Original Article

Interim Analysis of Outcome in Postoperative Cases of Squamous Cell Cancer of Oral Cavity Receiving Adjuvant Radiotherapy/Radiochemotherapy: An Observational Descriptive Study

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Abstract

Introduction: Squamous cell carcinoma of the oral cavity and lip is the most common type of head-and-neck cancer in India. Various tumor and treatment-related factors influence locoregional control. We aim to assess the impact of these prognostic factors on 2-year disease-free survival (DFS) in postoperative cases of cancer in the oral cavity. We present the interim analysis of our study. **Materials and Methods:** This was a prospective observational descriptive study conducted in the radiation oncology department. An interim analysis was performed at a minimum of 6 months following radiotherapy or sooner if an event occurred. Patients received either postoperative radiotherapy or chemoradiotherapy, depending on the presence of risk factors. We documented histopathological parameters and treatment-related factors. To evaluate the impact of risk factors on survival, we applied the log-rank test and Cox regression analysis. $P \leq 0.05$ was considered statistically significant. **Results:** A total of 22 patients were included in this interim analysis. The median DFS was 5.6 months. Kaplan–Meier survival analysis revealed that DFS was significantly poorer in patients with a higher pathological nodal (pN) stage ($P = 0.000$), those with positive lymphovascular invasion (LVI+) compared to those with negative LVI (142.62 ± 47.07 days vs. 253.61 ± 10.5 days; $P = 0.004$), and those with positive extranodal extension (ENE+) compared to patients without ENE (90 ± 40.41 days vs. 254.32 ± 9.54 days; $P = 0.000$). In univariate analysis using Cox regression, higher pN status (hazard ratio [HR]: 4.802; confidence interval [CI]: 1.236–13.482; $P = 0.021$) and LVI+ (HR: 15; CI: 1.39–177.72; $P = 0.029$) were found to be associated with poor survival outcomes. **Conclusions:** In this interim analysis, DFS was significantly impacted by high nodal burden, ENE+, and the presence of LVI. Other pathological prognostic factors and treatment-related factors did not significantly affect DFS.

Keywords: Cancer oral cavity, disease-free survival, nodal status, outcome, prognostic factors

Introduction

According to the GLOBOCAN 2022, oral cavity and lip cancer is the most common cancer among males in India, with 107,812 cases accounting for 15.6% of all cancer cases.[1] The most prevalent histological variant is squamous cell carcinoma, which is largely attributed to cultural habits such as chewing tobacco, gutka, betel nut, and smoking.

In India, 70%–80% of cases present at an advanced stage, necessitating combined modality treatment. Neoadjuvant chemotherapy may be administered in borderline operable and inoperable cases. After radical surgery, adjuvant radiotherapy is recommended for patients with a pathological tumor stage of pT3, pT4, N2, or N3, as well as those exhibiting positive perineural invasion (PNI+) or positive lymphovascular invasion (LVI+) to enhance locoregional control. In cases

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with high-risk features such as extranodal extension (ENE) and positive resection margins, concurrent chemoradiotherapy has also been advised.[2]

Key risk factors for locoregional failure and distant metastasis include tumor size, local tumor extent, lymph node status, ENE, margin status, LVI, PNI, tumor differentiation, and the worst pattern of invasion (WPOI) V.[3] Furthermore, treatment-related factors such as the surgery-to-radiotherapy interval (SRI), radiotherapy duration (RD), and total treatment time (TTT) can significantly affect disease-free survival (DFS).[4]

Locally advanced oral cavity cancer often results in poor outcomes, with approximately 30% of cases experiencing locoregional failure and 25% showing distant metastasis. The 5-year survival rate is around 50%.[5]

Our aim is to assess the burden of various histopathological prognostic features and treatment-related factors in our postoperative patients with oral cavity cancer, as well as their impact on DFS at 2 years. The reported DFS rates for oral cavity cancer cases at 1 year and 2 years are 78.4% and 68.9%, respectively.[6]

Materials and Methods

Study design

This study is a prospective observational descriptive research project. It was conducted following the ethical guidelines established in the Declaration of Helsinki and the ICMR guidelines. Written informed consent was obtained from all patients, and approval from the Institutional Review Board (IRB) and the Institutional Ethics Committee (IEC) has been granted for the study (ECR/769/INST/JH/2015/RR-21-166).

Inclusion criteria

All new cases of postoperative squamous cell carcinoma of the oral cavity requiring adjuvant treatment will be eligible for the study. Participants must be aged between 18 and 75 years and have a performance status (PS) of 0–2.

Exclusion criteria

Candidates will be excluded from the study if they meet any of the following conditions: PS > 2, presence of distant metastasis, cancer located in nonoral cavity sites, HIV-positive status, HBsAg positivity, hepatitis C virus positivity, tuberculosis, uncontrolled diabetes mellitus or hypertension, any psychiatric illness, cardiac disorders, pregnancy, dual malignancy, a previous history of cancer, prior radiotherapy, or the presence of any of these factors.

Sample size

The estimated sample size for this study was calculated using the following formula: estimated sample size: $4pq/d2$

p = prevalence from previous studies

q = 100 − P

d = allowable error (5%–20%).

According to the formula, a total of 270 patients will be included in the study based on a DFS rate of 78.4% at 1 year (as referenced in introduction citation "6"). To account for potential dropouts, estimated to be around 10% of the recruited patients, an additional 27 participants will be recruited. Therefore, the overall target is to enroll 301 patients. Recruitment will continue until the target number of patients is reached.

Study setting

Postoperative cases of oral cancer with squamous cell cancer as a histological type visiting the radiation oncology department as per the set inclusion criteria were included in the study. We are submitting the interim analysis with at least 6 months post-treatment status, or earlier if an event occurs. Cases were enrolled from February 2024 after IRB and IEC approval. At baseline, height, weight, and routine blood tests (complete blood count [CBC], kidney function test [KFT], and liver function test [LFT]) were recorded. Dental prophylaxis was advised prior to the start of radiotherapy. All patients were screened for any lung metastasis by chest X-ray posterior-anterior as minimum. Further metastatic workup was not done in view of very low incidence of metastasis to other sites. Patients were subjected to concurrent chemoradiotherapy or radiotherapy alone as per the detailed histopathological report. Radiotherapy was advised to patients having either of these factors, i.e., pT3, pT4, depth of invasion (DOI) >5 mm, any N+, LVI+, and PNI+. Concurrent chemotherapy (CCT) indications were positive margin, >N2 nodal status, and presence of ENE. Radiotherapy was for a total dose of 60–66 Gy/30–33#, 5 fractions/week, and CCT drug regimen was with weekly injection cisplatin at a dose of 35 mg/m^2. Radiation Therapy Oncology Group guidelines for contouring and Quantitative Analyses of Normal Tissue Effects in Clinics guidelines for organ at risk constraints were followed. Radiotherapy was delivered by 6 MV ELEKTA Synergy Linear Accelerator by volumetric-modulated arc therapy (VMAT)/two-dimensional (2D) technique. Weekly monitoring of CBC, LFT, KFT, and weight was done for all patients during radiotherapy. Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 was used to assess treatment-related toxicities on a weekly basis during radiotherapy. Supportive care was given as required in the form of analgesics, anti-inflammatory. Intravenous fluids, Ryle's tube feeding, soda-bicarbonate (baking soda), and salt gargles were advised to the patients as required. Treatment-related toxicity will be presented in another publication. Posttreatment monthly FU for 3 months, after that 3 monthly for 2 years for all patients was advised. DFS was calculated as the period of time without any evidence of locoregional recurrence from the completion of adjuvant treatment of radiotherapy/radiochemotherapy. SRI is defined here as an interval in days between surgery and radiotherapy initiation. RD is the total number of days to complete radiotherapy. TTT will be defined as the total time period from the surgery till completion of adjuvant radiotherapy.

Statistical analysis

The categorical variables were described as frequency or

percentage, mean, and median using descriptive statistics. Kaplan–Meier survival analysis was done to calculate DFS. Log-rank test and Cox regression analysis were applied to assess the impact of risk factors on survival. $P \leq 0.05$ was considered statistically significant.

Results

There were 22 patients for this interim analysis. The median age was 56 years (35–72 years). Males were in the majority 16 (72.7%). Tumor characteristics and treatment-related factors are presented in Table 1.

The most common primary tumor location was tongue ($n = 8$; 36%), followed by buccal mucosa ($n = 7$; 31%). Stage III was the most common ($n = 11$; 50.0%), followed by Stage IVA ($n = 9$ 40.1%) at presentation. In the pathological nodal (pN) 3 category ($n = 2$; 10.9%), there were 10 lymph nodes positive, putting these patients in the high-risk category for locoregional recurrence/failure. Tumor depth of more than 10 mm was observed in 12 (54.5%) cases and also intratumoral PNI in 12 (54.5%) cases. LVI positivity was seen in only 4 (18.2%) of cases. Only 4 (18.2%) cases could complete radiotherapy in 42 days. Nine (45.4%) patients could complete radiotherapy within 43–63 days, and the rest 8 (36.4%) patients took a longer time to complete their radiotherapy. Similarly, by 7–8 weeks, 14 (63.66%) patients could take up adjuvant radiotherapy. For 7 (31.8%) cases, SRI was more than 8 weeks. The TTT was within 100 days for 8 (36.4%) cases, and another 3 (13.6%) patients could complete all treatment in 101–110 days. For 11 (50%) cases, it was more than 110 days. The median DFS was 5.6 months (170.50 days). Two (9%) out of 22 patients had neoadjuvant chemotherapy with the regimen injection paclitaxel 175 mg/m^2 and injection carboplatin with Area under curve (AUC) 5–6, with a 3-weekly schedule. CCT was indicated in 3 (13.6%) patients. Patient 1 had cancer of the buccal mucosa and gingivobuccal sulcus, with N3b and ENE+ status. He could only tolerate 2 cycles of CCT with cisplatin injection. Another patient with a tongue as primary and ENE+ could receive 1 cycle of CCT, and she did not comply with subsequent cycles. Another patient with primary as central arch could not receive CCT as per physician discretion anticipating poor tolerance. Two (66%) out of three patients with ENE+ received radiotherapy at a dose of 66 Gy/33#/5#/week. One (33%) patient did not want to take beyond 30# of radiotherapy. All patients except one received conformal radiotherapy by VMAT, i.e., 21 (95.45%) and 1/22 (4.5%) by 2D, respectively, on 6 MV ELEKTA Synergy Linear Accelerator.

On Kaplan–Meier survival analysis, DFS was found to be significantly affected by nodal status, ENE+, and the presence of LVI. The mean survival was significantly lower in patients with pN3 with $P = 0.000$ [Figure 1]. In a similar manner, the presence of LVI affected the DFS, with a lower mean survival of 142.62 ± 47.07 days compared to 253.61 ± 10.5 days in patients without LVI (LVI−), resulting in a P value of 0.004 [Figure 2]. Moreover, also ENE positivity was associated with worse DFS, i.e., 90 ± 40.41 days vs. 254.32 ± 9.54 days ($P = 0.000$) [Figure 3]. In the current study, treatment-related factors such as the interval between surgery and radiotherapy, as well as RD, SRI, and TTT, were found not to impact DFS ($P > 0.005$). On Cox regression univariate analysis, pN status was associated with poor survival ($P = 0.021$, hazard ratio [HR]: 4.082; confidence interval [CI]: 1.236–13.482) and also LVI ($P = 0.029$, HR: 15; CI: 1.39–177.72). However, on multivariate analysis, none of the factors show a significant effect on DFS. Furthermore, pT, PNI, DOI, WPOI, close margin, and tumor location were not found to impact DFS in this interim analysis.

Locoregional failure was observed in 4 (18.2%) cases. There was no distant metastasis reported. Two (50%) out of four of these patients were put on metronomic therapy with oral methotrexate + celecoxib and subsequently methotrexate + erlotinib. One patient with a tongue as primary was sent for surgical resection. One patient defaulted after recurrence.

Discussion

Patients presenting with advanced disease and possessing aggressive tumor biology often fail to respond to even the most intensive combination therapies, leaving them with limited options for salvage treatment.[7,8] The first 2 years following treatment are particularly critical in head-and-neck cancer (HNC), as up to 84% of recurrences are observed during this time.[9] Moreover, early relapses or recurrences of oral cancer, occurring within 18 months, are associated with poorer survival outcomes compared to late relapses. The mortality rate for these early cases can be as high as 90%.[10]

In our observations, carcinoma of the tongue was the most common primary tumor ($n = 8$; 36.4%), with a predominance of Stage III cases ($n = 11$; 50.0%). Notably, 12 (54.5%) patients demonstrated a DOI >10.1 mm, and 12 (54.5%) patients presented with pathological N0 status. PNI was positive in 12 (54.5%) cases. In addition, 9 (40.9%) patients were classified as Stage IVA, and 4 (13.6%) patients had ENE+. All cases underwent adequate neck dissection. DFS was significantly impacted by high nodal burden ($P = 0.000$). Patients with ENE+ had a DFS of 90 days (±40.41) compared to 254.32 days (±9.54) for those without ENE ($P = 0.000$). The presence of LVI also affected DFS, with patients showing a DFS of 142.62 days (±47.07) versus 253.61 days (±10.5) in those without LVI ($P = 0.004$). In our interim analysis, pT, PNI, DOI, WPOI, close margin, and tumor location did not have a significant impact on DFS. Univariate Cox regression analysis indicated that higher pN status (HR: 4.802; CI: 1.236–13.482; $P = 0.021$) and LVI+ (HR: 15; CI: 1.39–177.72; $P = 0.029$) were associated with poorer survival. However, in multivariate analysis, none of these factors showed a significant effect on DFS. Factors such as pT, PNI, DOI, WPOI, close margin, and tumor location also did not influence DFS in this interim analysis.

Table 1: Tumor and treatment-related characteristics

Tumor characteristics	Patients ($n=22$), *n* (%)
Primary tumor location	
Buccal mucosa	7 (31.8)
Lower alveolus/GBS	5 (22.7)
Tongue	8 (36.4)
Lip	1 (4.5)
RMT	1 (4.5)
Tumor size (cm)	
pT1 (0–2)	3 (13.6)
pT2 (2.1–4)	10 (45.5)
pT3 (>4.1)	9 (40.9)
pN	
N0	16 (72.7)
N1	1 (4.5)
N2	3 (13.6)
N3	2 (9.1)
ENE	
ENE+	3 (13.6)
ENE−	19 (86.3)
Stage	
III	11 (50.0)
IVA	9 (40.9)
IVB	2 (9.09)
Tumor depth (mm)	
0–5	1 (4.5)
5.1–10	9 (40.9)
>10.1	12 (54.5)
Margin	
Free	18 (81.8)
Close	4 (18.2)
LVI	
LVI+	4 (18.2)
LVI−	18 (81.8)
PNI	
PNI+ intratumoral	12 (54.5)
PNI−	9 (40.9)
PNI indeterminate	1 (4.5)
WPOI	
WPOI (3)	14 (63.6)
WPOI (4)	6 (27.3)
WPOI – not available	2 (9.1)
RD (days)	
42	4 (18.2)
43–63	10 (45.4)
63–200	8 (36.4)
SRI (days)	
42	1 (4.5)
43–56	14 (63.66)
57–200	7 (31.8)
TTT (days)	
Up to 100	8 (36.4)
101–110	3 (13.6)
111–250	11 (50.0)
Locoregional recurrence	
Yes	4 (18.2)
No	18 (81.8)

GBS: Gingivobuccal sulcus, TTT: Total treatment time, SRI: Surgery-to-radiotherapy interval, RD: Radiotherapy duration, WPOI: Worst pattern of invasion, PNI: Perineural invasion, LVI: Lymphovascular invasion, ENE: Extranodal extension, pN: Pathological nodal stage, pT: Pathological tumor stage, RMT: Retromolar trigone

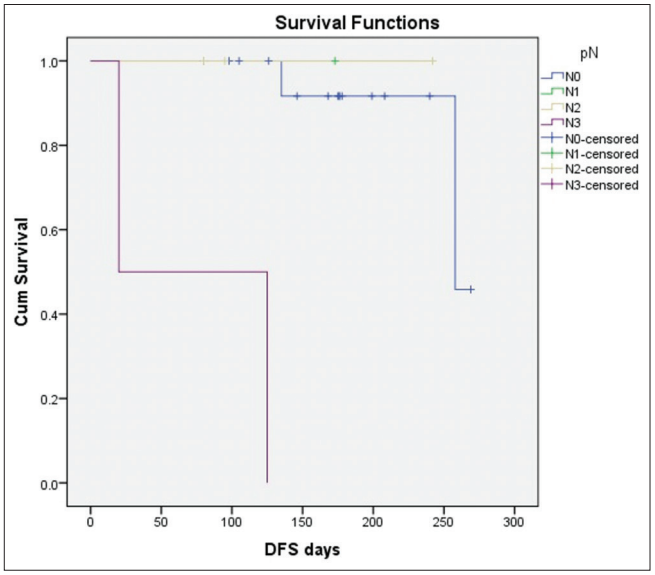

Figure 1: Kaplan–Meier survival curve showing poor survival with higher nodal status. No=pN0, N1=pN1, N2=pN2, N3=pN3

Tumor size and extracapsular spread adversely influence outcomes due to an increased risk of lymph node metastasis and challenges in achieving clear surgical margins. This ultimately affects locoregional control and overall survival (OS). The mortality risk in patients with recurrent disease exhibiting extracapsular spread in the primary tumor is 0.35 times higher than in those without this characteristic.[9,11]

In a retrospective analysis of 517 patients of oral squamous cell cancer, the authors investigated the possible risk factors impacting locoregional recurrence. All of the patients underwent radical primary surgery and appropriate neck dissection followed by adjuvant radiotherapy–chemotherapy as per standard. Tumor grade was found to be an independent predictor of locoregional recurrence on univariate as well as multivariate analysis ($P = 0.016$); however, other factors such as number of positive lymph nodes ($P = 0.041$), extracapsular spread ($P = 0.028$), and postoperative radiotherapy (PORT; $P = 0.018$) were found be having significant impact on univariate analysis only.[12] We could observe on Cox regression univariate analysis that pN status was associated with poor survival ($P = 0.021$, HR: 4.082; CI: 1.236–13.482) and also

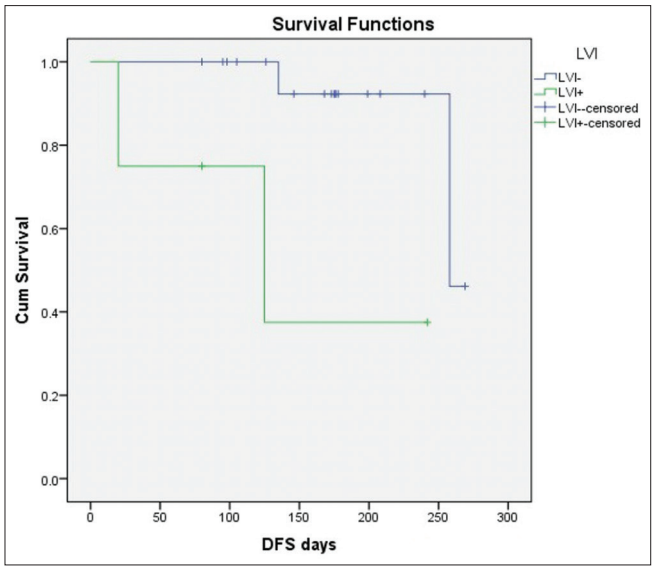

Figure 2: Kaplan–Meier survival curve showing poor survival with positive lymphovascular invasion positive. LVI+: Lymphovascular invasion positive; LVI−: Lymphovascular invasion negative

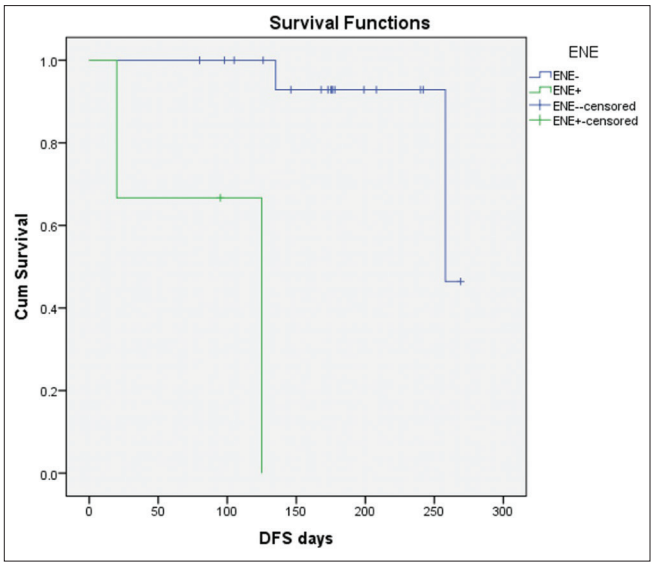

Figure 3: Kaplan–Meier survival curve showing poor survival with extranodal extension positive. ENE+: Extranodal extension positive; ENE−: Extranodal extension negative

LVI (P = 0.029, HR: 15; CI: 1.39–177.72). However, in the multivariate analysis, none of the factors showed a significant effect on DFS.

In a retrospective study of 691 treated cases of oral cancer patients, 159 recurrent cases were included in the study. The 5-year survival was 62% and 10-year survival was 47%. They also reported that 60% of recurrent cases were in the first 2 years. Margin status (P = 0.023), extracapsular spread in the primary tumor (P = 0.003), the timing of recurrence (P < 0.001), and performance of salvage treatment were found to be independently affecting the OS on multivariate analysis; however in the univariate analysis, several factors were found to have a significant impact on survival, including T stage, N stage, tumor grade, LVI), lymph node ratio, and treatment modality (P = 0.001). Furthermore, the analysis indicated that higher N stage was associated with poorer disease-free survival (DFS) outcomes (P < 0.001).[11] Another author could demonstrate the impact of nodal staging on survival by both univariate and multivariate analyses.[13]

Margin status is an independent prognostic factor and independent of T, N, tumor grading, extracapsular spread, and adjuvant treatment regimen for OS in multivariate analysis.[13] The risk of death following a relapse in patients with negative margins is 50% lower than in patients having positive margins.[11]

The presence of LVI signifies an aggressive biological tumor, an important risk factor for nodal metastasis, and has been associated with poor locoregional control and decreased OS.[14] In early postoperative cases with T1-T2N0 status, the presence of PNI, LVI, or DOI greater than 5 mm indicates that PORT has improved outcomes. This has been well observed in a retrospective study including 528 patients with primary as cancer oral tongue with pT1-pT2N0 status; a total of 147 cases (27.5%) received postoperative radiotherapy (PORT). Multivariate analysis indicated that patients with perineural invasion (PNI) and/or lymphovascular invasion (LVI) who underwent PORT experienced improved disease-free survival (DFS) rates (76% vs. 47%, P = 0.002). Additionally, a DFS benefit from PORT was observed in patients with a depth of invasion (DOI) greater than 5 mm (80% vs. 64%, P = 0.006).[15] However, some studies have reported no significant association between overall survival (OS) and PNI in relation to PORT. This lack of association may be attributed to factors such as small sample sizes, retrospective study designs, single-center studies, and various confounding factors.[16]

The presence of more than one high-risk factor also increases the local failure rate. A retrospective review of 130 patients with oral squamous cell carcinoma (OSCC) demonstrated that a significant proportion of patients exhibited at least one high-risk feature: positive margins in 52% of cases, close margins (between 0.1 and 5 mm) in 27%, and ECE in 45%. The study revealed that the combination of two high-risk factors—close or positive margins alongside ECE(+) led to poorer outcomes. Specifically, the 5-year locoregional control (LRC) rate was 37% compared to 70% (P = 0.001), the progression-free survival rate was 26% versus 60% (P < 0.001), and the overall survival rate was 13% compared to 43% (P < 0.001) when compared to patients with only a single high-risk factor.[17]

There has been much emphasis regarding the timing of adjuvant radiotherapy. Postoperative RT should be initiated within 6 weeks (42 days) of surgery for head-and-neck squamous cell cancer as per the recommendations of the American College of Radiology and National Comprehensive Cancer Network. Adjuvant RT in 6 weeks of surgery improves local control with an odds ratio of 2.89 in individuals receiving

RT during this window. However, it has been reported that for 55%–67% of patients, PORT could not be started within this time frame.[18,19] There are various operative and medical factors, which can lead to late appointments for adjuvant radiotherapy. Factors include prolonged hospital admission, fistula, chyle leak, venous congestion, wound breakdown, flap necrosis, and hematoma, abscess formation and the medical complications may include pneumonia, cardiac arrhythmias, heart failure, acute kidney injury, urinary tract infections, hypotension, dyselectrolytemia, and, also the instances where patients do not comply with medical advice. All these factors can delay the timing to start adjuvant treatment as well as prolongation of treatment package time (TPT).[20]

In a multicenter study prospective study with 1368 patients, 80% of patients had prolonged (>42 days) times to PORT initiation, and 26% of patients had treatment time intervals >46 days. In the analysis, S-PORT, T, and N were significant factors affecting OS on univariate analysis. However, on multivariate analysis, prolonged S-PORT showed an independent association with worse OS (66% vs. 77%) (HR: 1.39; 95% CI: 1.07–1.8).[21]

Optimal treatment time (OTT) is the length of time a patient receives radiotherapy. Danish Head and Neck Cancer Group recommends a maximum OTT of 41 days for moderately accelerated radiation treatment and 48 days for conventional treatment. TTP is the number of days between surgery and the end of the end of radiation therapy (RT). Surviving tumor cells undergo accelerated repopulation in response to RT. It has been proposed that TPT in a range of 68–100 days can represent an ideal TPT.[22,23]

Petery *et al*. conducted a retrospective study involving 214 patients with postoperative oral squamous cell carcinoma (OSCC), suggesting that the ideal duration of treatment is less than 105 days. Both terms have been used in the literature and refer to the same concept. The study analyzed various factors influencing event-free survival (EFS). The authors found that a TPT of less than 105 days (HR: 1.13, 95% CI: 0.691–0.841, P = 0.018), pathologic Stage IV (HR: 2.456, 95% CI: 1.423–4.240, P = 0.001), PNI(+) (HR: 1.66, 95% CI: 1.090–2.528, P = 0.018), and extranodal extension (ENE) (P = 0.012) negatively impacted EFS.[20] Additionally, a large retrospective cohort study involving 35,167 patients with nonmetastatic HNC who underwent definitive surgical dissection and adjuvant RT supported these findings. In this cohort, a TPT of less than 11 weeks was associated with improved overall survival (OS) when compared to a TPT of 12 to 13 weeks (HR: 0.90, 95% CI: 0.83–0.97).[24]

A retrospective cohort study involving a large sample of 16,733 HNC cancer patients, of which 41.4% had OCC, defined overall treatment time as the duration from surgery to the conclusion of radiotherapy. The overall treatment time of 13 weeks versus <13 weeks demonstrated higher mortality (HR: 1.07, 95% CI: 1.01–1.13, P = 0.029). The authors set the cutoff ideal overall treatment time should be <97 days. During radiotherapy, treatment breaks could be due to machine breakdown, poor tolerance due to mucositis, family issues, or lack of motivation to complete the treatment in the scheduled time.[23]

TTT, SRI, and RD were not found to impact DFS in our interim analysis. We have observed positive outcomes in DFS, despite the fact that in 7 cases (33.8%), the SRI was longer than 8 weeks. Additionally, 14 cases (63.6%) were able to commence radiotherapy within 7 to 8 weeks, and in 11 cases (50%), the treatment duration exceeded 110 days. However, these are preliminary observations, and their true impact will be more evident with longer follow-up time.

In this interim analysis with a median FU of 5.6 months, DFS was found to be significantly affected by high nodal burden, ENE+, and the presence of LVI. pT, PNI, DOI, WPOI, close margin, tumor location, RD, TTT, and SRI were not found to impact DFS in this interim analysis.

Limitation of the study

It is an interim analysis with a median FU of 5.6 months; this short interval may not reflect the impact of all prognostic factors in survival.

Conclusions

In our study, patients with high nodal burden, LVI, and ENE had poorer outcomes. For these locally advanced cases, which have been confirmed through imaging and pathology, there is a critical need to optimize treatment. NACT can help downstage the tumor, followed by optimal surgical management. Adjuvant chemoradiotherapy should ideally be initiated within 4–6 weeks after surgery to improve outcomes. In addition, any breaks in radiotherapy should be avoided by providing effective supportive care, including Ryle's tube feeding, intravenous fluids, analgesics, and anti-inflammatory medications. This is important because tumor repopulation can occur more rapidly following radiotherapy. The impacts of p53, HPV, or EGFR status on outcomes should also be explored and managed accordingly; however, further research in this area is needed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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