



OUTCOME OF RADICAL CHEMORADIOTHERAPY (CRT) IN UNRESECTABLE N3B HEAD AND NECK SQUAMOUS CELL CARCINOMA

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ABSTRACT

Background: Radical CRT has its established role in unresectable locally advanced head Neck Squamous Cell Carcinoma (LAHNSCC). Its effect has been seen collectively over N1, N2 and N3. None of the studies have been done to see its role solely in N3 patients. **Aim:** With the present study we want to see the actual outcome of this treatment modality in unresectable N3 disease. **Method:** We retrospectively evaluated 17 patients' who took CRT in cobalt-60 teletherapy unit between period of 1st January 2020 to 31st December 2023. Their data regarding sociodemographic details and tumour characteristics were collected. Primary outcome in terms of remission period after CRT and overall survival was seen. Data was statistically analyzed. **Result:** All the 17 patients were of N3b. T4 staging was present in 64.7% patients. Median remission period was 4 months and median overall survival was 7 months. During CRT, mucositis (Grade III/IV) was present in 41.2% patients and dermatitis (Grade II/III) in 76.5% patients. **Conclusion:** Radical CRT in cobalt-60 teletherapy unit has poor outcome in unresectable N3b LAHNSCC. Palliative radiotherapy with or without palliative chemotherapy can be given to such patients.

KEYWORDS : N3b, head and neck cancer, chemoradiotherapy, cobalt-60

INTRODUCTION

Despite acknowledging poor prognosis of unresectable N3 locally advanced head Neck Squamous Cell Carcinoma (LAHNSCC), it is appreciated that aggressive treatment improves survival and should be considered even for large tumor volume. The radical Chemoradiotherapy (CRT) has now been established as a standard of treatment for patients when Eastern Cooperative Oncology Group (ECOG) performance status is 2 or less based on several randomized studies (Dhaka et al., 2024), (Fietkau et al., 2020), (Cohen et al., 2014). But, these studies could not clearly define the outcome of N3-LAHNSCC due to less number (approx. 10%) of N3 patients. Additionally, their results were combined with N1 & N2 subgroups (approx. 90%). Very few studies have been done to evaluate the role of radical CRT in N3 LAHNSCC and even fewer have mentioned type of teletherapy used.

METHOD

All the patients who had completed their radical CRT from department of Radiotherapy, Sarojini Naidu Medical College, Agra between period of Jan 1, 2023 - Dec 31, 2023 for the unresectable N3 LAHNSCC were enrolled in this study. Consent was taken at the beginning of the treatment from all the patients that their data can be used in the future studies. For all these enrolled patients', data of sociodemographic details, staging of tumor and follow up progress were collected. Patient of nasopharyngeal and salivary gland cancer were excluded. Patients who took incomplete CRT or who didn't follow up with us after completing their treatment were excluded.

All the patients had received radiation using 2D technique to a total dose of 70 Gray in 35 fractions, 2 Gray/fraction, 5 fractions /week in cobalt-60. All these patients had received weekly Cisplatin with dose of 35mg/m² as concurrent

chemotherapy. Tumor response assessment was performed by direct laryngoscopy, computed Tomography (CT) or 18-fluorodeoxyglucose (18FDG) positron emission tomography (PET)-CT at 3 months post CRT. Tumor response was assessed as per the Response Evaluation Criteria in Solid Tumors 1.1 (RECIST) or the Positron Emission Tomography Response Criteria in Solid Tumors (PERCIST). Clinical follow-up consisted of physical examination every month.

Overall survival (OS) was taken from date of their first hospital visit to the last follow up or till death. Remission period is taken as the duration when signs and symptoms of cancer decreases or disappear after CRT. All the data were analyzed statistically.

RESULT

We identified 17 patients with N3 HNSCC who had received definitive CRT between Jan 1, 2023- Dec 31, 2023. During retrieval of data, it was found that all the 17 patients died at some point during the follow up. Median follow up was of 7 months with range between 1.5–15.0 months. Patient and tumor characteristics are detailed in Table 1. Majority (94%) of patients were males. Oropharynx (41.2%) and oral cavity (35.3%) were common primary tumor sites. Median age was 47 years with range of 25-69 years. Nearly 2/3rd of the patients were of T4 stage. All these 17 patients had neck node of size < 6 cm with extracapsular extension (N3b)..

Median overall survival (OS) was 7 months (range 1.5 -15). One-year overall survival for entire cohort was 12%. Table 2 shows that median remission period after radical CRT was of 4 months and it varied from 1 month to 6 months after receiving CRT. During CRT, mucositis (Grade III/IV) was present in 41.2% patients and dermatitis (Grade II/III) in 76.5% patients.

Table 1. Sociodemographic details and tumor characteristics

Characteristics	CRT (n=17)	Percentage (%)
Median Age in years (range)	47(25-69)	
Sex		
Male	16	94.1
Female	1	5.9
Primary tumor site		
Oral cavity	6	35.3
Oropharynx	7	41.2
Larynx	3	17.6
Hypopharynx	1	5.9
T- stage		
T1	1	5.9
T2	1	5.9
T3	4	23.5
T4	11	64.7
N3- stage		
N3a	0	0
N3b	17	100

Table 2. Post CRT remission period duration

Post CRT remission period duration	Total no. of patients yield remission for definite period after radical CRT (n=17)	Percentage (%)
1 month	2	11.8
2 months	1	5.9
3 months	6	35.3
4 months	2	11.8
5 months	1	5.9
6 months	5	29.4

DISCUSSION

Recommended treatment for unresectable N3 locally advanced head and neck squamous cell carcinoma is radical CRT based on multiple randomized trial and metaanalysis (Dhaka et al., 2024),(Fietkau et al., 2020),(Cohen et al., 2014),(Pignon et al., 2009). All these trials have very low percentage of N3 patients approximately 10 %. Outcome of N3 patients was poorly defined as their results were routinely combined with N1, N2. Few studies have been conducted to evaluate the outcome of N3 LAHNSCC and none of them have seen the effect of definitive CRT with respect to teletherapy unit used in treatment. Most of these studies have been done in high income countries. In low-income countries like India cobalt-60 teletherapy unit is still being used in many centers. With this study we evaluated the role of radical CRT in N3 LAHNSCC in cobalt-60 teletherapy unit.

This study demonstrates median overall survival of 7 months and median remission period of 4 months after completing radical CRT. One-year overall survival for entire cohort is 12%. These findings are incongruous with previous studies. Witek et al demonstrated that N3 outcome is similar in different treatment modalities like surgery, radiotherapy and CRT. With any of these modalities overall survival at 2 year and 5 year is 60% and 30% respectively (Outcomes for Patients with Head and Neck Squamous Cell Carcinoma Presenting with N3 Nodal Disease | Cancers of the Head & Neck | Full Text, n.d.). This finding can be due to many reasons – (a) Enrollment of high percentage of oropharyngeal cancer patients (70%) which has higher response rate than to oral cancer (0% enrollment). (b) Only 20% patients belonged to T4 stage. (c) Large percentage (60%) of patients were treated by IMRT technique. While in present study, significant proportion (35.3%) of oral cavity patients was included, 64.7% of the patients are of T4 stage, and patients were irradiated by 2D technique on cobalt-60 teletherapy unit. Sellami et al also evaluated outcome of CRT in N3 Head and Neck cancer with 2 year overall survival of 44% (Sellami et al., 2021). Their results were also not similar to the present study. There may be various reasons for this dissimilarity such as- (a) Majority of

the patients included in that study had oropharyngeal (38.5%) or hypopharyngeal (40.4%) cancer. Oral cavity patients were very less (7.2%). (b) They did not present separate results for T3 and T4 staging. (c) They irradiated those patients on LINAC based teletherapy. A Recent study done at Tata Memorial center demonstrated the role of CRT in unresectable locally advanced oral cavity cancer with median progression free survival of 6.4 months and median OS of 8.9 months concluding that role of radical chemoradiation is limited for unresectable locally advanced oral cavity cancer without nodal staging dependence (Patil et al., 2021).

CONCLUSION

With radical CRT, we could only give median remission period of 4 months with range of 1 month to 6 months and none of these patients gained complete response with it. These patients also got significant toxicities. It shows that Radical CRT in cobalt-60 teletherapy unit has poor outcome in unresectable N3 LAHNSCC. This group of patients can be offered palliative radiotherapy with or without palliative chemotherapy.

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