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Original Research

Pulmonary Function Changes in Carcinoma Breast Patients Treated with hypo-fractionated Radiotherapy

Divya Sharma	Department of Radiation Oncology, Sardar Patel Medical College, Bikaner, Rajasthan, India.
Mayur Khandelwal	Department of Radiation Oncology, Sardar Patel Medical College, Bikaner, Rajasthan, India.
Neeti Sharma	Department of Radiation Oncology, Sardar Patel Medical College, Bikaner, Rajasthan, India.
Shankar Lal Jakhar	Department of Radiation Oncology, Sardar Patel Medical College, Bikaner, Rajasthan, India.

Background: Radiation treatment in breast cancer has very pivot role. Post operative chest irradiation in carcinoma breast is necessary because it prevents recurrence. By radiation treatment survival increase but also it increases local toxicity. This study intends to assess the acute and late pulmonary in patients undergoing post-operative radiation with hypo-fractionated radiotherapy techniques.

Material and methods: A total of 40 female patients of breast cancer, treated by mastectomy, were taken in our study from January 2022 to July 2022 after having obtained informed consent. All patients had PFT`s before the start of RT and post RT at 3 months, 6 months and after 2 years to assess early and late side effects.

Results: Results shows that we can use hypo-fractionated regimes as no significant long-term toxicity found in our study.

Conclusion: Our study has shown that hypo-fractionated regimes are not detrimental to the effective and safe delivery of radiation post- mastectomy in breast cancer patients especially when concerning acute or late pulmonary damage, with data in this study revealing no clinically statistically significant acute or late pulmonary toxicity even at a follow up of 2 years.

Introduction

In the breast cancer protocol, radiation treatment is essential to reduce post operative recurrences [1]. also many prospective studies also show the same effects by post op RT and adjuvant chemotherapy and it improves survival in high-risk females [2, 3]. Previously conventional RT was using 50 Gy in 25 Fr, but due to larger fractions it was associated with late tissue reactions [4]. LQ model two components of cell killing are described

i.e. α- which is proportional to dose and, β- proportional to square of dose. Lower the ratio, greater the effect of change in RT fraction size on normal and malignant tissues [5]. Hypo-fractionated RT is getting popular due to less fraction size compare to conventional, and the results are comparable for both the regimes. However, limited data is available for late tissue reactions by using hypo-fractionated regime. Pulmonary complications post-RT are inevitable still the incidence remains unclear [6]. Majority of patients are clinically asymptomatic and so are under diagnosed. Given the long favorable overall survival post treatment in breast cancer patients, the impact on quality of life of patients due to pulmonary complications should be quantified and reported lung is irradiated

during RT to chest wall and it is acute and chronically reacting tissue, acute pneumonitis seen within 6 months of treatment and late complications like fibrosis seen after several months. Lung is particularly sensitive to fractionation, with α/β estimated to be about 3 Gy. In the present study after post operative hypo-fractionated RT, pulmonary function test (PFT) is examined to every patient.

Materials and Methods

This hospital-based prospective study was conducted in the Department of Radiotherapy, Acharya Tulsi Cancer treatment and research center Bikaner, Rajasthan. The study population consisted of 40 female patients registered from January 2022 to July 2022 with histological confirmed carcinoma breast who were candidates for post-operative RT and were willing to undergo follow-up according to the study guidelines with informed consent. Those patients with ages between 18 and 65 years, Stage 1–3, with Eastern Cooperative Oncology Group performance status ≤2 and with no history of the previous pulmonary disease were included in the study. The study was conducted after taking ethical clearance from the ethical committee. Informed consent was taken from each patient. At the time of study started, the following data were collected: Name, age, address, socioeconomic status, menopausal status, hematological and biochemical parameters, previous comorbidities, site of the primary tumor, stage at diagnosis, histopathological report, details of surgery performed, chemotherapy taken, and whether hormonal agents were being used. Radiotherapy was planned and administered after obtaining informed consent. All patients were asked to undergo a PFT to get a baseline value. Radiation was scheduled to begin within 3 weeks after chemotherapy. A dose of 40.05 Gy in 15 fractions was planned using gamma rays from a Cobalt 60 machine using medial and lateral tangential fields. Patients were treated in the supine position with the ipsilateral arm abducted, externally rotated, and placed above the head. The tangential field borders were determined clinically and marked by radiopaque wires. Boost doses of 10 Gy in 5 fractions were given to patients who had undergone BCS. During the simulation, the central lung distance (CLD) values for each patient were recorded. Every patient was monitored at 3 months and 6 months and 2 years following radiation with PFT. A detailed history was taken and a clinical examination was done to assess pulmonary toxicity. forced expiratory volume in 1 s (FEV1) values were recorded. Data were entered into Microsoft Excel and analysis was performed using the SPSS software and analyzed with the help of descriptive statistics such as mean, standard deviation (SD), percentage, and statistical tests such as one-way ANOVA test, and Chi-square test applied appropriately.

Results

In our present study a total of 40 patients were screened. Patient, tumor, and treatment characteristics are reported in Table 1.

Patient Characteristics	n = 40 (%)
Age	
<45yrs	10 (25)
>45 yrs	30 (75)
Smokers	6 (15)
Non-smokers	34 (85)
Histology Ductal	40 (100)
Nodal dissection	
Adequate (≥10)	32 (80)
Inadequate (<10)	8 (20)
Stage grouping	
I	4 (10)

II	20 (50)
III	16 (40)
Grade	
I	6 (15)
II	20 (50)
III	14 (35)
LVSI	
Present	9 (23)
Absent	31 (77)
ECE	
Present	5 (12)
Absent	35 (88)
Supraclavicular field	
Yes	34 (85)
No	6 (15)

Table 1. Patient, Tumor and Treatment Characteristics.

Majority of the patients were in 38 to 65 years age group with a median age of 47 years. Average length and width of tangential field were 18.5 ± 1.1cm and 8±1.24cm respectively. Average central lung distance measured was 1.9 ± 1.3cm. Median follow up was 18 months. The mean of FEV1, FVC, and DLCO before and after radiotherapy are summarized in Table 2.

PFT	Before	3 months	6 months	2 years		p value	
	RT (a)	(x)	(y)	(z)	x vs. a	y vs. a	z vs. a
FEV1	108.12	102.5	101.07	100.1	0.81	0.8	1
	(3.21)	(3.25)	(4.01)	(7.42)			
FVC	107.67	106.11	105.67	105.11	0.49	0.87	0.27
	(4.03)	(3.9)	(4.07)	(4.35)			
DLCO	95.8	94.2	93.1	90.5	0.9	0.06	1.1
	(4.9)	(5.01)	(5.4)	(9.9)			

Table 2. Variation in Mean (SD) Values of Pulmonary Function Tests (PFT) Data Presented as Mean with Standard Deviation in Parenthesis (expressed as percentage of predicted PFT).

showing no statistically significant difference. All measurements being expressed as a percentage of predicted values adjusted for age, gender, and height. The CTC (v 3.0) adverse effects grading is depicted in Tables 3, 4, and 5 reported as percentage decline of predicted values of pulmonary functions.

Grade	No. of patients
Gr 0	28 (70%)
Gr 1	12 (30%)
TOTAL	40 (100)

Table 3. Acute Pulmonary Toxicity (CTC v 3.0).

GRADE	No. of Patients (40)
Gr 0	27 (64)
Gr 1	7 (18)
Gr 2	7 (18)
Gr 3	0 (0)
TOTAL	40

Table 4. Late Pulmonary Toxicity.

	No ≥ Gr2 toxicity	With ≥ Gr2 toxicity	p- value
Age			
<45 years	15	1	0.16
>45 years	20	4	
Smoking			
Smokers/ Ex-smokers	6	1	0.06
Non-smokers	32	1	
Supraclavicular RT			0.36
Yes	37	5	
No	3	0	
Chemotherapy used			0.16
TAC	15	4	
AC→TC	19	2	
Hormonal therapy			0.29
Tamoxifen	10	0	
Aromatase inhibitors	16	3	

Table 5. Association between Demographic Variables and ≥ Grade (Gr) 2 Lung Toxicity.

Discussion

Hypo-fractionated RT was taken into consideration to decrease hospital burdens but several studies showed severe complications [7-9]. when we using fraction size more than 2 Gy it may produces late side effects [10]. In this study we use hypo-fractionated regime of 40 Gy in 15 fr adjuvant to chemotherapy. While modeling the schedules α/β values of 3 Gy for late changes and 10 Gy for early changes were considered. Using these values the biologically effective doses estimated are as follows; early/ late effects→ 53.8 Gy/ 80.3 Gy and 50.6 Gy/ 75.3 Gy for 40 Gy and 42.5 Gy schedules respectively. During chest wall irradiation, proximity organs are prone to get irradiated i.e. lungs. and one such toxicity is radiation pneumonitis and this toxicity is directly related to the areas irradiated to lung. The likelihood of pneumonitis increases when the tangential fields are combined with the axillary and / or supraclavicular field and adjuvant chemotherapy. Radiation pneumonitis is type of disease which is characterized by symptoms like fever, cough, dyspnea. Lignos et al [11] reported RP in 1% of patients after surgery and radiation. Radiation pneumonitis seen in 9 % patients with 3 fields technique + CTRT vs 13 % in 2 fields and sequential chemotherapy. Plataniotis GA et al [12] evaluated RP in hypofractionation setting (42.5 Gy/ 16#) by HRCT in early breast cancer patients, and reported minimal and minor effects on the underlying lung parenchyma and investigated lung toxicities with conventional RT. Also, these studies showed pulmonary changes in patients who underwent breast conserving therapy [11, 13-17]. In our present study, we studied % decrease in pulmonary function test, predicted values of FVC, FEC1 and DLCO, were investigated. After follow up for median time of 18 months we observed variation in pulmonary function test, but it was not statistically significant. However, regards the individual assessment and bifurcation of acute and late reactions 30% of the study population developed Gr 1 acute reactions, late reactions- 18% had Gr1, 18 % Gr2 late pulmonary toxicity. A study by Lind et al [18] reported that as compared to whole breast radiotherapy alone addition of axillary/ supraclavicular radiotherapy portals increased incidence of pulmonary complications. However, in our study Gr2 and above late pulmonary toxicity was observed in 15% patients treated with supraclavicular radiotherapy (p = 0.36). Lingos et al [11] found increased incidence of radiation induced lung injury in patients receiving chemotherapy concomitantly. In contrast, in our study, no statistically significant late reactions found in patients, received chemotherapy. our trial found no statistically significant late adverse effect in patients receiving chemotherapy. (p= 0.16). Several trials were done to see any impact of tamoxifen and other hormonal therapy on RP. There were 3 patients out of a total 16 receiving aromatase inhibitors who developed ≥ Gr2 lung reactions (p= 0.29). Some of

other trials had studied about other risk factors that contributed to radiation lung injury i.e. age, smoking [18, 19-24]. In our study there were 4 patients out of 24 aged>45 years who had ≥Gr2 late pulmonary toxicity, not statistically significant (0.16). Supraclavicular field was used to cover supraclavicular lymph node, out of 40 patients' supraclavicular field was irradiated in 37 patients and in these patients 5 patients had grade 2 toxicity.

In conclusion, to conclude we can say that using hypo- fractionated Radiotherapy regimes are safer option to treat post operative breast cancer when concerning about late and acute toxicities, with data in this study revealing no clinically statistically significant acute or late pulmonary toxicity even at a follow up of 2years.

Conflict of interest

No conflict of interest.

Informed Consent

Research involving human participants – Informed consent was obtained from all individual participants included in the study

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