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Research Article

Comparative Study Between 17 Gy in 2 Fractions and 36 Gy in 12 Fractions Radiotherapy to Primary Site for Palliation of Symptoms in Stage IV Non-Small Cell Lung Cancer

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Abstract

Background: Half of NSCLC patients present with stage IV disease where a cure is not possible. The use of a hypofractionated RT schedule has economic and logistic advantages for Radiation Oncology departments and a higher degree of patient convenience than conventional fractionation. *Objective:* To evaluate outcomes between 17 Gy in 2 fractions and 36 Gy in 12 fractions RT regarding relief of thoracic symptoms in IV NSCLC patients. *Methods:* This quasi-experimental study was done at the Radiation Oncology Department, NICRH from July, 2022 to June, 2023. A total of sixty (60) study participants were assigned into two groups, 30 in each arm. Arm-A received 17 Gy in 2 fractions, 1 week apart and Arm-B received 36 Gy RT in 12 fractions in two and half weeks. *Result:* About 68.33% of participants were between 40 to 60 years. In Arm-A, among 30 participants there were 22 (73.3%) male and 8 (26.7%) female. In Arm-A, 26 (86.7%) participants were in stage IVA and 4 (13.3%) were in stage IVB, and in Arm-B 28 (93.3%) participants were in stage IVA and 2 (6.7%) were in stage IVB. The response was evaluated in both arms. In Arm-A, 10 (33.3%) participants showed partial response (PR) and 11 (36.7%) participants showed partial response (PR) in Arm-B. According to ECOG-PS, In Arm-A, among 2 participants with PS ECOG -0, 1 participant developed a partial response and the other one had a stable disease. *Conclusion:* Hypofractionated RT with 17 Gy in 2 fractions renders similar symptom relief with minimum toxicities compared with 36 Gy in 12 fractions RT to a primary lesion in stage IV NSCLC.

Keywords

Hypofractionated, Non-Small Cell Cancer, Death, Palliation, Stage Iv

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1. Introduction

Globally, among all the alarming causes of death, Lung cancer is well recognized as the 2nd commonest cancer among all malignancies. Approximately 2.2 million (11.4%) new cases of lung cancer were diagnosed worldwide and 12,999 (8.3%) new cases in Bangladesh in 2020 [1]. According to the National Institute of Cancer Research and Hospital (NICRH) hospital-based cancer registry, the total number of lung cancer patients who attended the out-patient department was 2195, 2320 & 1712 in 2018, 2019 & 2020 respectively. Lung cancer was the most commonly diagnosed malignancy in those three years.

The total number of lung cancer patients detected was 6227 (17.4%) [2]. In a Surveillance Epidemiology and End Results (SEER) analysis involving all lung cancer histology, localized lung cancer was found in around 15% at the beginning of diagnosis; 22% had regional lymph node spread, and 56% had distant metastasis the remaining 7% of stages were not diagnosed properly.

Unfortunately, de novo metastatic case of NSCLC is approximately 50% and the remaining half of NSCLC progresses to stage IV from the localized or locally advanced stage [3]. Although any organ may be the site of metastasis from primary lung cancer; the adrenal glands (>50%), liver (30-50%), brain (20%), bones (20%), contralateral lung, pericardium, kidneys, and subcutaneous tissue are frequently found in case of metastatic spread [4].

Among all the stages, the 5-year survival rate for lung cancer is only 18%; the 5-year survival rate for those with stage IV (metastatic) disease at diagnosis is much lower approximately 2%. The median overall survival of stage IV patients with NSCLC ranges between 7.0 and 12.2 months depending on the treatment received, histologic types, and other exaggerated causes [5, 6].

Patients with 4th stage non-small cell lung cancers suffer from significant local symptoms for an example, superior vena cava obstruction, intractable cough, severe respiratory distress, chest pain & hemoptysis.

Because the life expectancy of most patients with metastatic NSCLC is measured in months, symptomatic management and improvement of quality of life are important treatment goals. Urgent palliative radiotherapy of the chest as a consequence of systemic or targeted therapy is the preferred treatment approach for such patients [7]. The main advantages of palliative radiotherapy are pain relief, control of hemorrhage, decrease in size of ulceration, improvement of dyspnea, removal of blockage of hollow viscera, and relief of pressure symptoms [8]. The effectiveness of palliative RT for pulmonary symptoms related to NSCLC ranges from 50% to 90%. In general, hemoptysis has the highest response rate (76-95%), followed by chest pain (50–80%), cough (50–65%), and dyspnea (37–60%). The optimal radiation schedule for palliation of these symptoms has not been determined [8]. Many studies have been performed to identify the optimal thoracic radiotherapy regimen for the palliation of symptoms in stage IV non-small cell lung cancer. Recommending palliative RT, radiation oncologists must decide on a total dose and dose per treatment (dose per fraction). This determines the total number of treatments (number of fractions) and consequently, the number of visits needed by the patients [10].

The perfect regimen would provide relief to the patients from all symptoms permanently; cause no adverse effects, extend progression-free survival, and require a short treatment time. A short-duration course of hypo-fractionated RT for palliation, if effective and not unduly toxic, would be an attractive alternative to more protracted regimens [9]. In reality, these targets are not 100% satisfiable but one should strive to maximize palliation and minimize adverse effects.

Hypofractionation refers to the delivery of the total radiotherapy dose in a small portion of fraction than would be used to deliver a traditional dosing scheme. The daily fraction size, therefore, is larger than the size given in standard fractionation. The total duration of radiation treatment therefore reduced significantly.

It decreases the unfavorable phenomenon of repopulation and allows a prompt & accelerated regression of neoplastic lesions within the lungs [11]. Previously similar clinical trials have established the equivalence of conventionally fractionated and hypo-fractionated radiotherapy in terms of tumor control and long-term toxicity for NSCLC. The lung is an intermediate to late responding tissue to radiation with an α/β estimated to be about 3 Gy (Van Leeuwen et al., 2018) where 17 Gy in 2 fractions is the radiobiologic equivalent of 45 Gy in 25 fractions or 36 Gy in 12 fractions by the linear-quadratic formula [12].

Radiation-induced damage usually occurs in such late-responding tissues months to years after the completion of radiation. In addition, the efficacy of radiotherapy fractionation schemes can potentially be predicted by calculating the BED which reflects the tumor type (doubling time), dose per fraction, and nominal total dose and may also take into account the time to complete therapy [13].

By analyzing the above trials, we can endeavor to complete a study of palliative radiation in our context to make a comparison between two schedules of 17 Gy in 2 fractions, 1 week apart, and 36 Gy in 12 fractions in two & half weeks in terms of symptom relief, local control, clinical response, and toxicities to see whether this approach would be for the palliative treatment of stage IV non-small cell lung cancer.

2. Methods

This Quasi-experimental study was performed from July 2022 to June 2023. This study was conducted at National Institute of Cancer Research and Hospital (NICRH), Dhaka. Patients with histopathologically/cytopathologically proven NSCLC presented with metastasis (stage IV) as the initial

presentation. They were selected from OPD who met the selection criteria of the study.

The process of informed consent was of utmost importance. Each participant was provided with comprehensive information about the study's purpose, procedures, potential risks and benefits. It was imperative that participants voluntarily and knowingly consented to their involvement and they had the opportunity to ask questions before agreeing to participate.

3. Selection of Patients

Inclusion criteria:

1. Age more than 18 years and less than 72 years.
2. Histopathologically/cytopathologically proven non-small cell carcinoma of lung.
3. Radiological / cytological evidence of metastasis.
4. De novo metastatic case of non-small cell lung cancer who presented with significant
5. Intra-thoracic symptoms that needed immediate palliation.

Exclusion criteria:

1. ECOG performance status >3.
2. Existence of synchronous multiple malignancies.
3. Previously treated with chemotherapy & thoracic radiotherapy.
4. Participants with hepatic and renal dysfunction
5. Recurrent cases.
6. Pregnancy.
7. Eligible participants who were unwilling to participate in the study.

The sample was collected by purposive sampling technique. A total of 60 patients were included in this study, distributed in two arms (A and B), 30 patients in each arm.

4. Intervention

Symptomatic and Supportive care:

1. Participants were managed symptomatically with antibiotics, steroids, analgesics, bronchodilators, diuretics, oxygen inhalation, and anti-ulcerates, and conservative management was given according to need throughout the treatment period.
2. Before specific intervention, participants with moderate to severe effusion were referred to NIDCH for pleurodesis.
3. Consultation with a palliative care unit specialist was done simultaneously.
4. For participants who presented with brain metastasis, urgent whole-brain RT was given.
5. Urgent palliative RT was delivered to the most painful sites for bone metastasis.

5. Specific Management

Radiotherapy was given as per protocol.

Thereafter, participants were sent for palliative systemic therapy and treated accordingly.

For Arm- A:

1. Total Dose- 17 Gy
2. Dose per fraction- 8.5 Gy
3. Number of fractions – 2
4. Number of fractions per week – 1
5. Duration – 8 days (Day 1 and Day 8)

For Arm-B:

1. Total Dose- 36 Gy
2. Dose per fraction- 3.0 Gy
3. Number of fractions -12
4. Number of fractions per week – 5
5. Duration- 2 and ½ weeks

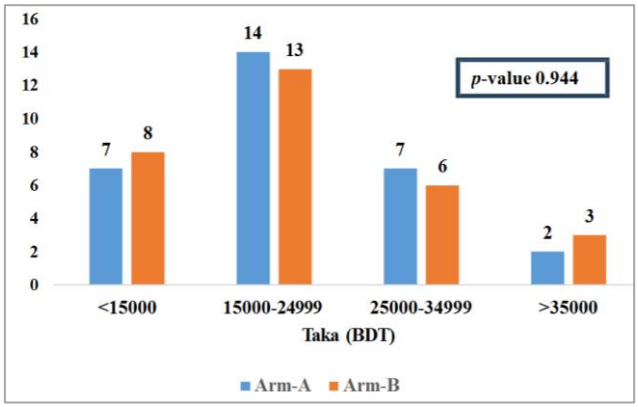
6. Statistical Analysis

Statistical analysis was done according to the study's objective using SPSS software version 27.0 for Windows (IBM SPSS Statistics for Windows, version 27.0, Armonk, NY: IBM Corp.) and graphs by MS Excel 2019. The analysis was done using independent t-tests for continuous variables, Chi-squared tests, and Fisher's Exact test for categorical variables. All reported *p*-values were two-sided, and a value less than 0.05 was regarded as significant.

Table 1. *Socio-demographic characteristics of the participants (n=60).*

Distribution of the participants according to age (n=60)					
Age group (in years)	**Arm A (n=30)**		**Arm-B (n=30)**		**p-value**
	No.	**%**	**No.**	**%**	
18-34	0	0	0	0	
35-44	7	23.3	8	26.7	0.748
45-54	10	33.3	9	30	

Distribution of the participants according to age (n=60)					
Age group (in years)	**Arm A (n=30)**		**Arm-B (n=30)**		**p-value**
	No.	**%**	**No.**	**%**	
55-64	8	26.7	9	30	
65-72	5	16.7	4	13.3	
Distribution of the participants according to gender (n=60)					
Sex	Arm A (n=30)		Arm-B (n=30)		p-value
	No.	%	No.	%	
Male	22	73.3	24	80	0.541
Female	8	26.7	6	20	
Distribution of participants according to occupation (n=60)					
Occupation	Arm A (n=30)		Arm A (n=30)		p-value
	No.	%	No.	%	
Farmer	18	60	16	53.3	
Day labor	2	6.7	3	10	
Business	0	0	5	16.7	0.179
Housemaker	8	26.7	6	20	
Service holder	1	3.3	0	0	
Factory worker	1	3.3	0	0	
Association of risk factors between two groups (N=60)					
Factor	Arm A (n=30)		Arm A (n=30)		p-value
	No.	%	No.	%	
Smoking	24	80	25	83.3	0.739 [ns]
Passive smoker	8	26.6	6	20	0.542 [ns]
Pre-existing pulmonary disease	5	16.7	4	13.3	0.718 [ns]
Occupational Exposure*	1	3.3	0	0	-



*BDT= Bangladeshi Taka

Figure 1. *Distribution of the study participants by socioeconomic status (n = 60).*

7. Result

Table 1 resembles the socio-demographic characteristics of the participants. Age distribution resembles normal distribution where the numbers of middle-aged participants were high in contrast to extreme age groups. About 68.33% of participants were between 40 to 60 years. In Arm-A, among 30 participants there were 22 (73.3%) male and 8 (26.7%) female. Among 30 participants in Arm-A, 18 participants (60%) were farmers whereas, in Arm-B, among 30 participants, only 5 (16.7%) were businessmen. The two arms had no significant statistical difference ($p > 0.05$) regarding risk factors. Figure 1 illustrates the distribution of the study participants by socio-economic status. Most of the participants in this study had monthly incomes between 15000 and 24,999 tk. For example, in Arm-A, 14 (46.7%) and 13 (43.3%) participants.

Table 2 shows distribution of participants according to TNM stage. In Arm-A, 26 (86.7%) participants were in stage IVA and 4 (13.3%) were in stage IVB and in Arm-B 28 (93.3%) participants were in stage IVA and 2 (6.7%) were in stage IVB with no significant statistical difference ($p > 0.05$).

Table 2. *Distribution of participants according to stage (N=60).*

Stage	Arm-A (n=30)		Arm-B (n=30)		*p*-value
	No.	%	No.	%	
Stage IVA	10	33.3	8	26.7	
Stage IVB	20	66.7	22	73.3	0.389^{ns}
Total	30	100.0	30	100.0	

Distribution of participants according to the presentation of symptoms is shown in table 3. The common presentation in both the groups was cough; 56 (93.3%). It was present in 28 (93.3%) participants in both arms. In Arm-A, it was then followed by respiratory distress in 28 (93.3%), hemoptysis in 24 (80%) and chest pain in 21 (70%) participants. Likewise, in Arm-B cough was followed by hemoptysis, dyspnea, and chest pain in 24 (80%), 23 (76.7%), 22 (73.3%), participants respectively.

Table 3. *Distribution of the participants according to presentation of symptoms (n=60).*

Distribution of the participants according to presentation of symptoms (n=60)					
Symptoms & signs	Arm A (n=30)		Arm-B (n=30)		p-value
	No.	%	No.	%	
Cough					
None	2	6.7	2	6.7	
Mild	4	13.3	6	20	0.554
Moderate	14	46.6	12	40	
Severe	10	33.3	10	33.3	
Hemoptysis					
None	8	26.6	6	20	
Mild	6	20	7	23.3	0.848
Moderate	12	40	11	36.6	
Severe	4	13.3	6	20	
Dyspnea					
None	2	6.6	7	23.3	0.320

Distribution of the participants according to presentation of symptoms (n=60)					
Symptoms & signs	**Arm A (n=30)**		**Arm-B (n=30)**		**p-value**
	No.	**%**	**No.**	**%**	
Mild	14	46.7	10	33.3	
Moderate	9	30	8	26.7	
Severe	5	16.7	5	16.7	
Chest pain					
None	9	30	8	26.7	
Mild	6	20	5	16.7	
Moderate	10	33.3	10	33.3	0.883
Severe	5	1.7	7	23.3	

Table 4 indicates clinical symptoms before and after RT in Arm-A and Arm-B. During analysis of dyspnea, Arm-A and Arm-B had initial TSS 47 & 41 respectively. Just after completion of RT, 6th and 24th weeks after radiotherapy the score was 38, 32 & 26 respectively in Arm-A and the score was 40, 28 & 20 respectively in Arm-B. The chest pain was also evaluated by symptom score. Initially it was 41 in Arm-A and 46 in Arm-B. Just after completion of RT, 6th and 24th weeks after radiotherapy the score was 16, 13 & 11 respectively in Arm-A and the score was 19, 15 & 12 respectively in Arm-B. Regarding skin toxicities, very few participants developed grade 1 or 2 dermatitis and one participant in Arm-B developed grade 3 dermatitis.

Table 4. *Clinical symptoms before and after RT in Arm-A and Arm-B (n=60).*

Grading of dyspnea about RT	**Arm-A (n=30)**		**Arm-B (n=30)**		***p*-value**
	No.	**%**	**No.**	**%**	
Before LRRT					
None	2	6.7	7	23.3	
Mild	14	46.7	10	33.3	0.320^{ns}
Moderate	9	30	8	26.7	
Severe	5	16.7	5	16.7	
After completion of RT					
None	4	13.3	7	23.3	
Mild	16	53.3	10	33.3	0.403^{ns}
Moderate	8	26.7	9	30	
Severe	2	6.7	4	13.3	
After 6th week of RT					
None	8	26.7	12	40	
Mild	14	46.7	13	43.3	0.386^{ns}
Moderate	6	20	2	6.7	
Severe	2	6.7	3	10	

Grading of dyspnea about RT	Arm-A (n=30)		Arm-B (n=30)		*p*-value
	No.	%	No.	%	
After 24th week of RT					
None	10	33.3	14	46.6	
Mild	15	50	13	43.3	0.688[ns]
Moderate	4	13.3	2	6.7	
Severe	1	3.3	1	3.3	

Grading of chest pain in relation to RT	Arm-A (n=30)		Arm-B (n=30)		*p*-value
	No.	%	No.	%	
Before LRRT					
None	9	30	8	23.3	
Mild	6	20	5	16.7	0.883[ns]
Moderate	10	33.3	10	33.3	
Severe	5	16.7	7	23.3	
After completion of RT					
None	17	56.7	16	53.3	
Mild	11	36.7	10	33.3	0.782[ns]
Moderate	1	3.3	3	10	
Severe	1	3.3	1	3.3	
After 6th week of RT					
None	19	63.3	18	60	
Mild	10	33.3	10	33.3	0.795[ns]
Moderate	1	3.3	1	3.3	
Severe	0	0	1	3.3	
After 24th week of RT					
None	20	66.6	18	60	
Mild	9	30	11	36.7	0.715[ns]
Moderate	1	3.3	1	3.3	
Severe	0	0	0	0	

Table 5. *Grading of Toxicities with RT completion (n=60).*

Grading of skin toxicity in relation to RT	Arm-A (n=30)	n (%)	Arm-B (n=30)	n (%)	*p*-value
Before LRRT					
No	30	100	30	100	

Grading of skin toxicity in relation to RT	Arm-A (n=30)	n (%)	Arm-B (n=30)	n (%)	*p*-value
After 1st week during RT					
G1	0	0	0	0	
G2	0	0	0	0	-
G3	0	0	0	0	
G4	0	0	0	0	
After 2nd week during RT					
G1	8	26.7	12	40	0.177^{ns}
G2	3	10	6	20	
G3	0	0	1	3.3	
G4	0	0	0	0	
After 6th Week of RT completion					
G1	4	13.3	5	16.6	0.754^{ns}
G2	1	3.3	1	3.3	
G3	0	0	0	0	
G4	0	0	0	0	
After 24th Week of RT completion					
G1	0	0	0	0	-
G2	0	0	0	0	
G3	0	0	0	0	
G4	0	0	0	0	

Grading of cough in relation to RT	Arm-A (n=30)		Arm-B (n=30)		*p*-value
	No.	%	No.	%	
Before LRRT					
None	2	6.7	2	6.7	0.554^{ns}
Mild	4	13.3	6	20	
Moderate	14	46.7	12	40	
Severe	10	33.3	10	33.3	
After completion of RT					
None	5	16.7	3	10	0.819^{ns}
Mild	7	23.3	9	30	
Moderate	14	46.7	15	50	
Severe	4	13.3	3	10	
After 6th week of RT					
None	5	16.7	4	13.3	0.792^{ns}

Grading of cough in relation to RT	**Arm-A (n=30)**		**Arm-B (n=30)**		***p*-value**
	No.	**%**	**No.**	**%**	
Mild	8	26.7	10	26.7	
Moderate	13	43.3	14	46.7	
Severe	4	13.3	2	6.7	
After 24th week of RT					
None	7	23.3	7	23.3	0.948 ^{ns}
Mild	10	33.3	12	40	
Moderate	12	40	10	33.3	
Severe	1	3.3	1	3.3	

Grading of esophagitis in relation to RT	**Arm-A (n=30)**	**n (%)**	**Arm-B (n=30)**	**n (%)**	***p*-value**
Before LRRT					
No	30	100	30	100	
After 1st week during RT					
G1	1	3.3	1	3.3	*0.754^{ns}
G2	0	0	0	0	
G3	0	0	0	0	
G4	0	0	0	0	
After 2nd week during RT					
G1	5	16.7	7	23.3	0.554^{ns}
G2	1	3.3	2	6.7	
G3	0	0	0	0	
G4	0	0	0	0	
After 6th Week of RT completion					
G1	3	10	4	13.3	*0.500^{ns}
G2	0	0	0	0	
G3	0	0	0	0	
G4	0	0	0	0	
After 24th Week of RT completion					
G1	0	0	0	0	-
G2	0	0	0	0	
G3	0	0	0	0	
G4	0	0	0	0	

Grading of pneumonitis in relation to RT	Arm-A (n=30)	n (%)	Arm-B (n=30)	n (%)	*p*-value
Before LRRT					
No	30		30		
After 1st week during RT completion					
G1	0	0	1	13.3	-
G2	0	0	0	0	
G3	0	0	0	0	
G4	0	0	0	0	
After 2nd week during RT					
G1	0	0	1	13.3	-
G2	0	0	0	0	
G3	0	0	0	0	
G4	0	0		0	
After 6th Week of RT completion					
G1	4	13.3	6	20	0.253^{ns}
G2	1	3.3	1	3.3	
G3	0	0	0	0	
G4	0	0	0	0	
After 24th Week of RT completion					
G1	0	0	1	3.3	-
G2	0	0	0	0	
G3	0	0	0	0	
G4	0	0	0	0	

Table 5 resembles the grading of toxicities with RT completion. Regarding skin toxicities, very few participants developed grade 1 or 2 dermatitis, and one participant in Arm-B developed grade 3 dermatitis. Esophagitis was slightly higher in Arm-B but the observed difference was not statistically significant ($p > 0.05$) with Arm-A.

Table 6 reveals distribution of participants according to response. Response was evaluated in both arms. In Arm-A, 10 (33.3%) participants showed partial response (PR) and 11 (36.7%) participants showed partial response (PR) in Arm-B. Stable disease was observed in 13 (43.3%) participants in Arm-A and 14 (46.7%) participants in Arm-B. 7 participants (23.3%) in Arm-A and 5 participants (16.7%) in Arm-B developed progressive disease. Although, Arm-B showed arithmetically better response compared to Arm-A, it was not statistically significant (*p*-value >0.05).

Table 6. *Distribution of participants according response 6th weeks after RT (N=60).*

Response	Arm-A No.	%	Arm-B No.	%	*p-value*
Complete response	0	0	0	0	

Response	Arm-A		Arm-B		*p-value*
	No.	**%**	**No.**	**%**	
Partial response	10	33.3	11	36.7	0.811[ns]
Stable disease	13	43.3	14	46.7	
Progressive disease	7	23.3	5	16.7	

Table 7 shows the participants' responses according to ECOG-PS. In Arm-A, among 2 participants with PS ECOG -0, 1 participant developed a partial response and the other one had stable disease. In cases of PS with ECOG-1, 5 participants developed a partial response, 4 participants had stable disease, and 2 participants developed progressive disease. In Arm—B, 11 participants developed partial response, 14 had stable diseases, and 5 had progressive diseases.

Table 7. *Response of participants according to Performance status (N=60).*

ECOG	Arm-A		Arm-B		*p-value*
	No.	**%**	**No.**	**%**	
ECOG 0	2		5		
Complete response	0	0	0	0	
Partial response	1	50	3	60	0.809[ns]
Stable disease	1	50	2	40	
Progressive disease	0	0	0	0	
ECOG 1	11		9		
Complete response	0	0	0	0	
Partial response	5	45.5	3	33.3	0.303[ns]
Stable disease	4	36.4	4	44.4	
Progressive disease	2	18.1	2	24.4	
ECOG 2	10		7		
Complete response	0	0	0		
Partial response	4	40	2	28.6	0.606[ns]
Stable disease	5	50	3	42.8	
Progressive disease	1	10	2	28.6	
ECOG 3	7		9		
Complete -response	0	0	0	0	
Partial response	1	14.3	3	33.3	0.247[ns]
Stable disease	2	28.6	5	55.5	
Progressive disease	4	57.2	1	11.1	

8. Discussion

This research was conducted in Department of Radiation Oncology, National Institute of Cancer Research and Hospital, Mohakhali, Dhaka, to compare the effectiveness and clinical response of two palliative radiotherapy schedules of 17 Gy in 2 fractions versus 36 Gy in 12 fractions in reducing intrathoracic symptoms in stage IV non-small cell lung cancers.

The study population was in the age range of 35-72 years. The majority of incidence was seen in the age range of 45-54 years in both arms. Minimum age was 35 years in Arm-A, 37 years in Arm-B. Maximum age was 70 years in both arms. Age distribution resembles normal distribution where the median age of this study was 53 years. According to the Hospital Based Cancer Registry (HBCR) of NICRH (2018-20), the mean age was mean age 58.36 years, SD ±12.36 years in 2020. There was no significant difference in mean age. However, Attia et al. (2015) conducted a study of palliative hypo fractionated radiotherapy in South Egyptian participants with stage III and IV non-small cell lung cancer between March 2013 and March 2015 and found a median age of 68 years. The possible reason for dissimilarity is that most of the participants in this study belong to low socioeconomic conditions where there is a lack of awareness and thereby their exposure to tobacco occurs early and the development of carcinoma also occurs early [14].

In Arm A, the male and female participants were 22 (73.3%) and 8 (26.7%), respectively, and the ratio was 2.8:1. In Arm B, male and female participants were 24 (80%) and 6 (20%), respectively and the ratio was 4:1. So, the overall distribution was 76.7% male and 23.3% female which was close to the finding of the Hospital Cancer Registry Report 2018-2020, NICRH where 83.9% of total lung cancer participants were male and 16.1% of them were female in 2020. There was no significant difference in sex distribution among Arm A and Arm B. The majority of males is in almost all the previously listed studies except in the American study by Cross et al. (2004) in which females were 61% of the study population [9].

In this study's observation, the overall common presentation in both the groups was cough; 56 (93.3%). It was present in 28 (93.3%) participants in both arms. In Arm-A, it was then followed by respiratory distress in 28 (93.3%) participants, hemoptysis in 24 (80%), and chest pain in 21 (70%) participants. Likewise, in Arm-B cough was followed by hemoptysis, dyspnea, and chest pain in 24 (80%), 23 (76.7%), and 22 (73.3%) participants respectively. There was no significant difference between the two groups regarding presenting complaints. The finding was similar to the observation of Corner et al. (2005) and Attia et al. (2015) where cough, breathlessness, hemoptysis, and chest pain were the most common presentations [12, 15].

The chest pain was also evaluated by symptom score. Initially, it was 41 in Arm-A and 46 in Arm-B. Just after completion of RT, in the 6^{th} and 24^{th} weeks after radiotherapy, the score was 16, 13 & 11 respectively in Arm-A and the score was 19, 15 & 12 respectively in Arm-B. No statistically significant differences were found in chest pain palliation. These results were identical to the results of the prospective randomized trials [16, 17]. All these studies showed a significant palliation of the intra-thoracic symptoms after the hypo-fractionated regimen of 17 Gy in two fractions, which was equal to that achieved by more protracted regimens. These results, however, were challenged by a few studies, which demonstrated better palliation in participants given higher radiation doses. These discrepancies can at least partially be explained by different fractionation schedules, various endpoints, and differences in evaluation tools used in studies [18]. Many studies emphasized the importance of relying more on participant self-assessment than on physician evaluation.

Regarding skin toxicities, very few participants developed grade 1 or 2 skin reactions, and one participant an Arm-B grade 3 reaction. The difference was not statistically significant. Several studies including a study done by Attia et al (2015) did not mention skin toxicities. Highly conformal radiotherapy using high megavoltage energy could be the reason for a low to no percentage of participants developing skin toxicities [12].

Finally, this study illustrated that in most participants, a short course of radiotherapy with only two visits improves the common symptoms as effectively as longer courses without more side effects. The estimated α/β ratio for lung cancer is 3. The BED of 17 Gy radiation in 2 fractions is approximately 65.17 Gy, almost equal to the BED of 36 Gy in 12 fractions. Data indicates hypo-fractionated radiotherapy with 17 Gy in 2 fractions renders similar symptom relief with minimum and manageable toxicities compared with 36 Gy in 12 fractions in metastatic NSCLC. Moreover, the participants will have to come to the hospital only two times for treatment in the case of Arm-A which will greatly reduce the cost in terms of hospital expenditures & stay in cities. On the other hand, as a greater number of patients can be treated with hypo-fractionated radiotherapy in less time, it will be a huge opportunity to manage the long queue for radiation in a high-volume resource-constrained center like NICRH.

9. Conclusion

The study proved that hypo-fractionated and short-course palliative thoracic radiotherapy with 17 Gy in 2 fractions is non-inferior to 36 Gy in 12 fractions in participants with metastatic NSCLC, even with poor performance status and short expected survival time, in terms of relief of immediate intra-thoracic symptoms, minimum and manageable toxicities, and cost-effectiveness.

Abbreviations

ECOG	Eastern Cooperative Oncology Group

LLRT	Locoregional Radiation Therapy
NSCLC	Non-Small Cell Lung Cancer
NICRH	National Institute of Cancer Research and Hospital
RT	Radiotherapy
SEER	Surveillance Epidemiology and End Results

Conflicts of Interest

The authors declare no conflicts of interest.

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