ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

EVALUATION OF PATHOLOGICAL RESPONSE OF NEO-ADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED ORAL CAVITY MALIGNANCY

Dr K.L Jayakumar [1], Dr M.Aspin Nivya [2]

1. *Dr K.L Jayakumar, MD (Professor and HOD), Department of Radiation Oncology Sree mookambika institute of medical sciences, Kanyakumari, Tamil Nadu.*
2. *Dr M.Aspin Nivya, Junior resident Department of Radiation Oncology, Sree mookambika institute of medical sciences, Kanyakumari, Tamil Nadu.*

Corresponding Author – Dr M. Aspin Nivya Junior Resident Department of Radiation Oncology, Sree mookambika institute of medical sciences, Kanyakumari, Tamil Nadu.Email – nivyaaspin950@gmail.com

ABSTRACT

Background: Locally advanced oral cavity cancers have poor prognosis despite all multimodality local treatments. In these patients, neoadjuvant chemotherapy may be helpful because it can reduce the size of the tumour and enable final surgery.

Materials and methods: Prospective observational study: secondary data analysis of patients treated with neoadjuvant chemotherapy (NACT) for a year after they were diagnosed with locally advanced oral cavity cancers. Patient characteristics, chemotherapy received, toxicity, clinical response rates, available local treatments, and pathological response rates were all examined in the data analysis. SPSS version 20 was used for the statistical analysis.

Results: The study included 60 patients, of whom 27 of 60 (45%) were female and 33 of 60 (55.0%) were male. Most of the patients were in the age range of 51 to 60. Smoking, alcoholism, and tobacco/pan chewing were the most prevalent risk factors. Prior to definitive treatment, the clinical responses were documented following NACT, and all 60 patients received a TPF regimen as neo-adjuvant chemotherapy for two or three cycles. Total of 31% of responded to Neoadjuvant chemotherapy.

Conclusion: Locally advanced oral cavity cancers that are technically incurable were successfully transformed into operable diseases by NACT. Clinical and pathological findings

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

of response rates are significantly correlated after NACT. After NACT, there is no rise in the incidence of surgical complications.

Keywords: Oral cavity cancers, neoadjuvant chemotherapy, Smoking.

INTRODUCTION

The sixth most frequent type of cancer reported worldwide is oral cancer. With an age-adjusted incidence of 20 cases per 100,000 people, India has one of the highest rates of oral cancer worldwide [1]. Over 60% of patients in developing nations like India present with locally advanced illness [2]. The majority of oral cancers are squamous cell carcinoma and as per American Joint Committee on Cancer (AJCC) 8th edition, T4a tumors (moderately advanced disease) are conventionally considered resectable tumors, whereas T4b tumors are unresectable [3]. However, due to the high surgical morbidity linked to T4a oral cavity tumours, some may be technically unresectable if they exhibit characteristics such as disease, bone and muscle involvement and extensive skin infiltration [4].

It is difficult to achieve local control of locally advanced oral cavity cancers with just surgery or radiation therapy. Chemotherapy has been used more frequently recently, either as a neoadjuvant (chemotherapy before definitive surgery or radiation).The treatment of locally advanced, technically incurable oral cavity cancer is still a clinical conundrum [6]. Pignon JP et al.,[7-9] in their meta-analysis included 31 trials on induction chemotherapy in head and neck cancer, failed to demonstrate significant survival benefits.There were fewer cancers of the oral cavity in these trials, which included a comprehensive group of all head and neck cancer subsites. But according to recent studies like TAX 323 and 324, patients with advanced head and neck squamous cell carcinoma who received a three-drug neoadjuvant chemotherapy (NACT) regimen that included taxane (docetaxel), cisplatin, and 5-fluorouracil

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

(TPF) had a better prognosis than those who received a two-drug NACT regimen that only included cisplatin and 5-fluorouracil (PF). Once more, though, these trials covered all head and neck subsites, not just cancers of the oral cavity. In order to improve the overall outcome, a prospective observational analysis of patients with locally advanced T4a oral cavity cancer-(buccal mucosa and tongue) who were offered NACT was conducted. The goal was to make the patients resectable.

Materials and methods

A total of 60 patients with good performance status, muscle involvement, patients with skin infiltration, bone involvement, and lesions crossing midline were included. Patient with poor performance status, metastatic disease, involvement of the skull base, encasement of the carotids and involvement of the masticator space (cT4b) were excluded. Patients underwent clinical examination and specific measurements of primary and nodal disease were noted as target I and target II lesions respectively. Contrast studies of local part (contrast-enhanced computerised tomography (CECT) of the base of skull to sternal notch for all oral cavity primaries except tongue for which magnetic resonance imaging was required) and CECT Chest for metastatic work up was also performed in these patients. The size of the lesions was also recorded before starting the neoadjuvant chemotherapy (NACT). The chemotherapy regimen of choice was docetaxel 75 mg/m2, cisplatin 75 mg/m2 and 5 flurouracil 750 mg/m2(TPF). Response assessment was done clinically after completion of each cycle of chemotherapy. Further chemotherapy cycles were offered to the eligible patients up to a maximal of two to three cycles depending on the clinical response of the patients and tolerability. Reassessment imaging was done after 2 to 3 cycles of neo-adjuvant chemotherapy, and assessed the radiological response, using Standard World Health Organization (WHO) RECIST1. A: For dichotomous data, we used the 1 criteria to assess the response after NACT.

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

Complete Response: Disappearance of all target lesions (any pathologic lymph node must have reduction in short axis to 30% reduction in the sum of the highest diameter of the target lesions, using as comparison the baseline total of the diameters.

Partial response: a 30% or greater drop in the target lesions' longest diameter sum, using the baseline sum of the diameters as a benchmark.

Stable disease: not meeting the criteria for reduction (above) sufficient to qualify as a partial response or for increase (above) sufficient to qualify as progressive disease.

Progressive disease: 20% or an absolute increase of 20% in the sum of the longest diameter of the target lesions

Surgery was performed in tumours with complete or partial response or in a few cases with stable disease. These patients subsequently received definitive radiotherapy if progressive or stable disease. Patients who achieved a complete response or partial response proceeded to surgical modalities with or without reconstructions and adjuvant therapy in the form of radiotherapy was planned for patient with cT4a. In the first year these patients were followed-up monthly, followed by two monthly follow-up in the second year and three monthly follow-up in the third year, Biannual followed up after that.

Results

Table 1 shows that of the 60 patients with locally advanced oral cancers who were enrolled in this study, 25 of 60 (41.67%) were female and 35 of 60 (58.33%) were male.

Table 1: Gender distribution of the patients

Gender	No. of patients	Percentage
Male	17	56.6

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

Female	13	43.3

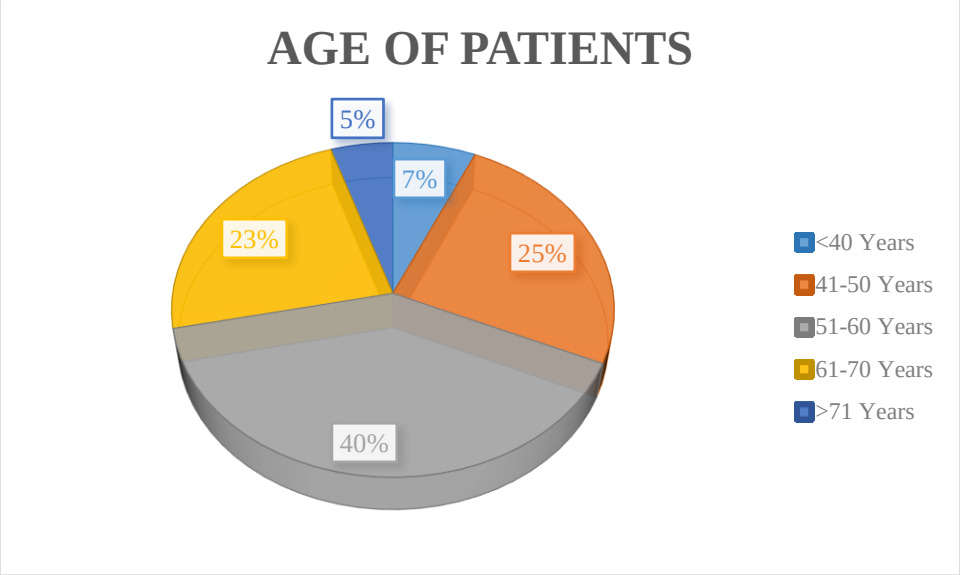

Figure 1: Age distribution of the patients

Table 2: Risk factors

Risk factors	No. of patients	Percentage
Tobacco/Pan chewer	23	76.6
Smoker	25	83.33
Alcoholic	18	60

Table 3: Subsites of lesion

Subsites	Number	Percentage
Buccal mucosa	35	58.33
Lower alveolus	15	25.00
Tongue	5	8.33
Floor of mouth	2	3.33
Upper alveolus	3	5.00

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

Table 4: Response to therapy

Response	No. of patients	Percentage
Progressive disease	33	55.00
Partial response	11	18.33
Complete response	4	6.67
Stable disease	12	20.00

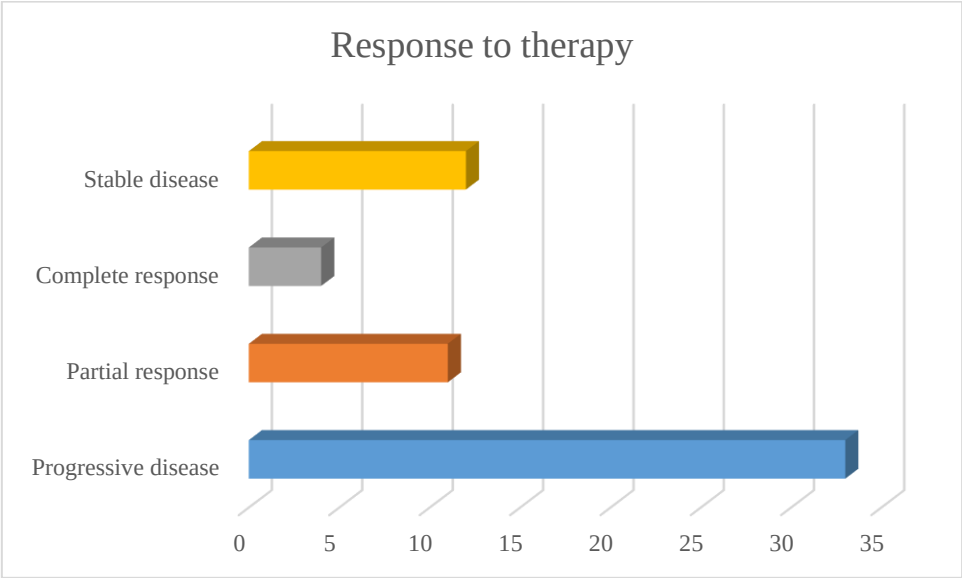

Figure 2: Response to therapy

In the surgery group, the disease-free survival was 12 months, while in the RT group, it was 16 months. The overall survival rate was 25% in the RT group and 50% in the surgery group (P value = 0.822). The overall mortality rate was 73.7% in the RT group and 22.2% in the surgery group (P value - 0.001).

Discussion

Stage I and II cancers of the oral cavity require a single modality management strategy, whilst stage III and IV cancers require a multimodality approach [10]. Clearly,

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

improvements to radiation techniques, especially intensity-modulated radiation therapy (IMRT), have led to increased local-regional control of the tumour [11]. However, distant recurrences increasingly impact overall survival. To cure this problem, into 2012, the investigators hypothesized that chemotherapies set as induction or neoadjuvant in the presence of definitive narrow based treatment/surgery would significantly act on the obtainer of something attorney in contrast, as well as to reduce comes back and invade wrinkle [12].Several of the Phase 3 trials that have evaluated the addition of a taxane agent (either docetaxel or paclitaxel) to induction cisplatin and 5-fluorouracil (5-FU) therapy have shown improved response rates, disease-free survival, and overall survival in patients treated with this triplet induction chemotherapy[13].

Our study demography, thus highlighted that, males were predominant gender (58.33%), in comparison to females (41.67%). The most common age group was between 51 - 60 years. In line with our study, males were predominantly affected in the study on the "Socio demographic profile of oral cancer patients residing in Tamil Nadu" [14]. In another such cohort study 44.5% were smokers and 39.8 % were alcoholics, which were also comparable to our study, 53.33 % of smokers and 38.33 % of alcoholics respectively.

Patil et al. published a retrospective study of 123 patients with technically unresectable locally advanced oral cavity cancers[15]. The patients received neoadjuvant chemotherapy (NACT) including TPF or TP followed by an assessment of resectibility. The response rate of the three drug was 32% which was similar to the data available with our study.

Dhruv Patel et al., investigated the feasibility for the down staging of locally advanced oral cancers with three cycles of TPF (docetaxel, cisplatin, 5FU) followed by response assessment prior to surgery in 32 patients [16]. In this study, 12 out of 32 patients

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

(37.5%) were classified as good responders, including two patients (6.67%) with a Complete Response (CR). Compared to our study with 25 % response rate including patients only.

Resectability rate in our study was comparable to that of the study of TAX 324 study who had a resectability rate of 30 % and similar to that of Joshi et al, who observed a resectability rate of 30.9 % among patients with locally advanced oral cancers receiving 2 cycles of neoadjuvant chemotherapy[17].

An international, multicenter, randomized, open label, phase 3 TAX 324 trial which compared the survival benefit for 3 cycles TPF vs 3 cycles of PF in the same population (locally advanced oscc, stage III and stage IV) got better outcome than current study as phase 1–2 Clinical report in Tax 324 group were on April 2004. Similar to our study led to a median overall survival of 35 months and 50% survival rate in the surgery group[18].

In a study by Zhonget. al, in 109 unresectable patients treated with neoadjuvant TPF x 2, surgery and adjuvant RT 2-year OS was 68.2% [19]. Overall survival of 50 % and a disease free survival of 48 % respectively were recorded in our study.

One another limitation of our study which may play a critical role is – Patients who are good responders to the neoadjuvant chemotherapy are only taken for surgery hence the conventional belief that patients turned up for surgery do better as the disease biology is in their favour.

Certain oral cavity cancers not amenable to upfront surgery can achieve 30 % resectability and 50 % survival with neoadjuvant chemotherapy with TPF regimen. According to the clinical response and outcome in this patient, we suggest that neoadjuvant chemotherapy may be an effective and safe approach for R0 resection[20]. It may also relate

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

to improved survival among resected patients, and could be regarded as the standard of care in this setting.

Conclusion

In a developing nation like India, moderately advanced oral cavity cancer presents a significant therapeutic challenge. About half of patients with moderately advanced oral cavity cancers that are technically incurable can have their cancers resectable with NACT. In general, the most crucial treatment option for these patients is still surgery. To prove the benefits of NACT in moderately advanced oral cancers, larger prospective randomised trials involving three medication regimens are required.

Reference

1. Kulkarni MR. Head and neck cancer burden in India. Int J Head Neck Surg 2013; 4:29–35
2. Pfister DG, Spencer S, Brizel DM, Burtness B, Busse PM, Caudell JJ, et al. Head and neck cancers, version 1.2015. J NatlComprCancNetw 2015; 13:847–55
3. Patil VM, Noronha V, Joshi A, Muddu VK, Gulia S, Bhosale B, et al. Induction chemotherapy in technically unresectable locally advanced oral cavity cancers: Does it make a difference?. Indian J Cancer 2013; 50:1–8
4. Kirkwood JM, Miller D, Weichselbaum R, Pitman SW. Predefinitive and postdefinitive chemotherapy for locally advanced squamous carcinoma of the head and neck. Laryngoscope 1979; 89:573–81
5. Lustig RA, DeMare PA, Kramer S. Adjuvant methotrexate in the radiotherapeutic management of advanced tumors of the head and neck. Cancer 1976; 37:2703–8

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

6. Jacobs C. Adjuvant and neoadjuvant treatment of head and neck cancers. SeminOncol 1991; 18:504–14
7. Pignon J, Bourhis J, Domenge C, Designé L. Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: Three meta-analyses of updated individual data. MACH-NC collaborative group. Meta-analysis of chemotherapy on head and neck cancer. Lancet 2000; 355:949–55
8. Pignon JP, le Maître A, Maillard E, Bourhis J MACH-NC Collaborative Group. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients. RadiotherOncol 2009; 92:4–14
9. Posner MR, Hershock DM, Blajman CR, Mickiewicz E, Winquist E, Gorbounova V, et al. Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer. N Engl J Med 2007; 357:1705–15
10. National Comprehensive Cancer Network: NCCN Clinical Practice. Guidelines in Oncology: Head and Neck Cancers, Version 1201210.6004/jnccn.2020.0031http://www.nccn.org/professionals/physician_gls/pdf/headand-neck.pdf
11. B Cho Intensity-modulated radiation therapy: a review with a physics perspectiveRadiatOncol J2018361110
12. SJ Wong M Machtay Y Li Locally recurrent, previously irradiated head and neck cancer: concurrent re-irradiation and chemotherapy, or chemotherapy alone?JClin Oncol2005241726538
13. Tata Institute of Social Sciences (TISS), Mumbai and Ministry of Health and Family Welfare, Government of India. Global Adult Tobacco Survey GATS 2 India 2016-17

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

14. VM Patil V Noronha A Joshi VK Muddu S Gulia B Bhosale Induction chemotherapy in technically unresectable locally advanced oral cavity cancers: does it make a difference?Indian J Cancer201350118
15. D Patel E Saldanha B Joseph S Ghosh V Dhakad S Desai Role of Neoadjuvant Chemotherapy in Oral Cavity SCC: A Surgical Oncologists Experience at Tertiary Care Institute - DhruvPatelEur J Clin Oncol20073114
16. A Joshi VM Patil V Noronha S Juvekar A Deshmukh P Chatturvedi Is there a role of induction chemotherapy followed by resection in T4b oral cavity cancers?Indian J Cancer201350434955
17. R Haddad A O'Neill G Rabinowits R TishlerFoKhuri D Adkins Induction chemotherapy followed by concurrent chemoradiotherapy (sequential chemoradiotherapy) versus concurrent chemoradiotherapy alone in locally advanced head and neck cancer (PARADIGM): A randomised phase 3 trialLancet Oncol201314325764
18. JH Lorch O Goloubeva RI Haddad K Cullen N Sarlis R Tishler Induction chemotherapy with cisplatin and fluorouracil alone or in combination with docetaxel in locally advanced squamous-cell cancer of the head and neck: long-term results of the TAX 324 randomised phase 3 trial - Jochen H LorchLancet Oncol20111221539
19. LP Zhong CP Zhang GX Ren W Guo WN William J Sun Randomized phase III trial of induction chemotherapy with docetaxel,cisplatin, and fluorouracil followed by surgery versus up-front surgery in locally advanced resectable oral squamous cell carcinomaJClin Oncol201331674451
20. A Parmar M Macluskey NM Goldrick DI Conway AM Glenny JE Clarkson Interventions for the treatment of oral cavity and oropharyngeal cancer:

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 03, 2025

chemotherapyCochrane Database Syst

Rev20071212CD00638610.1002/14651858.CD006386.pub4