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Role of Palliative Radiotherapy to Chest in Advanced Non-Small Cell Lung Carcinoma in Improving Quality of Life and Tumor Response

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Abstract: ***Purpose: Role of Palliative Radiotherapy to chest in advanced Non-Small Cell Lung Carcinoma in improving quality of life and tumor response. Methods and Material: This retrospective comparative dosimetric study is based on the data of patients with histologically proven lung carcinoma treated with palliative radiotherapy to the thorax. Patients were treated with a dose of 30 Gy in 10 fractions at 3Gy per fraction daily six days a week. Radiotherapy is given through cobalt 60 source by conventional treatment. Further, the patients were on follow-up for 3 months and the response was assessed inform of control of symptoms with quality of life after treatment and objective tumor response based on the degree of reduction in the size of tumor on CT scan. The EORTC QLQ-C30 and EORTC QLQ-LC13 questionnaires were used to assess changes in QoL. Assessments were performed before starting radiotherapy and atthe completion of rt & 3 months after rt. Results: Total numbers of Non-Small cell carcinoma lung patients involved in this study are 40 out of which 80% are male and 20% are female. The median age was 65.9 (range 50-75). Out of 40 patients, 4 patients does not report after first visit & 4 patients were not able to complete treatment. So, 32 patients received palliative radiotherapy to the lung. Chest pain and dyspnea at the walk &climbing significantly improved after Radiotherapy when compared to baseline (P<0.001) while cough (P<0.001), hemoptysis (P<0.001) significantly improved after three months of rt in QLQ-LC13 scores. Of the QLQ-C30 scale, Dyspnea significantly improved after radiotherapy when compared to baseline (P<0.001) while fatigue (P<0.05), role functioning (P<0.001) insomnia (P<0.05) and loss of appetite (P<0.001) significantly improved after three months of rt. There is partial tumor response seen by ct scan after 3 months of RT. Conclusion: The present study attempts to analyze the Response of Palliative Radiotherapy to chest and confirms the palliation of respiratory symptoms and improved QoL in a substantial proportion of patients of NSCLC. The mechanism by which palliation of symptoms and improvement of QoL is achieved is through tumor size reduction only.***

Keywords: Paliiative Radiotherapy, Non Small Cell Lung Carcinoma, Quality Of Life, Local Control, QLQ-C30 questionnaire, QLQ LC-13 questionnaire

1. Introduction

Throughout the World, the leading cause of Cancer related Death is Lung Carcinoma with an estimated of 1.59 million deaths per year around the world. The global incidence is 13% of the total cases of cancer (1). According to GLOBOCON 2020-In India, lung cancer constitutes 5.5 percent of all new cancer cases and 7.8 per cent of all cancer related deaths in both gender (2). Types of Lung Carcinoma (Based on histological and clinical characteristics):

- Non-Small Cell Lung Carcinoma (80%-85%)
- Small Cell LungCarcinoma (15%-20%)

The main etiological factor responsible for almost 90% of cases of lung cancer is cigarette smoking (3). Passive smoking is also at increased risk of developing lung cancer (4). Exposure of radon and other occupational exposures like asbestos, arsenic, chromium, nickel and vinyl chloride also increases lung cancer risk. Smoking has a multiplicative or compounding effect with some of these agents (5).

A key role is played by Radiotherapy in the management of lung cancer and is used in almost all patients as a curative and palliative treatment (6). Almost all patients with advanced loco-regional or metastatic non-small cell lung cancer will, at some point, have symptoms like hemoptysis, breathing difficulties and chest pain compelling for the treatment. The treatment of metastatic disease with thoracic symptoms is palliative in nature and this group of patients has a poor median survival of between 2 and 9 months (7). Therefore, shorter hypo-fractionated radiotherapy treatments take advantage of this limited survival period and palliate the symptoms of patients, provided that the quality of palliation is equivalent and morbidity is not increased. Since the lung cancer constitutes a large proportion of malignancy and so the workload of all radiotherapy departments, and shorter fractionation schedules will allow increased treatment-machine time for potentially curable patients (8).

The European Organization for Research and Treatment of Cancer (EORTC) questionnaires (QLQ-C30 and QLQ-LC13) are used in this retrospective study to assess changes in respiratory symptoms and QoL using a group of patients with histopathological proven non-small cell lung carcinoma having poor prognostic features treated by external beam radiotherapy to chest (9). The main goal of treatment in these patients was symptom palliation like control of hemoptysis, dyspnea, and chest pain with preservation of quality of life (10). Objective tumor response was assessed by comparing the tumor size on chest ct scans before and after 3 months of completion of treatment and response was categorized according to RECIST 1.1 Criterion (11).

2. Materials and Methods

Study Population: This was a retrospective analysis of patients who received palliative radiotherapy for lung cancer. Patients who had biopsy-proven Carcinoma lung with stages ranging from AJCC (8^{th} edition) IIIB to IVB, karnofsky performance status of 60-80were included in this study.32 patients (80%) were male and eight (20%) were female. The mean age at diagnosis was 65.9 years, ranging from 50 to 75 years. All patients were treated by external beam radiotherapy to the chest.

Radiotherapy: All patients were given External beam Radiotherapy via teletherapy cobalt machine using 2 fields anterior-posterior/ posterior-anterior treatment. All patients received a dose of 30 Gy in 10 fractions with 3 Gy per fraction daily six days a week.

QoL assessment: The questionnaire used here is EORTC QLQ-C30 (version 3.0) to assess QoL. This questionnaire is composed of 30 questions organized into five functional scales (physical, role, emotional, cognitive, and social), three symptom scales (fatigue, pain, and nausea & vomiting), a global health/QoL scale, and some single items assessing additional symptoms (dyspnea, sleep disturbance, constipation, and diarrhea) (12).

For the assessment of respiratory symptoms, the EORTC lung cancer module (QLQ-LC13) was used, in this supplemental questionnaire 13 questions are included concerning symptoms frequently present in lung cancer patients like cough, hemoptysis, shortness of breath, chest pain, etc. (13).

The more the score is high it represents the better level of functioning in the functional and global health status/QoL scales. But for the symptom scales, higher scores represent a greater degree of symptoms. Patients were assessed before the start of radiotherapy, at the completion and 3 months after the completion of treatment. The patient participation was ensured in the study during the first visit to the Radiation Oncology Department. Firstly, the informed consent was taken then; the questionnaire was distributed to the patients who were asked to answer it. The same was repeated after completion and 3 months of completion of the treatment.

Objective tumor response: It was assessed by comparing the tumor size on chest CT scans before and after 3 months of completion of treatment. A complete response was defined as complete disappearance of target lesion while partial response is at least a 30% decrease in the sum of diameters of target lesion (14).

Statistics: To assess the response rate for symptoms, four categories were assigned for each symptom scale. For the single-item scales (hemoptysis, cough, pain arm/shoulder, pain chest wall, and loss of appetite), four ranges of scores were defined: 1 = nil, 2 = mild, 3 = moderate, and 4 = severe. For the multi-item scales (dyspnea and fatigue), there are four ranges of scores, based on the converted score ranging from 0 to 100: 0 = nil, 1 to 34 = mild, 35 to 67 = moderate, and 68 to100 = severe (15).

Firstly, the baseline score was calculated for the patients before starting of treatment and further follow-up score was calculated. If the follow up score was lower than the baseline, the patient was considered palliated while if the score increased then it indicated deterioration of patient.

The Wilcoxon Signed Rank test was used to determine changes in QLQ-C30 and QLQ-LC13 scores between baseline and each follow-up visit (i. e., after rt and 3 months after rt) (16).

3. Results

Patient demographics: Total number of patients taken was 40. Patient demographics are shown in Table 1. Eighty percent of participants were male and twenty percent were female. Their median age was 65.8 years (range 50-70), and their median KPS score at baseline is 70 (range 30-90). Out of 40, four patients do not report after first visit and four patients were not able to complete the treatment.

Compliance: Of the 40 patients who gave their informed consent at the beginning of the study, 36 returned the questionnaire before radiotherapy (90%). At 3 months the compliance was 88.8% (32 of 36 patients alive). Most patients did not return the questionnaire because they were in the terminal phase of their illness.

Table 1: Patients Demographics (N = 16)

Age (years)	
N	40
Mean ± SD	65.9 ± 8.4
Inter-quartiles	50-75
Median (range)	65.9 (50-75)
Karnofsky Performance Scale	
N	40
Mean ± SD	67 ± 16
Inter-quartiles	60-80
Median (range)	70 (30-90)
Gender	
Male	32 (80%)
Female	8 (20%)

QLQ-C30 score comparisons between baseline and each follow-up visit-fatigue, role, emotional, dyspnea, insomnia and loss of appetite significantly improved from baseline at different time points during follow-up (Table 2). Dyspnea significantly improved after radiotherapy when compared to baseline ($P<0.001$) while fatigue ($P<0.05$), role functioning ($P<0.001$), insomnia ($P<0.05$) and loss of appetite ($P<0.001$) significantly improved after three months of radiotherapy.

Table 2: QLQ-C30 Mean Score Values for Each Symptom Item at Baseline and Follow-up

Symptom Scales/Items	Data Collection Period		
	Before rt	After rt	At 3 months
Physical functioning	47.91	57.5	62.91
Role functioning	47.91	70.83	76.04**
Cognition functioning	62.5	69.79	72.91
Emotional functioning	56.77	71.87	79.16*
Social functioning	53.12	68.75	78.12*
Fatigue	59.02	45.13	34.02*
Pain	60.41	40.62	23.95**
N&V	36.45	26.04	12.5*

Dyspnea	70.83	54.16	33.33**
Insomnia	58.33	50	37.5*
Appetite	68.75	54.16	39.58**
Global Health	40.62	45.31	56.77

QLQ-30 scores were compared between baseline and at each follow-up visit. Scores that show significant differences at the indicated follow-up period are bolded.

Significant differences were calculated using Wilcoxon Signed Rank.
QLQ-LC13 score comparisons between baseline and each follow-up visit-Coughing, hemoptysis, chest pain, dyspnea at walk & climbing significantly improved from baseline at different time points during follow-up. Chest pain and dyspnea at walk &climbing significantly improved after rt when compared to baseline (P<0.001) while cough (P<0.001) and hemoptysis (P<0.001) significantly improved after three months of rt.

Sore mouth, peripheral neuropathy, alopecia and dyspnea at rest did not significantly change during any follow – up period (Table 3).

Table 3: QLQ-LC13 Mean Score Values for Each Symptom Item at Baseline and Follow-up

Symptom Scales/Items	Data Collection Period		
	before rt	after rt	at 3 months
Cough	3.31	2.5	2.06**
Hemoptysis	2.6	1.8*	1.4**
Sore Mouth	1.68	1.75	1.87
Dysphagia	1.5	1.5	2.06**
Peripheral Neuropathy	1.62	1.37*	1.31*
Alopecia	1.37	1.37	1.81
Pain in Chest	3.06	2.5**	2.06**
Pain in Arm	2.25	1.87	1.25*
Pain Other	1.93	1.75	1.68
Dyspnea at rest	2.25	1.93	1.87
Dyspnea at walk	2.93	2.37*	2.31*
Dyspnea at climb	3.43	3.2*	3.31**

*P0.05, **P0.001

QLQ-LC13 scores were compared between baseline and at each follow-up visit. Scores with a significant difference at the indicated follow-up period are bolded. Significant differences were calculated using Wilcoxon Signed Rank.

Objective tumor response: It was assessed by comparing the tumor size on chest ct scan before and after 3 months of completion of treatment. There was partial response seen in almost all patients and there was no complete response seen in any of the patients.

4. Discussion

The above-mentioned study is used to compare changes in respiratory symptoms and QoL using standardized QoL questionnaires in a group of patients with advanced and/or metastatic NSCLC treated with conventional palliative radiotherapy (30Gy in 3 #). These questionnaires are ideal in this study as they have the main focus on patient and tumor site. Before starting treatment there were some doubts regarding the compliance of patients as these patients generally have a poor performance status, the present study has recorded excellent palliation of hemoptysis, cough and dyspnea and good palliation of fatigue, loss of appetite & insomnia. There are no significant changes in Sore mouth, peripheral neuropathy, alopecia and dyspnea at rest during any follow – up period there is partial tumor response seen by ct scan after 3 months of rt. Additionally, group of patients with an objective tumor response had better palliation of dyspnea.

J. A. LANGENDIJK et al. performed a prospective study investigating changes in respiratory symptoms and quality of life (QoL) in patients with locally advanced and metastatic non-small cell lung cancer (NSCLC) receiving thoracic radiotherapy (15), suggesting that conventional thoracic radiotherapy offers palliation of respiratory symptoms and improved QoL in a substantial proportion of patients with locally advanced and metastatic NSCLC (17, 18). The authors indicated the need to include QOL as a meaningful endpoint when evaluating management of advanced lung disease; a sentiment echoed by other authors as well (19-21).

Salvo et al. reviewed QOL assessment tools for patients who received palliative radiotherapy for advanced lung cancer and lung metastases. This result of this study encouraged investigators to include validated, specific QOL instruments such as the EORTC QLQ-LC13 or the FACT-L due to the specificity of these instruments in measuring lung-cancer-specific symptoms [24].

Kaitlin Koo et al. investigated quality of life (QOL) in patients receiving palliative radiotherapy (RT) for advanced lung cancer/lung metastases using the EORTC QLQLC13 and the EORTC QLQ-C15-PAL questionnaires suggesting, fatigue, pain, insomnia and physical functioning significantly improved at their respective follow-ups and none of the QLQ-LC13 scores significantly improved or deteriorated at any follow-up (16).

It is interesting to note that in our study, none of the physical functioning symptoms and global QOL status assessed by the QLQ-30 significantly improved or deteriorated during any follow-up period. However, there was a stabilizing role of palliative radiotherapy in this context. Langendijk et al. reported that palliative radiotherapy was effective in improvement of global QOL as assessed by the QLQC30. There is evidence in the literature suggesting that symptoms experienced by this group actually worsened during and immediately following RT, and then returned to baseline levels (23, 24).

As the disease is very progressive in nature along with poor prognosis, there is a loss of follow-up in the group representing that our study mainly reflects palliation of symptoms in good prognosis patients and does not truly represent the population. There should be more efforts directed towards analyzing the outcomes of patients that were lost to follow-up as a loss of follow-up is the common limitation of most of the similar studies.

In conclusion, Palliative radiotherapy is a well-tolerated therapeutic modality that preserves the quality of life of patients and control of thoracic symptoms. Tumor reduction is also an important part of response, but it is not the only

mechanism for palliation of symptoms and Qol improvement (15).

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