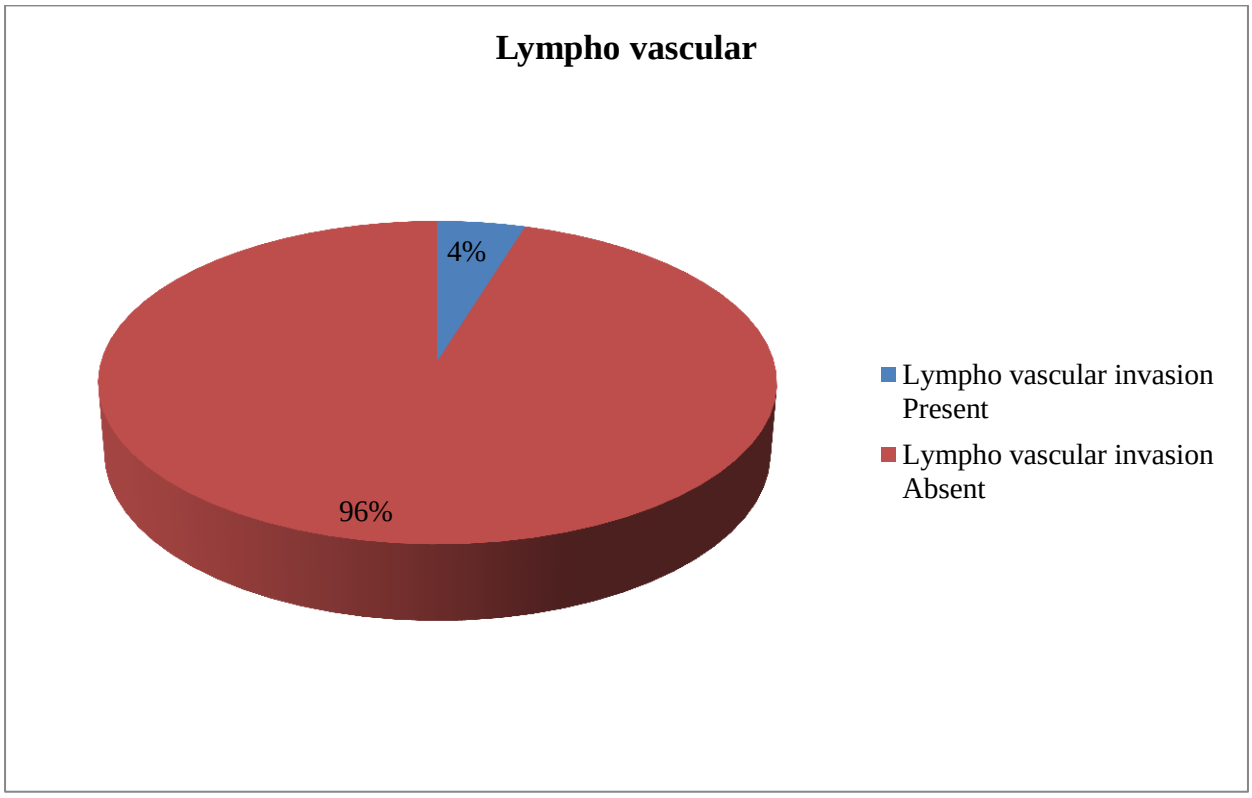


Figure 9: Pie diagram showing Lympho vascular invasion among patients

Table 13: Percentage of Lymphnode positive

		No of Patients	%
Lymphnode status	Negative	19	76.0%
	Positive	6	24.0%

In 76% of the patients no Lymphnodes were involved and in 24% of patients lymphnodes were positive for tumour deposits.

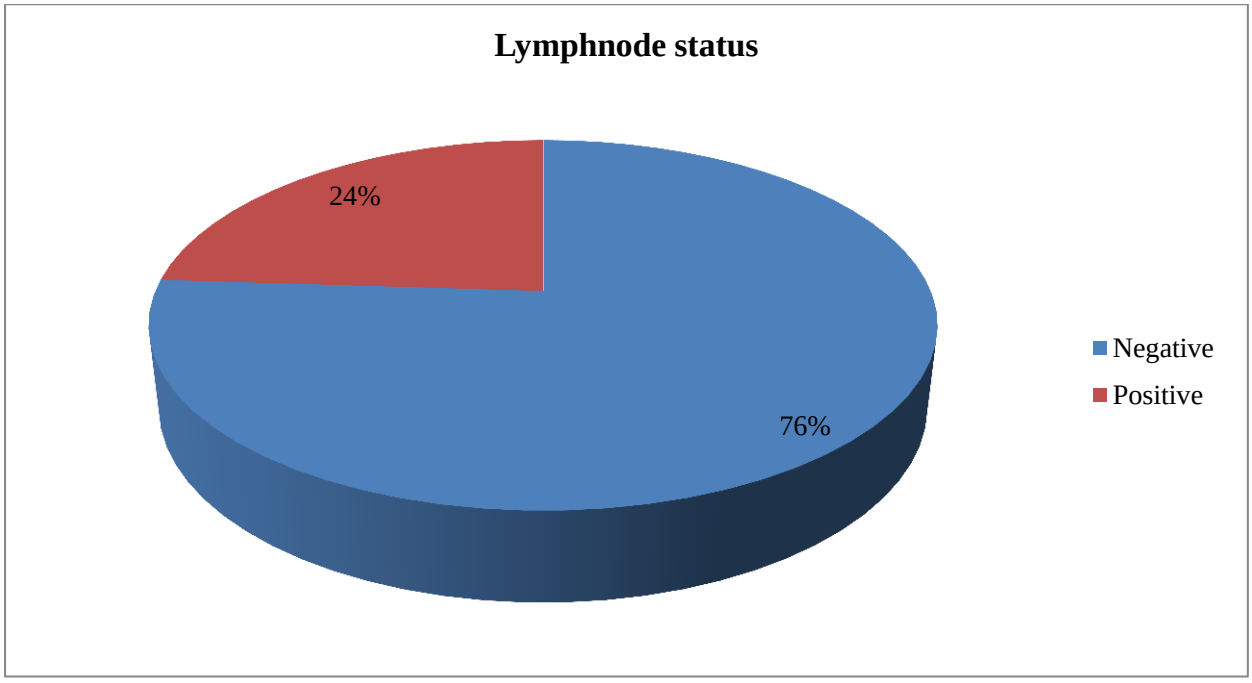


Figure 10: Pie diagram showing Percentage of Lymphnode positive

Table 14: Treatment distribution among patients

		No.of patients	**%**
Treatment	Surgery	1	4.0%
	Surgery + RT	22	88.0%
	Surgery + RT + CT	2	8.0%

Mean fractions of RT given 32.29 ± 7.068 fractions (the dose was 2Gy per fraction)

Majority of the patients underwent Surgery + RT as treatment (88%), 8% underwent Surgery + RT + CT and 4% (1 patient) underwent only surgery.

The patient who received only surgery was a patient with verrucous carcinoma. She underwent composite resection with ITF clearance and reconstruction for the same. On HPE surgical margins were clear with no positive lymph nodes, bone/ lymphovascular invasion. Hence she did not require any adjuvant treatment and was advised only observation and regular follow up.

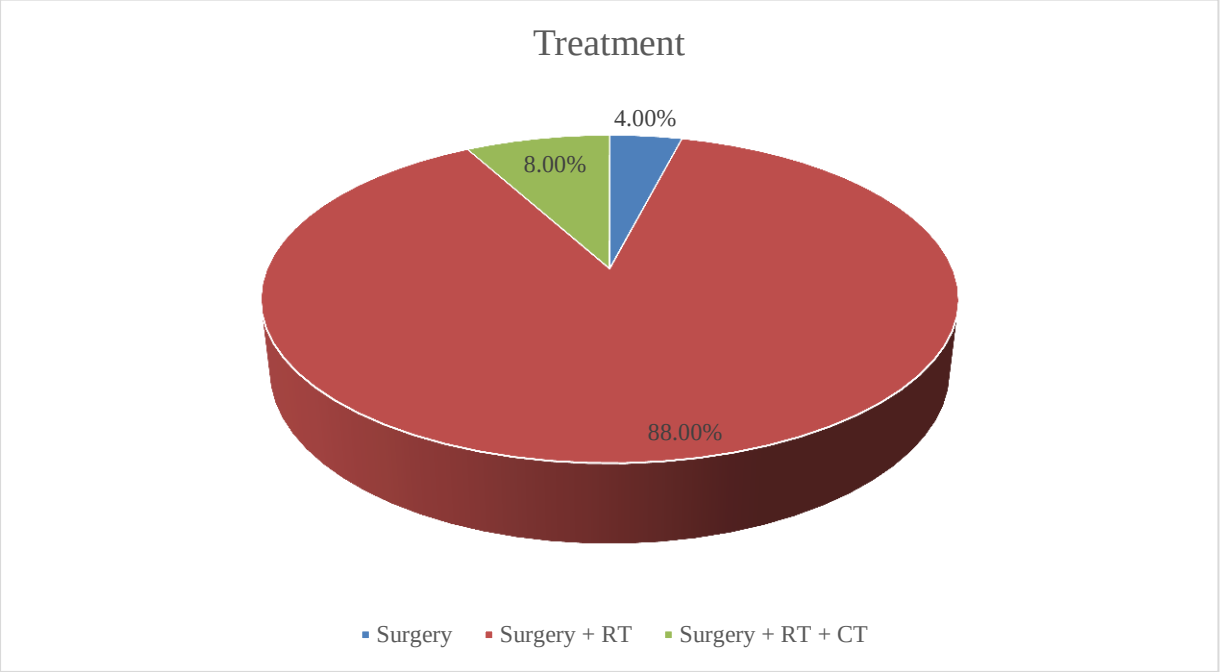


Figure 11: Pie diagram showing Treatment distribution among patients

Table 15: Functional outcome among patients

		No of Patients	%
Mastication	Soft diet	13	52.0%
	Normal diet	12	48.0%
Speech	Can speak and understood well	23	92.0%
	Can speak but not clearly	1	4.0%
	Deaf mute since birth	1	4.0%
Microstomia	Present	2	8%

In this study 52% of the patients were able to take soft diet orally and 48% were able to take normal diet. 92% of the patients could speak well and were understood clearly. Microstomia was seen among 8% of patients.

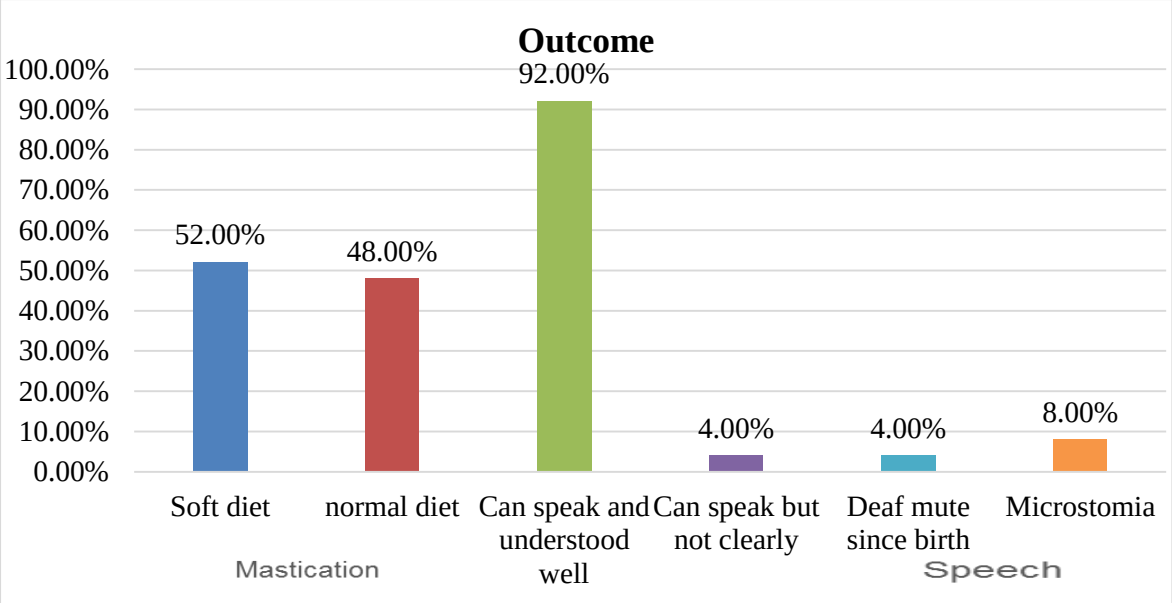


Figure 12: Bar diagram showing functional outcome among patients

Table 16: Complications among patients

		No of Patients	%
Complications	Infection	7	28.0%
	Flap Failure	2	8.0%
	Fistula	1	4.0%
	Osteitis	1	4.0%

28% of the patients had post operative wound infection, majority of these patients had chest wound infection. None of these patients required debridement, they all responded to conservative treatment. 8% (2 patients) had flap failure. 1 patient had necrosis of the distal end deltopectoral flap for which debridement and secondary suturing was done following which there were no further complications. The other patient had limited necrosis of pectoralis major myocutaneous flap at the recipient site for which debridement was done and the wound healed by secondary intention. 4% (1 patient) had orocutaneous fistula 4 months after completion of treatment. The patient was treated conservatively and the wound healed by secondary intention. 4% (1 patient) had Osteitis at the site of partial maxillectomy. She did not require any surgery for the same and responded to conservative treatment.

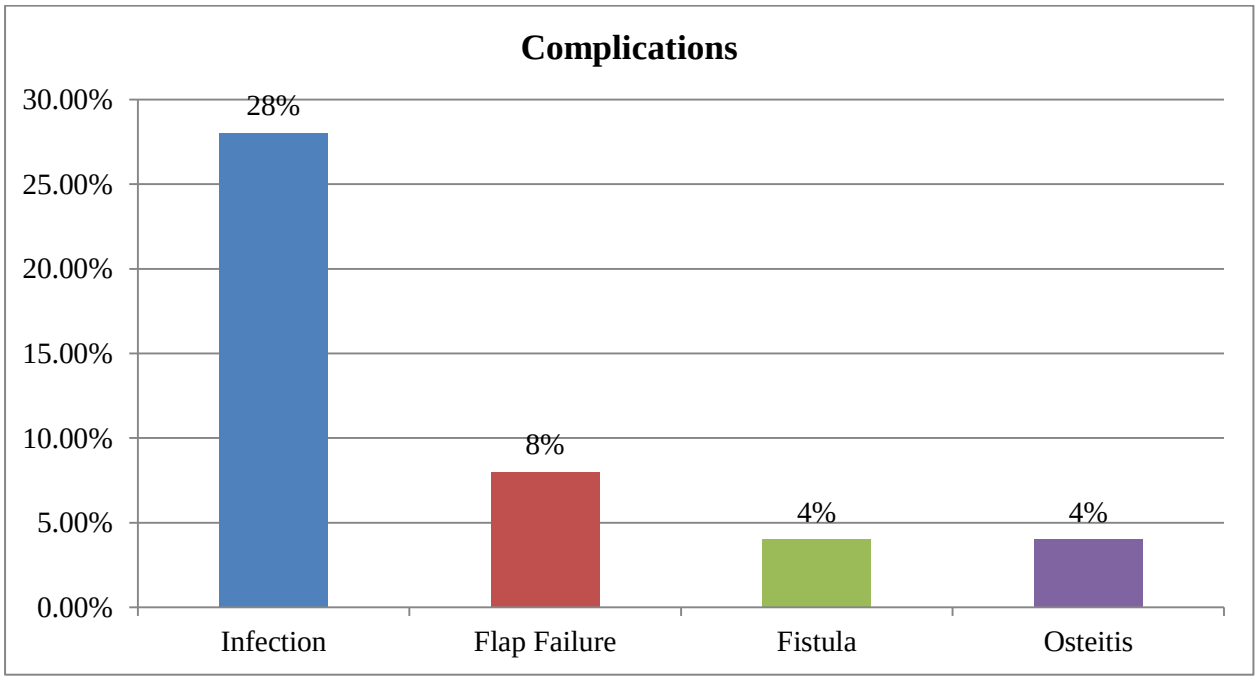


Figure 13: Bar diagram showing Complications among patients

Table 17: Recurrence and Mortality among patients

		No of Patients	%
Recurrence	Recurrence absent	22	88.0%
	Local recurrence present	3	12.0%
Death	Alive and disease free	20	80.0%
	Patients who died due to disease	2	8.0%
	Patients who died due to other cause	3	12.0%

In this study 12% of patients (3 patients) had local recurrence. 2 out of these 3 patients died due to the disease & 3 other patients died due to other cause. The range of follow up period was from 19 months – 6 months with a mean follow up of 12 months.

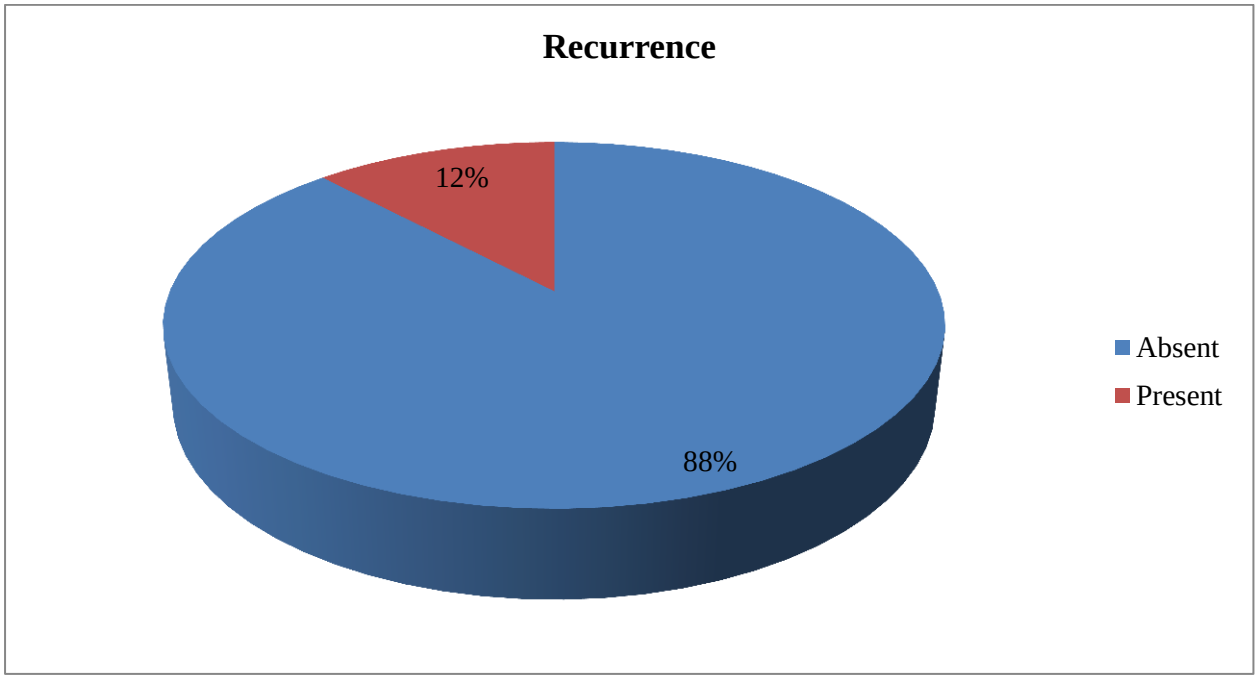


Figure 14: Pie diagram showing Recurrence among patients

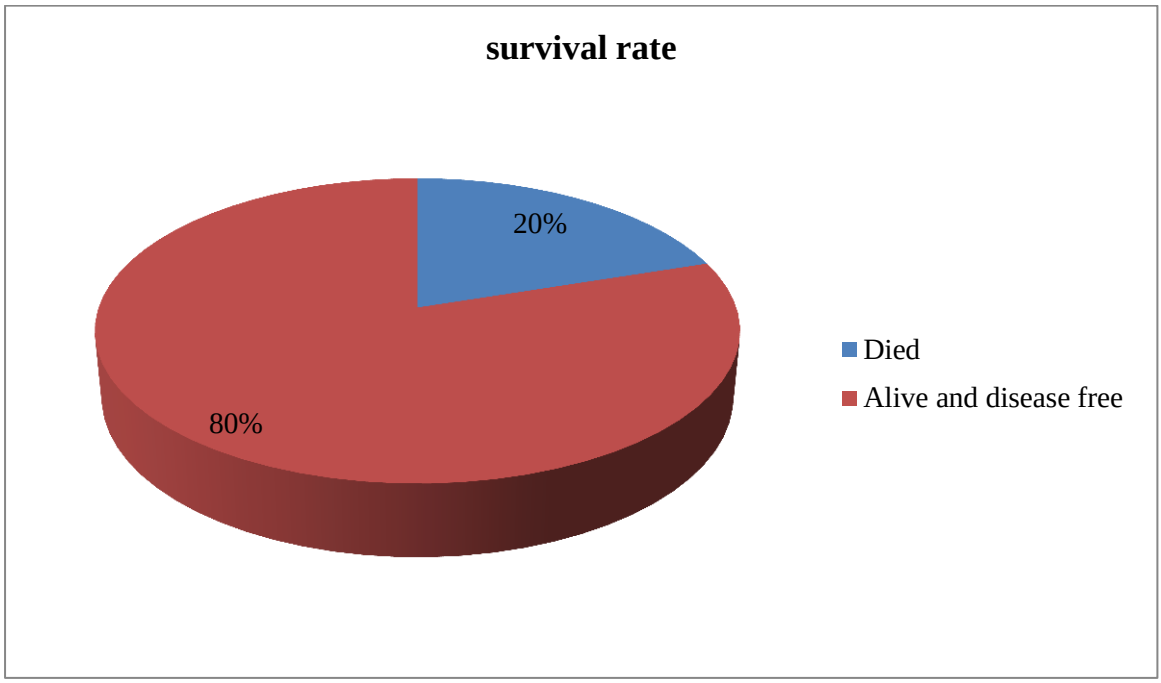


Figure 15: Pie diagram showing bar diagram showing survival rates among patients

Table 18: Comparison of Outcome between Tumor staging

		Tumor staging				P value
		T4a		T4b		
		No of Patients	%	No of Patients	%	
Mastication	Soft duet	4	33.3%	9	69.2%	0.073
	Normal diet	8	66.7%	4	30.8%	
Speech	Can speak and understood well	11	91.7%	12	92.3%	0.367
	Can speak but not clearly	1	8.3%	0	0.0%	
	Deaf mute since birth	0	0.0%	1	7.7%	
Microstomia	Present	0	0.0%	2	15.4%	0.156
	Absent	12	100%	11	84.6%	

There was no significant difference in mastication, speech and Microstomia incidence among patients in both T4a and T4b stage of tumor.

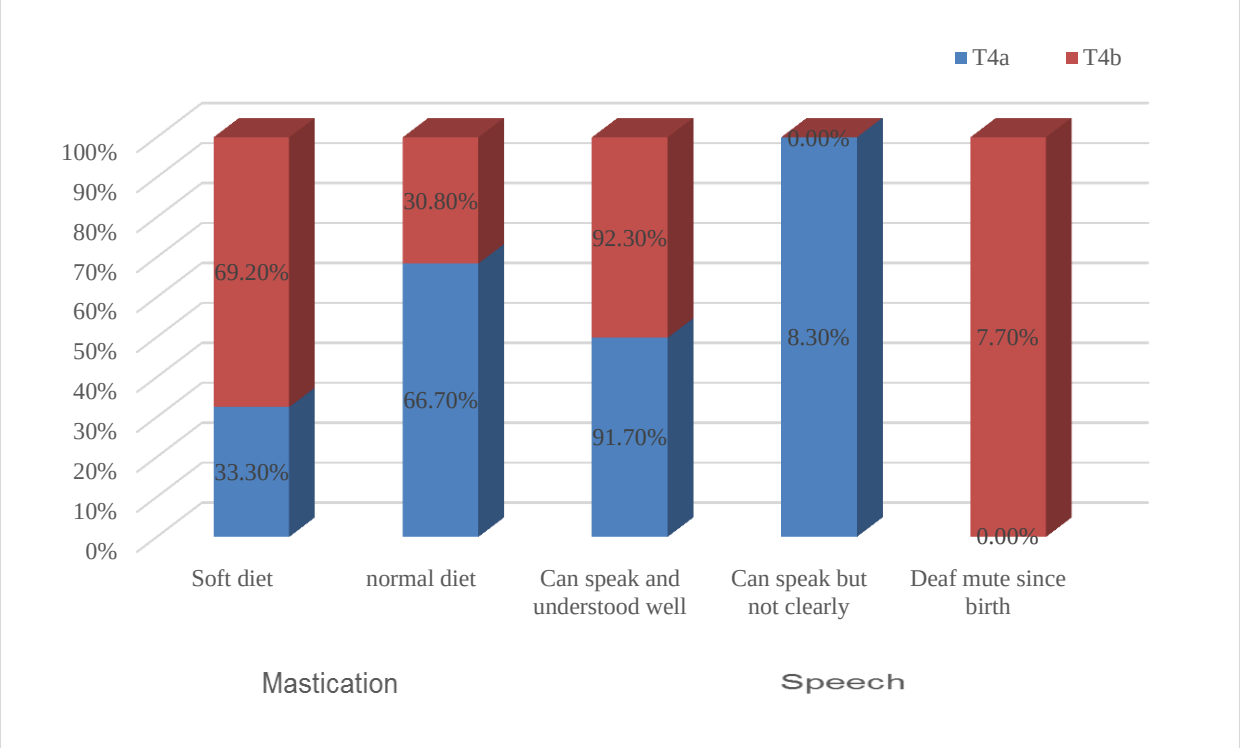


Figure 16: Bar diagram showing Comparison of functional outcome between T stagings

Table 20: Recurrence and Death comparison with tumor staging

		Tumor staging				P value
		T4a		T4b		
		No of Patients	%	No of Patients	%	
Recurrence	No recurrence	12	100.0%	10	76.9%	0.076
	Recurrence present	0	0.0%	3	23.1%	
Final Outcome	Alive and disease free	11	91.7%	9	69.2%	0.161
	Died	1	8.3%	4	30.8%	

In T4a patients none of them had recurrence and in T4b 23.1% had recurrence. 8.3% of patients in T4a stage and 30.8% of patients in T4b had mortality during the follow up. There was no significant difference between patients with T4a and T4b tumours with respect to recurrence and survival.

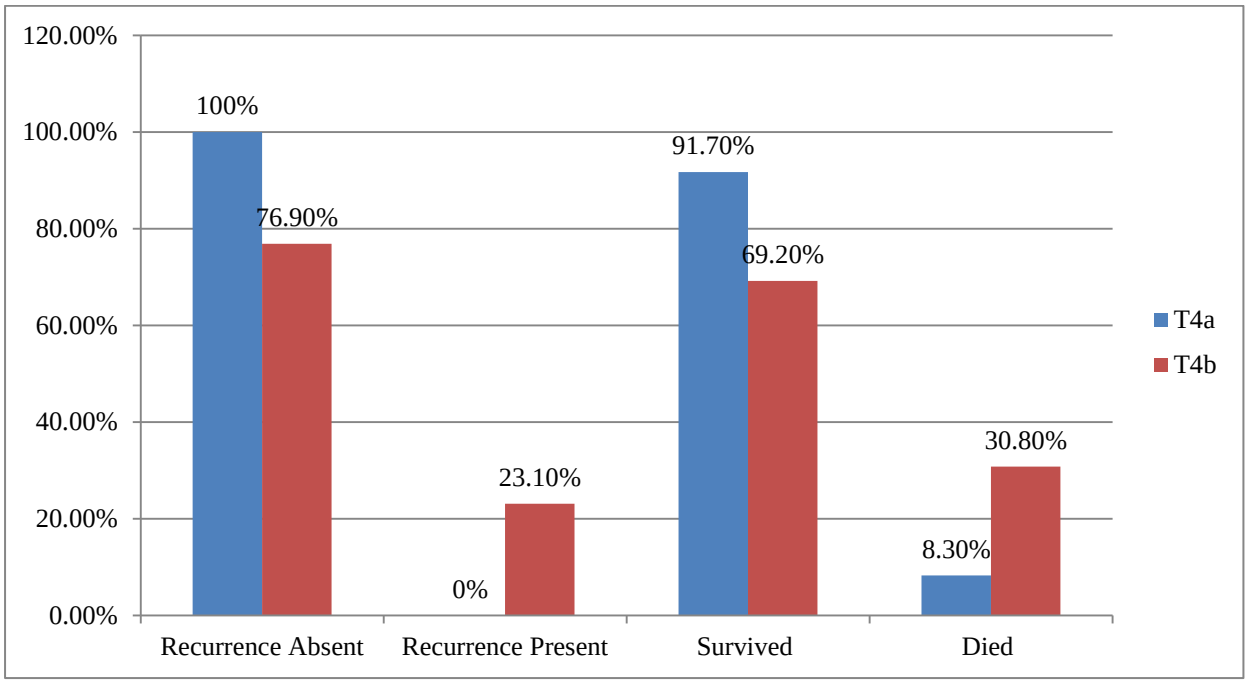


Figure 17: Bar diagram showing Recurrence and Death comparison with T staging

Image 1. Carcinoma left buccal mucosa T4aN2bM0

Image 2. pre operative ulceroproliferative growth consistent with SCC in left buccal mucosa involving RMT

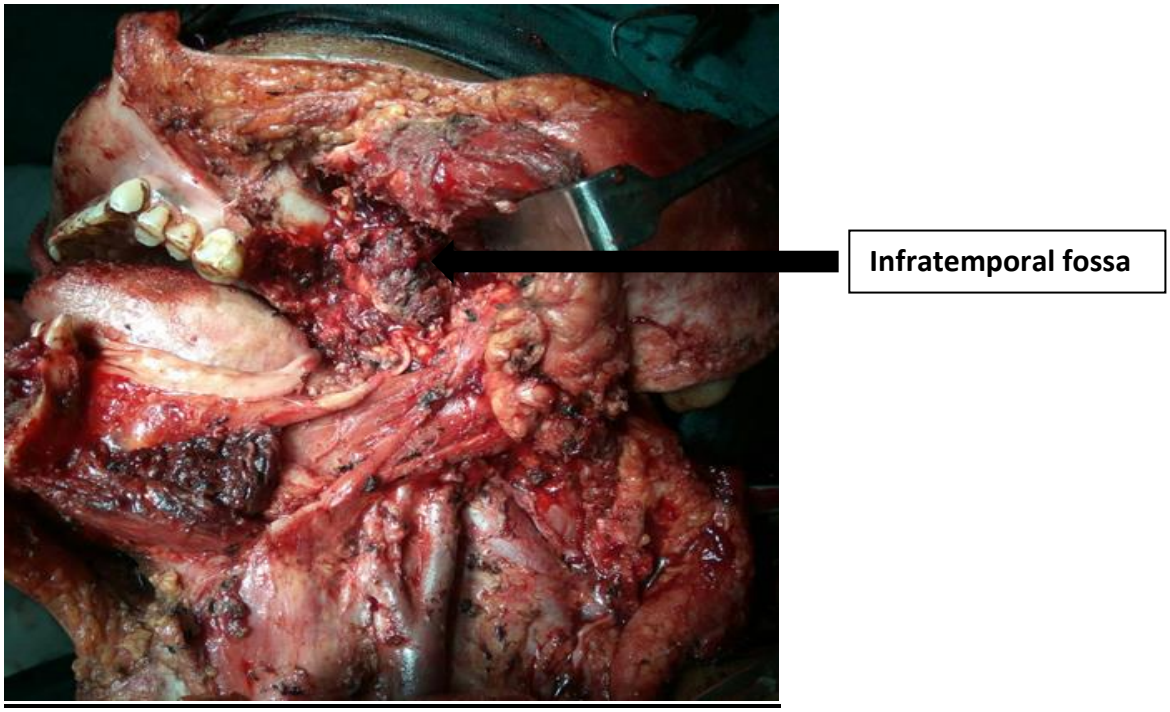


Image 3. composite resection completed

Image 4. post operative status with trismus

Image 5. intra operative (composite resection) image showing verrucous carcinoma of left buccal mucosa

image 6.after completion of bite resection and neck dissection

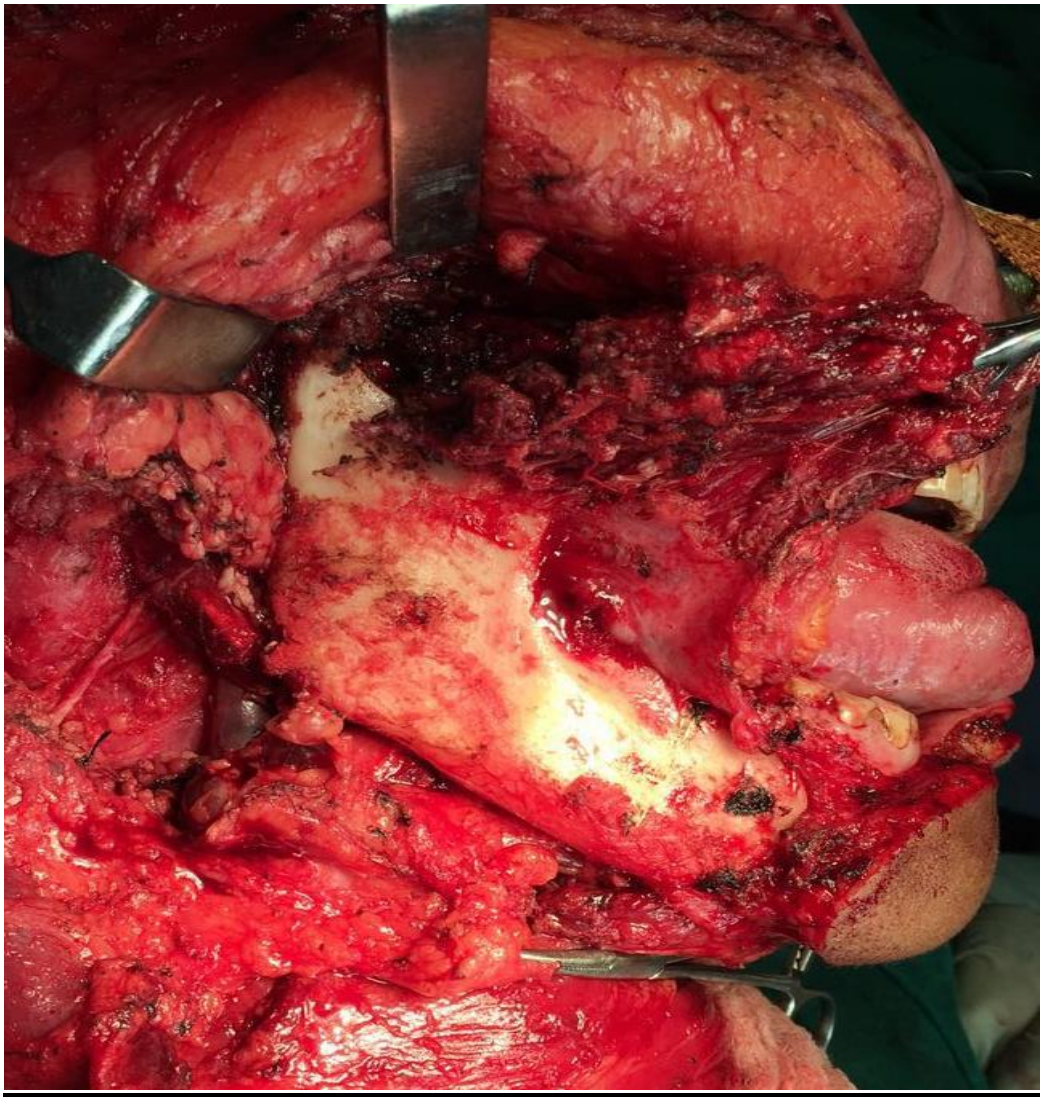


Image 7. tumour tissue being resected away from sigmoid notch of mandible

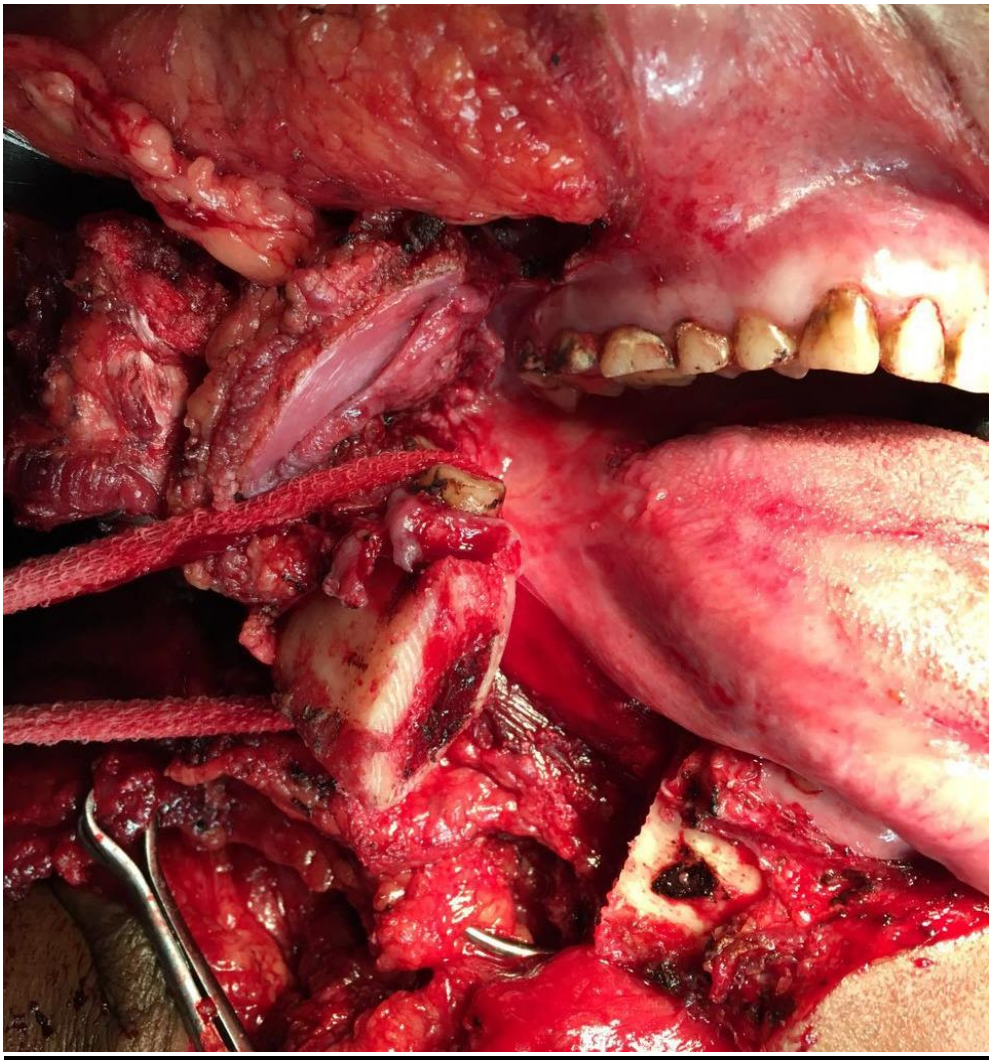


Image 8. mandibulotomy

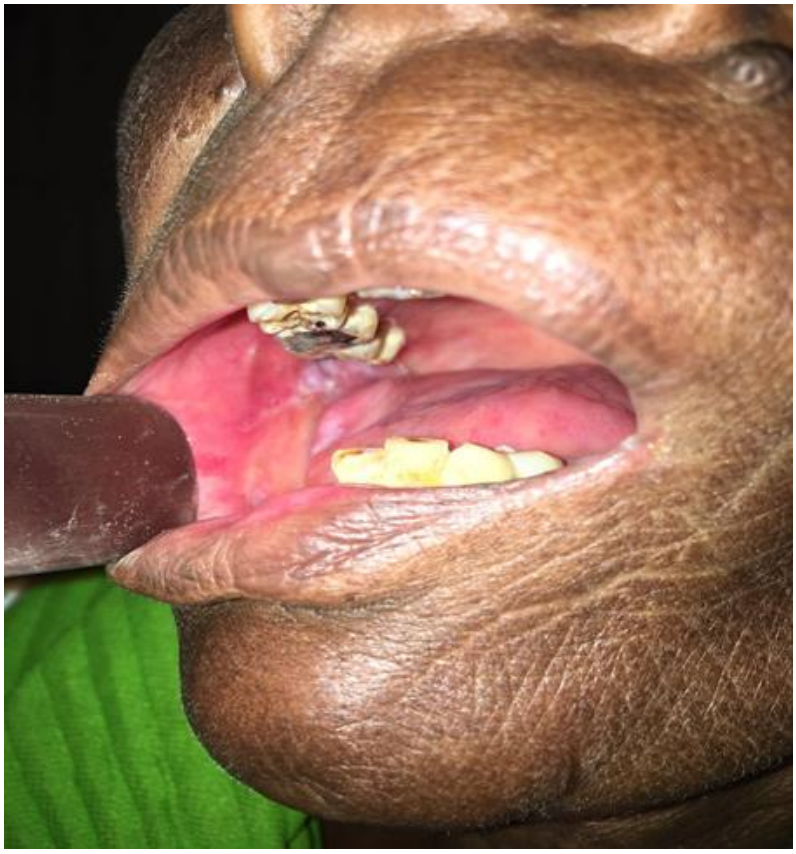


Image.9 healthy pmmc flap in situ at follow up

Image 10. Post operative patient at 6 month follow up

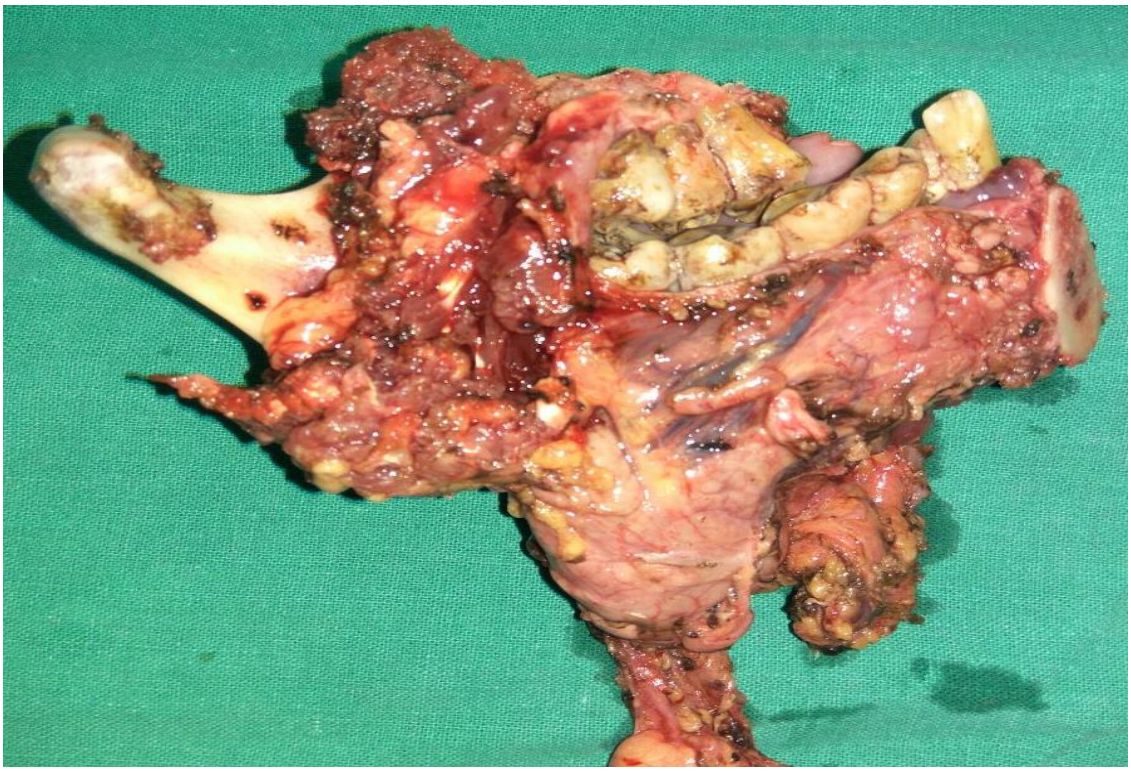


Image 11. surgical specimen of bite resection

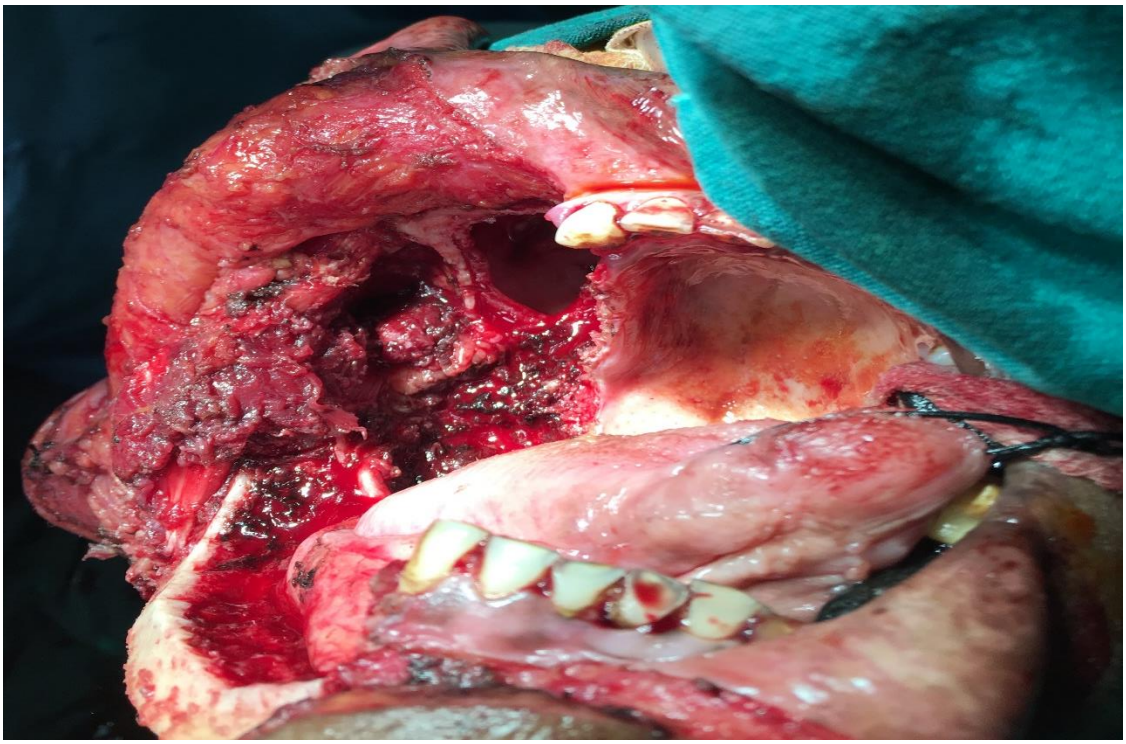


Image.12 defect after composite resection and compartment clearance of ITF showing roof if ITF

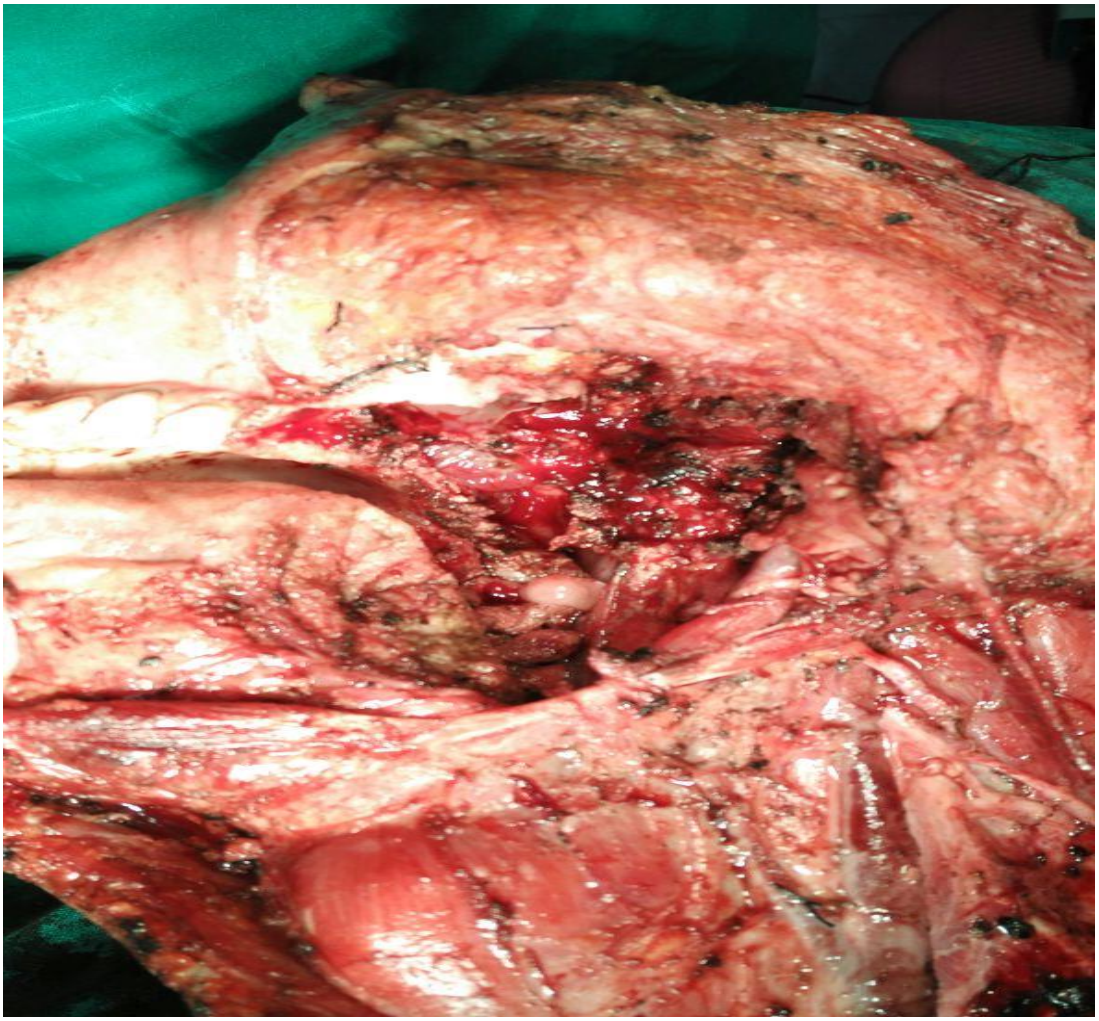


Image 13. intra operative image after compartmental clearance of infratemporal fossa

Image 14. surgical specimen of bite resection with neck dissection

Image 15. osteitis in the partial maxillectomy cavity

Image 16. orocutaneous fistula

Image 17. improvement in trismus following treatment (from grade II to grade I)

Image 18. Post operative case of carcinoma of RMT with healthy PMMC flap in situ

DISCUSSION

DISCUSSION

This study was done at R.L.Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar between Dec 2014 - April 2016. It included 25 patients. 72% of whom were females and maximum incidence was seen in the age group 41-50 years. The most common site involved was buccal mucosa (18 out of 25 patients) followed by lower alveolus (5 patients). The above findings can be attributed to the habit of chewing tobacco quid (kaddi pudi) among the ladies in this region. In an epidemiological study done in this region , head and neck cancer accounted for 30% of all malignancies, the commonest subsite being buccal mucosa[34]. Our findings were similar to the above study.In this study only patients with locally advanced disease were included. T4aN0: 3 patients, T4aN1: 4 patients, T4aN2a: 3 patients, T4aN2b: 2 patients, T4bN0: 1 patient, T4bN1: 2 patients, T4bN2a: 6 patients, T4bN2b: 3 patients & T4bN2c: 1 patient.

Majority of the patients in this region present with locally advanced disease which can be attributed to poverty, ignorance and lack of awareness among the people in this region .Other studies involving epidemiology, awareness and superstitions of this region have found similar findings[35,36,37].

17 out of 25 patients in our study presented with grade I trismus, 5 patients had grade II trismus ,2 patients had grade III trismus and only 1 patient had no trismus at presentation. There was no statistically significant difference involving the grade of trismus and T staging (T4a and T4b tumours) preoperatively. This finding can be explained by the fact that all the patients in our study had T4 disease and the current AJCC staging includes only the extent of tumour spread and not the depth and involvement of muscles of mastication.

All the patients in this study underwent composite resection with neck dissection followed by reconstruction. Due to the difficulty in achieving negative margins in soft tissue (muscles of

mastication) in such advanced tumors, a compartmental resection of infratemporal fossa was performed. A similar study performed in Mazumdar-Shaw Cancer Center showed that it was possible to achieve negative margins in majority of locally advanced oral cancer cases by performing a compartmental resection and clearance of masticator space[29].

The surgically excised specimen was then sent for histopathological examination where the surgical margins, especially soft tissue margins, lymphnode metastasis, involvement of bone and lymphovascular invasion were documented. Majority of the specimens (68%) showed well differentiated squamous cell carcinoma and 20% showed moderately differentiated squamous cell carcinoma. Only a small percentage of the specimens (4% each) showed poorly differentiated squamous cell carcinoma and verrucous carcinoma.

The surgical margins were found to be negative in all the cases. However in 48% of patients margins were close (< / = 4mm from the tumour after formalin fixation). 4mm was taken as cut off for close margins after formalin fixation i.e </= 4mm was considered as close margins and >4mm was considered as clear margins[38]. This cut off was taken in view of earlier study done in this institution correlating surgical margins on table and after formalin fixation which showed upto 30-40% reduction in tumour size[39]. Among the patients with near margins the superior margin was found to be close in 58.33 % (7 patients), the posterior margin was found to be close in 25% (3 patients), the inferior margin was found to be close in 16.67% (2 patients).This can be explained by the fact that the muscles of mastication extend superiorly into the infratemporal fossa and it is very difficult to know the true extent of tumour in these soft tissues (muscles of mastication) therefore requiring compartmental resection removing all the muscles of mastication[29,40]. In our study there was no significant

difference in margins of resection when T4a tumors were compared with T4b. This is because all patients underwent a compartment resection.

Mandibular erosion was present in 20% of cases both radiologically and on histopathology. Majority of the remaining patients had soft tissue involvement abutting the mandible requiring a mandibular resection. All these patients had hemimandibulectomy as the muscles of mastication were involved and it would not have been oncologically safe to preserve the mandible[41,42,43].

Only 1 patient had lymphovascular involvement.

In 24% of patients in our series cervical lymphnodes were found to harbor tumour deposits and 76% of patients had only reactive lymphnodes. This can be explained by the fact that majority of the patients had malignancy of buccal mucosa and a few had malignancy of upper alveolus which do not have rich lymphatic drainage (unlike tongue).

24 out of 25 patients received adjuvant treatment as they had locally advanced disease. 22 out of 25 patients underwent post operative radiotherapy and two patients (T4b) received post operative chemotherapy + radiotherapy as they had adverse histological features such as margins being too close and multiple lymph nodes being positive. Only one patient who had verrucous carcinoma with clear margins of resection on histopathology did not receive adjuvant treatment.

Post operatively patients were followed up to assess the locoregional control and functional outcome with regards to mouth opening, mastication, speech etc. the same variables were documented by other studies in which compartment resection was done for locally advanced oral cancers. Out of the 17 patients (68%) who had grade I trismus preoperatively 5 patients

(29.4%) continued to have Grade I trismus and the trismus increased from grade I to grade II in 9 patients (52.9%) and 3 patients (17.6%) had no trismus following the complete treatment. The 5 patients who had grade II trismus pre operatively had maximum relief after surgery 4 patients (80%) were completely relieved of trismus post operatively and in 1 patient (20%) it reduced to grade I trismus. This improvement in post operative trismus in those patients presenting with grade II trismus was found to be statistically significant. However the patients who had higher grade of trismus (grade III) pre operatively 3 patients (8%) continued to have grade III trismus post operatively.

The above findings can be explained by the fact that pain and pterygoid spasm was relieved after surgery (compartment resection) however major reconstruction using conventional (PMMC flap) and post operative radiotherapy contributed to post operative trismus in few cases particularly grade I. The other studies where compartment resection for oral cancer extending to infratemporal fossa was done, have only mentioned acceptable mouth opening following treatment but have not graded trismus[29,31,40].

Other surgical complications were also documented in our study which included post operative infection, fistula formation, microstomia and deformities were also documented. There was no statistically significant difference in outcome between the T4a and T4b with regards to these complications.

After a mean follow up of 1 year with minimum follow up of 6 months, 19 patients are alive and disease free (80%). 3 patients expired due to other cause (12%) and 3 patients had local recurrence (12%). 2 of the patients with recurrence expired and 1 patient refused any further treatment.

All the 3 patients with local recurrence (1 male and 2 female patients) had T4b disease. All 3 patients had advanced regional disease (N2a : 1 patient and N2b: 2 patients) pre operatively.

Though all these 3 patients underwent compartmental resection of ITF during the time of composite resection the superior margin was close (3mm in 1 patient and 2mm in 2 patients). Among these 3 patients all had multiple lymphnode involvement on HPE an 1 patient (with N2a) had extracapsular spread. Out of these 3 patients 1 had received post operative chemoradiation as adjuvant therapy, 1 had received only radiation as adjuvant therapy and the other was a defaulter of radiation (he received only 10/33 fractions of radiation).

A similar study conducted by Liao et al in Taiwan published in the year 2006 showed that oral cancer below the sigmoid notch of mandible has a favourable outcome after adequate treatment and the outcome is less favourable when the disease extends above the sigmoid notch inspite of compartment clearance of ITF[40]. However some of these patients who would have been otherwise condemned to palliative treatment only, were found to have reasonably good locoregional control.

In another study conducted in Taiwan and published in the year 2007, the outcomes of resection between T4a and T4b OSCC were compared. This study had 181 patients among whom 48 patients had T4b disease. The 5 year survival outcomes between T4a and T4b (not extending high up in the ITF) were comparable (80% vs 78% local control). However the disease free survival between T4a and T4b was 63% vs 65%. In their study the independent prognostic factors which affected 5 year survival were N2 status preoperatively, extracapsular spread from lymph nodes and poor differentiation.

The study done at Mazumdar Shaw Cancer Centre , India and published in the year 2012 involving 30 patients who underwent compartment clearance for ITF along with composite

resection for OSCC showed only 2 recurrences. These patients had extension till the pterygomaxillary fissure[29].

In our study we had almost similar results with 3 local recurrences out of 25 patients (12%). In both our study and Mazumdar Shaw Cancer Centre study close margins were a poor prognostic factor (superior margin). In our study the disease free survival was comparable between T4a and T4b tumours (inferior to sigmoid notch of mandible). However the sample size is small. More number of patients with longer follow up would be desirable in future to know the long term outcome.

In this study we found that patients with T4b disease who would have otherwise received only palliative treatment, had reasonably good locoregional control till date. Advanced nodal disease (multiple nodes and extracapsular spread) and close margins (<4mm) had a poor outcome in our study.

Similar outcome was found in the Taiwanese study and Mazumdar Shaw Cancer Centre study.

CONCLUSION

CONCLUSION

- There is a high prevalence of oral cancers among lower socioeconomic group, especially females, in Kolar region.
- Majority of the patients present with locally advanced disease , namely T4a and T4b tumours.
- Close margins (</= 4mm margins after formalin fixation) was found in 48% (12 out of 25 patients). The most common site for close margins in the resected specimen was found at the superior margin. This is because of involvement of muscles of mastication in infratemporal fossa and the technical difficulty in accessing this area.
- A significant number of patients in this region present with T4b disease.
- Compartment clearance of ITF involves removal of muscles of mastication at the time of composite resection for oral cancer.
- It is difficult to ensure adequate surgical margins superiorly during compartment resection in ITF and in our study 48% of patients were found to have close margins (</= 4mm). In most of these cases the superior margin was close.
- Some of the T4b tumours (involving ITF) have an outcome which is comparable to T4a (tumours not reaching high in ITF). Some of these patients who would have otherwise received palliative care only will benefit by compartment clearance of ITF along with composite resection, neck dissection and adjuvant treatment.
- Following composite resection and compartment clearance, a few patients who did not have trismus pre operatively may develop low grade trismus due to reconstruction, radiation and fibrosis. However patients who present with grade II trismus due to involvement of muscles of mastication can have improvement and be partially relieved of trismus following compartment clearance.

- Close margins, multiple lymph node metastasis, and extranodal spread from lymphnodes are bad prognostic factors and adversely affect the outcome.
- The mastication and speech in most of the patients after compartmental clearance of ITF is acceptable.
- With the present knowledge of anatomy, better surgical equipment and refined surgical techniques in compartment resection of ITF is a safe surgery in experienced hands.
- This compartment clearance of ITF will definitely provide hope of good locoregional control in a significant number of patients staged T4b (pre operatively) who would have otherwise be condemned as inoperable.
- .Larger studies of this type involving multiple institutions are desirable to objectively assess the long term outcome in patients with oral cancer extending to ITF.
- Based on the histopathological report patient received adjuvant treatment which was either post operative radiotherapy or post operative chemotherapy + radiotherapy.
- At follow up the functional outcome of patients was documented with regards to mouth opening, mastication & speech.
- The pre operative and post operative grading of trismus was also compared and analysed. We found that in those patients with grade II trismus pre operatively there was a statistically significant improvement in trismus following surgery.
- We also found that the functional outcome of patients with T4b tumours was comparable to those with T4a tumours.
- After completion of treatment patients were followed up and at each follow up the patients were assessed for locoregional control along with functional outcome.
- In our study we had 3 recurrences. 2 of which had T4b tumours and 1 had T4a tumour. All three had local recurrence. The former two patients (8%) were treated

palliatively for the recurrence but both succumbed to the disease. The latter patient refused further treatment.

- 3 patients (12%) died due to other cause.
- The remaining 80% of patients are alive and disease free.
- By performing a compartmental resection of infratemporal fossa in oral cancers involving this space it is possible to get clear margins in majority of the patients.

SUMMARY

SUMMARY

Head and neck malignancies account for about 30% of cancers in India.1/3rd of these are oral cancers.These cancers are common in and around kolar district due to the habit of betel nut/tobacco chewing and the use of quid.many present in the advanced stage (T4a and T4b tumours).Earlier such cases were considered inoperable and they received only palliative treatment. Recently few studies have shown that it is possible to resect these tumors with acceptable morbidity. A study conducted in Taiwan by Liao et al has shown that patients with locally advanced OSCC extending upto the level of sigmoid notch of mandible are operable and can have good locoregional control following surgery and adjuvant treatment. We aimed to study the functional outcome and assess the locoregional control following surgery and adjuvant treatment in patients with locally advanced oral cancers extending to ITF.

25 patients were included in our study. 72% of whom were females and maximum incidence was seen in the age group 41-50 years. The most common site involved was buccal mucosa (18 out of 25 patients) followed by lower alveolus (5 patients). The above findings can be attributed to the habit of chewing tobacco quid (kaddi pudi) among the ladies in this region.

17 out of 25 patients in our study presented with grade I trismus, 5 patients had grade II trismus ,2 patients had grade III trismus and only 1 patient had no trismus at presentation. There was no statistically significant difference involving the grade of trismus and T staging (T4a and T4b tumours) preoperatively.

After radiological and histopathological confirmation of OSCC extending to ITF, all patients underwent composite resection with compartment clearance of ITF with reconstruction followed by adjuvant treatment based on HPE.

Post operatively patients were assessed for functional outcome with regard to trismus, speech and mastication and also for locoregional control.

The surgical margins were found to be negative in all the cases. However in 48% of patients margins were close (< / = 4mm from the tumour after formalin fixation). The majority of close margins were found in the superior margin (58%) as it is difficult to know the exact extent of tumour in this region of ITF (muscles of mastication). Hence we did a compartmental resection of this space removing the muscles of mastication in order to get clear margins and better locoregional control.

24 out of 25 patients received adjuvant treatment as they had locally advanced disease. 22 out of 25 patients underwent post operative radiotherapy and two patients (T4b) received post operative chemotherapy + radiotherapy as they had adverse histological features such as margins being too close and multiple lymph nodes being positive.

Out of the 17 patients (68%) who had grade I trismus preoperatively 5 patients (29.4%) continued to have Grade I trismus and the trismus increased from grade I to grade II in 9 patients (52.9%) and 3 patients (17.6%) had no trismus following the complete treatment. The 5 patients who had grade II trismus pre operatively had maximum relief after surgery 4 patients (80%) were completely relieved of trismus post operatively and in 1 patient (20%) it reduced to grade I trismus. This improvement in post operative trismus in those patients presenting with grade II trismus was found to be statistically significant. However the patients who had higher grade of trismus (grade III) pre operatively 3 patients (8%) continued to have grade III trismus post operatively.

Almost all our patients were able to speak and were understood clearly following treatment. 52% of our patients were able to take soft diet orally and the other 48% were able to take normal diet orally after the completion of treatment.There was no statistically significant difference in the functional outcome between patients with T4a and T4b tumours.

A similar study conducted in Mazumdar Shaw Cancer Centre, India showed similar results and that patients with T4b tumours after compartmental resection of ITF can have acceptable functional outcome.

After a mean follow up of 1 year with minimum follow up of 6 months. 19 patients are alive and disease free (80%). 3 out of 25 patients expired due to other cause (12%) and 3 other patients had local recurrence (12%). 2 of the patients with recurrence expired and 1 patient refused any further treatment.

Close margins (mainly superior margin) were considered to be a poor prognostic factor in both our study and Mazumdar Shaw Cancer Centre study. In our study the disease free survival was comparable between T4a and T4b tumours (inferior to sigmoid notch of mandible). However the sample size is small and longer follow up would help in better assessing the outcome in these patients.

Now, with better surgical techniques these patients with locally advanced OSCC who would've otherwise been given only palliative treatment can be offered surgery followed by adjuvant treatment which will give a better locoregional control with acceptable functional outcome.

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ANNEXURE

ANNEXURE I

INFORMED CONSENT

TITLE OF THE PROJECT: OUTCOME OF SURGICAL RESECTION IN LOCALLY ADVANCED ORAL MALIGNANCY EXTENDING TO INFRATEMPORAL FOSSA

I/we have been explained in a language understandable to me the advanced nature of my illness and the standard treatment protocol.

I/we have also been informed regarding the recent advances in science in terms of surgery for locally advanced oral malignancy which will involve removal of the tumour in its entirety+ part of the jaw bone+ tumour deposits in the neck (lymph nodes) with reconstruction of the defect which will be followed by radiotherapy/chemotherapy. The associated complications such as bleeding, difficulty in chewing/speech and facial deformity have been enlisted to me.

I/we have had the opportunity to ask questions regarding various aspects of this study and my questions have been answered to my satisfaction.

I/we am aware that I am entitled to refrain/withdraw from the study at any point and the further course of treatment will not be compromised.

I/we, the undersigned agree to participate in this study and authorize the collection and disclosure of my personal information as outlined in this consent form.

Subject's/guardian's name and signature/thumb impression:

Date: Name and signature of witness:

Place:

Date: Name and signature of principle investigator:

ANNEXURE II

OUTCOME OF SURGICAL RESECTION IN LOCALLY

ADVANCED ORAL MALIGNANCY EXTENDING

TO INFRATEMPORAL FOSSA

PROFORMA

Name of the patient Date

Age Hospital No:

Sex

Occupation

Address

Phone NO:

Chief complaints	Yes/No	since
Presence of ulcer/mass in oral cavity		
Presence of mass/swelling in the neck		
Restricted mouth opening		

History of presenting illness	Yes/no	since
Able to insert 0/1/2/3 fingers in the mouth		
Difficulty in chewing food		
Difficulty in swallowing food		
Difficulty in speaking		
Halitosis		
Excessive salivation		
Burning sensation in oral cavity		
Weight loss		
Generalised weakness		
Loss of appetite		
Loosening of teeth		

Past history	Yes/no	Since	On treatment If yes, since
Hypertension			
Diabetes mellitus			
Pulmonary tuberculosis			
Bronchial asthma			
Epilepsy			

Treatment history	Yes/no	date
Previous surgery		
Chemotherapy		
Radiotherapy		

Family history:

Personal history	
Appetite	
Diet	

Habits/addictions	Yes/no	Quantity/day	since
Tobacco/betel nut chewing			
Bidi smoking			
Cigarette smoking			
Alcohol consumption			

General physical examination

Height weight pallor

Temperature pulse BP

Local examination

Oral cavity:

Lips

Trismus +/- grade

Orodental hygiene

Gingiva

Buccal mucosa

Upper alveolar surface

Lower alveolar surface

Retromolar trigone

Floor of mouth

Tongue

Hard palate

Jaw movements: side to side movements-

Forward and backward movements-

Oropharynx:

Soft palate

Anterior pillar

Tonsil

Posterior pillar

Base of tongue

Posterior pharyngeal wall

Face:

Neck:

Lymph nodes	Yes/no
Significant If yes,	
Size	
Level	

Investigations:

Hb Tc Dc PLC BT CT

Biopsy report:

Pre op CT scan findings

Treatment:

Surgery

Radiotherapy

Chemotherapy

HPE report:

Margins

Nodes

Follow-up:

Trismus (grade)

Mastication	0	1	2	3

Speech	1	2	3

Complications if any:

Post-op infection:

Deformity:

Locoregional control:

Recurrence

Local

Regional

Death

Due to diesaese

Other cause

Trismus:

Grade 0 : no trismus

Grade I : 4-6 cms

Grade II : 2-4 cms

Grade III : 1-2 cms

Grade IV : < 1 cm

mastication grading scale:

0- Cannot take orally

1- Can take liquids only

2- Can take semi-solid diet but not solids

3- Can take solids

Speech grading scale:

1- Cannot speak/ speaks but not understood

2- Can speak and partially understood

3- Can speak clearly and understood well

sl.no	age	sex	ip no	diagnosis	Side	Site	Tstaging	Nstaging	Mstaging	trismus	biopsy	surgery	hpe	margins	bone/ lymphovascular	nodes	adjuvant Rx	po- trismus	mastication	speech	complications	recurrence	Death
1	63y	f	56738	Ca left buccal mucosa T4bN1M0	left	buccal mucosa	T4b	1	0	+ (gr 3)	SCC	WE+L partial maxillectomy+ITF clearance+MRND	well.diff SCC	nearest margin 5mm sup	-	0/13 positive	33 Fr RT	+ (gr 3)	soft diet	can speak and understood well	osteitis of bony cavity at op site	no recurrence	Alive
2	45y	f	106142	Ca left buccal mucosa T4bN2bM0	left	buccal mucosa	T4b	2b	0	+ (gr 2)	SCC	WE +L HM +L MRND + PMMC recon.	well.diff SCC	nearest margin 2 mm sup	-	0/13 positive	35 Fr RT	no trismus	normal diet	can speak and understood well	microstomia	Present (Local)	Alive
3	68y	m	175059	Ca left buccal mucosa T4bN2cM0	left	buccal mucosa	T4b	2c	0	+ (gr 2)	SCC	WE +R HM +L MRND + PMMC + DP recon	well.diff SCC	nearest margin 5 mm post	-	0/23 positive	35 Fr RT	no trismus	normal diet	can speak and understood well	post op chest wound infection	no recurrence	died (other cause)
4	40y	m	30105/2015	Ca left lower alveolus T4bN2bM0	left	lower alveolus	T4b	2b	0	+ (gr 1)	SCC	WE+ L HM+ ITF clearance+L MRND + PMMC recon	mod. Diff SCC	nearest margin 7mm sup	bone erosion +	0/21 positive	36 FR RT	+ (gr 2)	normal diet	can speak and understood well	post op wound infection	no recurrence	Alive
5	80y	f	172529	Ca left buccal mucosa T4bN2aM0	left	buccal mucosa	T4b	2a	0	+ (gr 1)	SCC	WE+L HM+ ITF clearance+ L MRND+PMMC recon	well diff SCC	nearest margin 5 mm sup	-	0/19 positive	33 Fr RT	+ (gr 2)	soft diet	can speak and understood well	-	no recurrence	Alive
6	42y	m	52815/2015	Ca right buccal mucosa T4bN2aM0	right	buccal mucosa	T4b	2a	0	+ (gr 3)	SCC	WE+R HM+ITF clearance+R MRND+PMMC recon	mod. Diff SCC	nearest margin 2mm sup	-	0/12 positive	10 FR RT	+ (gr 3)	soft diet	deaf mute since birth	-	Present (Local)	died (disease)
7	40y	m	25204	Ca left buccal mucosa T4aN0M0	left	buccal mucosa	T4a	0	0	+ (gr 1)	SCC	WE+L HM+Upper alveolectomy+L MRND+PMMC recon	well diff SCC	nearest margin 8mm post	-	0/8 positive	36 FR RT	no trismus	normal diet	can speak and understood well	-	no recurrence	Alive
8	33y	m	25214	Ca left retromolar trigone T4aN1M0	left	retromolar trigone	T4a	1	0	+ (gr 1)	SCC (verrucous)	WE+L HM+Upper alveolectomy+L MRND+PMMC recon	well diff SCC	nearest margin 7mm post	-	0/24 positive	35 Fr RT	+ (gr 1)	normal diet	can speak and understood well	orocutaneous fistula	no recurrence	Alive
9	42y	f	252143	Ca left lower alveolus T4aN2aM0	left	lower alveolus	T4a	2a	0	-	SCC	WE+L HM+L MRND+PMMC+DP Recon	well diff SCC	nearest margin 5mm sup	-	0/23 positive	35 Fr RT	+ (gr 1)	soft diet	can speak and understood well	dp flap failure	no recurrence	Alive
10	60y	f	232008	Ca right lower alveolus T4bN2aM0	right	lower alveolus	T4b	2a	0	+ (gr 1)	SCC	WE+R HM+ITF clearance+R MRND+PMMC recon	well diff SCC	nearest margin 5mm post	bone erosion +	0/14 positive	35 Fr RT	+ (gr 2)	soft diet	can speak and understood well	-	no recurrence	Alive
11	50y	f	68566	Ca right buccal mucosa T4aN2aM0	right	buccal mucosa	T4a	2a	0	+ (gr 1)	SCC	WE+R MRND+ RFFF recon	well diff SCC	nearest margin 1 cm inf	-	0/12 positive	33 Fr RT	no trismus	normal diet	can speak and understood well	-	no recurrence	Alive
12	62y	f	250669	Ca left buccal mucosa T4aN2bM0	left	buccal mucosa	T4a	2b	0	- (gr 1)	SCC	WE+L HM+L infra. Maxillectomy+MRND+PMMC recon	well diff SCC	nearest margin 1 mm sup	-	3/22 positive	35 Fr RT	+ (gr 2)	soft diet	can speak but not clearly	-	no recurrence	died(other cause)
13	70y	f	203306	Ca left buccal mucosa T4bN0M0	left	buccal mucosa	T4b	0	0	+ (gr 1)	SCC	WE+L Tot.maxillectomy+MRND+PMMC recon	well diff SCC	nearest margin 1.5mm post	-	0/8 positive	36 FR RT	+ (gr 2)	soft diet	can speak and understood well	-	no recurrence	died(other cause)
14	55y	f	247143	Ca left buccal mucosa T4aN1M0	left	buccal mucosa	T4a	1	0	+ (gr 1)	SCC	WE+HM+MRND+PMMC recon	verrucous Ca	nearesr margin 5mm sup& bone	-	0/21 positive	no RT required	no trismus	normal diet	can speak and understood well	-	no recurrence	Alive
15	40y	f	290502	Ca right buccal mucosa T4bN2aM0	right	buccal mucosa	T4b	2a	0	+ (gr 1)	SCC	WE+HM+MRND+PMMC recon	well diff SCC	nearest margin 4mm sup	-	1/11 positive	35 Fr RT	+ (gr 2)	soft diet	can speak and understood well	shoulder deformity	no recurrence	Alive
16	50y	f	305255	Ca right buccal mucosa T4bN1M0	right	buccal mucosa	T4b	1	0	+ (gr 2)	SCC	WE+R HM+R MRND+PMMC recon	mod. Diff SCC	nearest margin 2mm sup	bone erosion +	4/16 positive	CT/RT (5 cycles, 36 RT)	no trismus	soft diet	can speak and understood well	post op chest wound infection	no recurrence	Alive
17	60y	f	305515	Ca right lower alveolus T4aN1M0	right	lower alveolus	T4a	1	0	+ (gr 2)	SCC	WE+HM+MRND+PMMC +DP recon	well diff SCC	nearest margin 3mm inf	bone erosion +	0/17 positive	35 Fr RT	+ (gr 1)	normal diet	can speak and understood well	chest wound gaping	no recurrence	Alive
18	46y	f	320246	Ca left buccal mucosa T4aN2bM0	left	buccal mucosa	T4a	2b	0	+ (gr 2)	SCC	WE+L HM+MRND+PMMC recon	mod. Diff SCC	nearest margin 5mm sup+post	-	0/11 positive	35 Fr RT	no trismus	normal diet	can speak and understood well	flap failure	no recurrence	Alive
19	60y	f	235937	Ca left upper alveolus T4aN0M0	left	upper alveolus	T4a	0	0	+ (gr 1)	SCC	WE+SOHD+RFFF recon	well diff SCC	nearest margin 5 mm sup	-	0/6 positive	30 Fr RT	+ (gr 1)	soft diet	can speak and understood well	-	no recurrence	Alive
20	70y	f	16983	Ca left buccal mucosa T4aN0M0	left	buccal mucosa	T4a	0	0	+ (gr 1)	SCC	WE+HM+MRND+PMMC recon	mod diff SCC	nearest margin 2mm post	-	0/20 positive	30 Fr RT	+ (gr 1)	normal diet	can speak and understood well	-	no recurrence	Alive

21	45y	f	328249	Ca right buccal mucosa T4bN2bM0	right	buccal mucosa	T4b	2b	0	+ (gr 1)	SCC	bite resection+MRND+PMMC recon	poorly diff SCC	nearest margin 4 mm ant	lymphovascular invasion+	5/15 positive + ECS	33 fr RT + 3 cycles CT	+ (gr 1)	normal diet	can speak and understood well	wound gaping at recipient site	Present (Local)	died(dis)
22	70y	f	303993	Ca right buccal mucosa T4aN2aM0	right	buccal mucosa	T4a	2a	0	+ (gr 1)	Scc	WE+MRND+HM+PMMC recon	well diff SCC	nearest margin 4 mm sup	-	0/12 positive	33 Fr RT	+ (gr 1)	normal diet	can speak and understood well	-	no recurrence	Alive
23	47y	m	383336	Ca left lower alveolus T4bN2aM0	left	lower alveolus	T4b	2a	0	+ (gr 1)	SCC	WE+MRND +HM+PMMC +dp recon	well diff SCC	nearest margin 2 mm inf	-	0/20 positive	35 Fr RT	+ (gr 2)	soft diet	can speak and understood well	post op wound infection	no recurrence	Alive
24	60y	f	236679	Ca right buccal mucosa T4aN1M0	right	buccal mucosa	T4a	1	0	+ (gr 1)	scc	WE+MRND+HM+PMMC recon	well diff SCC	nearest marin 2 mm sup	-	2/20 positive	33 Fr RT	+ (gr 2)	soft diet	can speak and understood well	-	no recurrence	Alive
25	21y	m	327724	Ca right buccal mucosa T4bN2aM0	right	buccal mucosa	T4b	2a	0	+ (gr 2)	scc	WE+MRND+HM+PMMC +DP recon	mod diff scc	nearest margin 2 mm post	bone erosion +	2/28 positive	CT/RT (5 cycles, 36 RT)	+ (gr 2)	soft diet	can speak and understood well	post op wound infection	no recurrence	Alive