ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 9, Issue – 1, January – 2024 , Page No. : 57 – 65

Evaluation of Recurrence in T3-T4 Squamous Cell Carcinoma of Mandible

[1]Dr. Sugandha Kaushik, BDS, MDS, Resident, Department of Oral and Maxillofacial Surgery, ITS Dental College, Greater Noida.

[2]Dr.Ashish Sharma, BDS , MDS, Professor and Head, Department of Oral and Maxillofacial Surgery, GDC, Bangalore

[3]Dr.Nilotpal Mishra, BDS , MDS, Senior Lecturer, Department of Oral and Maxillofacial Surgery, ITS Dental College And Hospital Greater Noida

[4]Dr.Ambika Luthra,BDS , MDS, Professor, Department of Oral And Maxillofacial Surgery, ITS Dental College And Hospital Greater Noida

[5]Dr.Gauri Gupta, Senior Lecturer, Department of Oral and Maxillofacial Surgery, ITS Dental College and Hospital Greater Noida

[6]Dr. Shweta Pandey, BDS, MDS, Resident, Department of Oral and Maxillofacial Surgery, ITS Dental College, Greater Noida.

Corresponding Author: Dr. Sugandha Kaushik, BDS, MDS, Resident, Department of Oral and Maxillofacial Surgery, ITS Dental College, Greater Noida.

Citation this Article: Dr. Sugandha Kaushik, Dr. Ashish Sharma, Dr. Nilotpal Mishra, Dr. Ambika Luthra, Dr. Gauri Gupta, Dr. Shweta Pandey, "Evaluation of Recurrence in T3-T4 Squamous Cell Carcinoma of Mandible", IJMSIR- January - 2024, Vol – 9, Issue - 1, P. No. 57 – 65.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Objective: Aim of this retrospective single center study was the analysis of recurrence and survival rate of patients suffering from T3-T4 oral Squamous cell carcinoma (OSCC) of mandible.

Study design: 49 patients with OSCC reported between 2011- 2017 to our department of oral and maxillofacial surgery. Among which only cases with t3-t4 lesion were involved in the study. Data acquisition consisted of analysis of operation reports, radiographic records, histopathological analysis and follow-up data.

Results: Mean age was 58 yrs , 15 males and 4 female patients included in the study and the results showed that 7 cases showed recurrence over a period of 4 yrs, recurrence in t3 lesion was in 4 patients(30%) and t4 lesion was in 3 patients (50%) , overall recurrence rate was 37% (7 patients).

Conclusion: Wide excision of the lesion should be performed with a minimum of 2mm healthy tissue, postoperative radiotherapy plays a vital role in improving the overall survival rate of the patients modified neck dissection plays an important role in improving the survival outcome and preventing recurrence, thereby improving the quality of life.

Keywords: Multifactorial, Data Acquisition, Papilloma Virus.

Introduction

Malignancies of the oral cavity represent approximately 5 % of all cancer diseases [1]. Incidences of newly diagnosed OSCC worldwide range between 200,000-350,000 per year making OSCC the sixth most common cancer disease[2].Alcohol and tobacco abuse can significantly increase the risk of OSCC , the etiopathogenesis of OSCC is multifactorial as there are multiple factors involved with the occurrence of OSCC like environmental and genetic , the risk of development of Squamous cell carcinoma of oral cavity in is significantly higher in immune compromised individuals and chronic betel nut chewers , the role of human papilloma virus has been proven in literature for being a causative of oral Squamous cell carcinoma of oral cavity . Predominantly floor of mouth, buccal mucosa, and tongue are the most commonly involved in Squamous cell carcinoma . From a clinical point of view, OSCC remains asymptomatic for a long time and can only be detected by the patient and the examiner through an in duration and color change of the oral mucosa[3].There are two fundamental categories of bone involvement. The initial type is characterized by erosive changes, wherein the mandibular bone retreats in the presence of a advancing tumor margin, such as in verrucous carcinoma. In this variation, there is a disruption of cortical continuity, resulting in a U-shaped or scalloped excavation of the medullary bone. Radiographically, this manifests as a clearly defined radiolucency without discernible bone spicules. The second type is infiltrative, where the carcinoma extends into cancellous bone, producing radiographs displaying an indistinct and irregular lesion. A third type, more commonly observed with adenoid cystic carcinomas infiltrating bone, demonstrates a spread through the bone marrow without causing significant bone destruction and minimal changes on radiographs. The primary route of entry into the mandible is documented to be through the alveolar crest and lingual cortex, particularly when the tumor is positioned medially in the mandible[13,14]. Other infiltration pathways are also documented, with spread through the canal of the inferior alveolar nerve being particularly significant in contexts emphasizing mandible preservation[15]. For the sake of quality of life, preserving mandibular continuity is crucial, provided it is oncologically safe.

Diagnosis is based on clinical examination, imaging like computed tomography (CT), magnetic resonance imaging (MRI), orthopantomography (OPG) and sonography as well as histopathology on FFPE-samples of the tumor [4]. Surgical resection of the complete tumour in combination with modified neck dissection is the mainstay in successfully treating the OSCC. Maintaining surgical outcome depends upon the wide excision of the tumour mass along with removal of 2mm of healthy tissue which will significantly reduce the chances of recurrence. An adjunctive therapy which include radiotherapy and chemotherapy aids in improving the survival outcome and also improves the quality of life, In OSCC mandible two types of resection can be done marginal or segmental mandibulectomy along with MRND.

Materials and Methods

Patient: A total of 49 patients reported with OSCC between 2011-2017, among all these cases only T3-T4 lesions were included in the study and rest excluded from the study. Among the patient included in the study 15 were male and 4 were female patients.

Operational Data: Operation reports between the years 2011 and 2017 were retrospectively screened for all OSCC of mandible treated for resection procedures in

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combination with MRND along with adjunctive treatment including chemotherapy and radiotherapy.

T3 – T4 lesion cases were included in the study, Patients with T1-T2 lesions, with distant metastasis, who have undergone any prior treatment were excluded from the study.

Retrospectively patient's data records were analyzed including histopathological reports, and radiographic records.

Histologically verified and graded SCC of the oral cavity, attached to and/or suspected or visibly displaying invasion into the mandible.

Surgical Protocol: Wide excision of the lesion with segmental resection or hemimandibulectomy was done in combination with Modified neck dissection, following which Reconstruction with locoregional flap was done. Post operatively all the patients underwent radiotherapy.(fig 1, fig 2,fig 3)

Locoregional radiotherapy was done with Cobalt 60 External Radiator (Theratron 1000) of 60 Gy (2 Gy/day, 5 days a week) at least 3 weeks after wound healing.

The minimum range of the segmental resection was from the mental foramen to the mandibular gingiva, to prevent possible perineuralspread into the inferior alveolar nerve region. To allow for conclusive follow-up data the minimum interval between operation and data acquisition was 4 years. Survival analysis for these patients was performed by Kaplan-Meier estimate.

Statistical Analysis: Statistical analysis was conducted using Microsoft® Excel Version 2016 (Microsoft® Excel, California, USA) and the statistic software R Version 3.1.3.

Pie-Chart was graphed to test for gender distribution, and recurrence in both t3 and t4 lesion group (fig 4), Kaplan-Meier survival curves were calculated and a log-rank test was used to test for equality of various survival curves, p value level was set to $p \leq 0.05$ which is statistically significant (fig 5) .

Result

This is a single center retrospective study where all the patients with oral Squamous cell carcinoma were analysed between 2011- 2017, a total of 49 patients reported to the department and among those patients only the patients with lesion size T3 and T4 were included in the study, all the patients were neck positive. A total of 19 patients were included in the study.

Fifteen male and four female were included in the study , Nine patients were diagnosed with SCC lower gingivabuccal sulcus, Four were diagnosed with SCC of lower alveolus, Three patient with SCC of lower GBS involving floor of the mouth, and two patients with primary intraosseous lesion respectively. Patients with T3 lesions were 13 and T4 lesion were 6.

All the patients were treated according to the standard protocol which involved removal of the tumour mass with procedures including segmental or hemimandibulectomy in combination with MRND, all the patients received radiotherapy as adjunctive procedure.

The results stated out that on basis of recurrence the T3 lesions showed a recurrence of 37% (4 patients) and the t4 lesions showed a recurrence of 50% (3 patients) over a period of 4 yrs.

Kaplan- Meier Survival Analysis was done to check for the recurrence rate of the patients, overall recurrence rate was found out to be 37% for a follow-up period of 4 years.

Discussion

Squamous cell carcinoma (SCC) stands out as the most prevalent malignant tumor within the oral cavity, with SCC of the mandibular alveolus accounting for 7.5–17.5 percent of cases, exhibiting the lowest survival rates

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among oral carcinomas (Langdon et al., 1977) [16]. This particular type of carcinoma is three times more prevalent than maxillary alveolar carcinoma. In the broader context, carcinoma of the oral cavity represents 4% of all malignancies in men and 2% in women, predominantly manifesting as oral Squamous cell carcinomas (OSCC) (Cunningham et al., 1986) [5].

The established etiology of OSCC often links its occurrence to the use of tobacco and alcohol, with these substances being identified as the most common etiological agents (Chang et al., 2004) [6]. The mandible, playing a crucial role in mastication, deglutition, speech, and airway maintenance, faces the risk of decreased quality of life when subjected to resection, leading to the loss of essential functions, reduced mouth opening, scarring, and deformity. The complexity of mandibular reconstruction further adds to the overall morbidity, considering potential disturbances at the donor site.

Depending on the extent of invasion, different barriers influence further progression. Cortical bone, fascia, and periosteum are recognized as relatively tumor-resistant structures, while medullary bone provides a poor barrier to tumor spread. Consequently, mandibular resection is often performed with a minimum 1-cm margin when cancellous bone involvement is suspected, frequently requiring segmental resection. The primary treatment approach remains surgery, with or without radiation and chemotherapy, tailored to the tumor extent and stage (Forastiere et al., 2001; Pignon et al., 2000; Shah and Gil, 2009) [7,8,9].

The goals of therapy include cure, organ preservation, restoration of form and function, reduction of associated morbidities, and improvement or maintenance of the quality of life. OSCC proximal to the mandible tends to invade the bone through direct extension or perineural spread (Nomura et al., 2005; Pandey et al., 2007; Rao et al., 2004) [10,11,12]. The reported incidence of mandibular invasion varies from 12 to 56% in the literature.

Polya and von Navratil et al emphasized that lymphatics of the tongue and floor of the mouth traverse the mandibular periosteum en route to cervical nodes. In contrast, Marchetta et al. (1964) and Carter et al. (1980) conducted studies indicating that carcinomatous involvement of the mandible occurs through direct invasion rather than lymphatic spread. Considered a surgical disease, especially in stage III and IV, the degree of bone involvement dictates the extent of tumor resection, emphasizing the need for careful cleaning of neck lymph nodes during primary tumor resection.

The standard treatment protocol involves surgery and postoperative radiotherapy, with combination treatment yielding the most success. Post-surgical combined radiotherapy and chemotherapy enhance overall survival rates, despite inevitable associated adverse effects. Soderholm et al. conducted a study comparing five treatments in a series of 159 patients and found no differences in 5-year survival rates between treatments for stage I and II tumors. In contrast, stage III and IV tumors treated with radiation therapy alone exhibited poor survival. The importance of adjuvant radiation therapy in affecting the 5-year survival rate was inconclusive, with earlier diagnosis appearing as the key factor in increasing survival rates [17].

However, De Vincente et al.'s study on a database of 196 patients contradicts Soderholm et al., stating that radiation therapy in stages III and IV did not negatively influence patient survival. The influence of adjuvant radiotherapy on survival time should not be isolated but considered in conjunction with other tumor characteristics and treatment variables, including site, size, lymph node involvement, perineural spread, etc.

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Selective neck lymph node dissection significantly lowers the recurrence rate [18].

Relapse is defined as the return of the disease after treatment. It can be classified as tumor recurrence in those cases where tumor cells are not eliminated by treatment and regrow, or second primary tumors (SPTs) when an independent carcinogenetic process is responsible for the development of a new tumor. The major cause of recurrence after a long term period of follow-up is field cancerization where there can be more than one primary zone of cancer , another factor that can explain the recurrence of the OSCC is micro-metastasis , in which there are cells of the cancer which remain undetected in PET-CT and can lead to recurrence of the disease over a long follow-up period. In our presented study 37% of cases showed recurrence over a period of 4 yrs.

The study concludes that postoperative adjuvant radiotherapy has a positive impact on patient survival, with an overall recurrence noted in 37% of patients. Specifically, a lower recurrence rate of 27.25% is observed in T3 lesions compared to 50% in T4 lesions. These findings align with studies by De Vincente et al., Guerra et al., and Hoffmanova et al.

Conclusion

In conclusion, the current study underscores the significance of understanding and addressing Squamous cell carcinoma (SCC) in the mandibular alveolus, which represents a considerable proportion of oral malignancies with notably lower survival rates. The intricate balance between preserving essential functions of the mandible and the imperative need for resection to combat the disease poses challenges in maintaining the patient's quality of life.

While surgical intervention remains the primary treatment modality, the complexity intensifies when considering mandibular reconstruction and potential donor site disturbances. The interplay of tumor characteristics, such as site, size, and involvement of surrounding structures, plays a crucial role in determining the extent of resection and subsequent treatment strategies.

The investigation into the efficacy of adjuvant therapies, including radiotherapy and chemotherapy, reveals a nuanced landscape. While combination treatments show promise in improving overall survival rates, the influence of adjuvant radiation therapy on the 5-year survival rate remains inconclusive and necessitates a comprehensive consideration of various tumor and treatment variables.

Selective neck lymph node dissection emerges as a pivotal aspect in reducing recurrence rates, emphasizing the importance of meticulous surgical techniques. The positive impact of postoperative adjuvant radiotherapy on patient survival, as evidenced by a lower recurrence rate in specific tumor categories, aligns with findings from related studies.

In essence, this study contributes to the evolving understanding of SCC in the mandibular alveolus, shedding light on the intricate dynamics of treatment strategies, factors influencing survival outcomes, and the ongoing pursuit of refining therapeutic approaches for improved patient outcomes.

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Legend Figure and Tables

Figure 1: Patient treated with hemi-mandibulectomy with ex articulation combined with MRND

Figure 2: Patient treated with hemi-mandibulectomy combined with MRND, followed by reconstruction with PMMC

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Figure 3: Patient treated with hemi-mandibulectomy with combined with MRND

Figure 4: Chart representation for recurrence in individual group

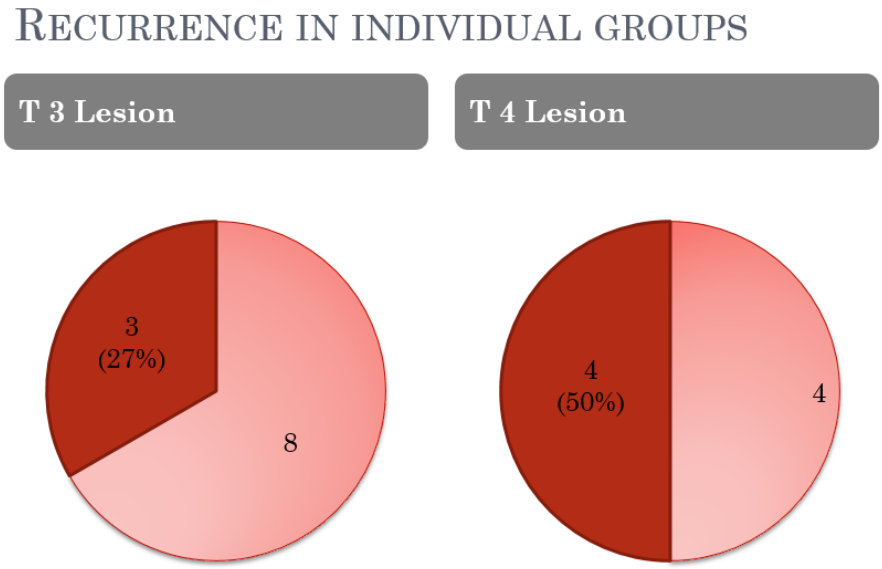

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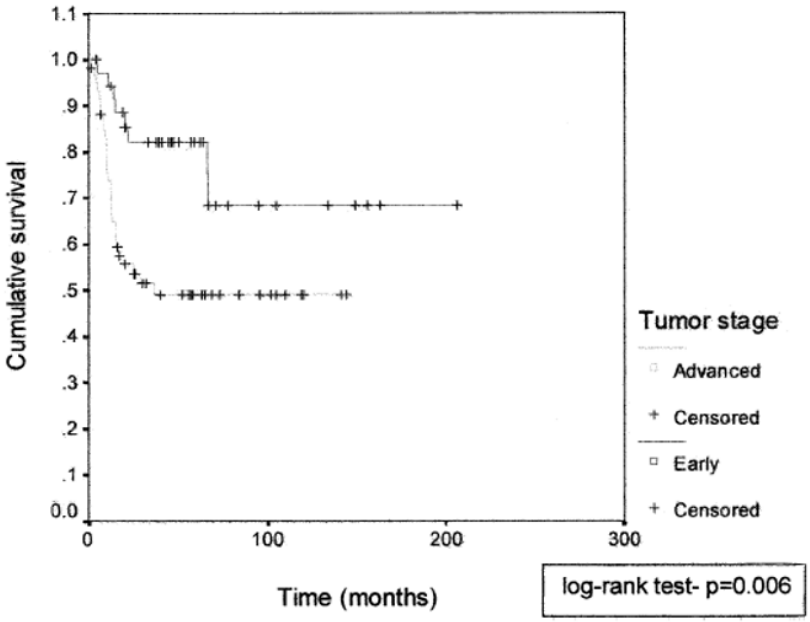
Figure 5: Kaplan- Meier analysis for recurrence and survival rate of the patients with T3 and T4 lesion.



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