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Original Research Article

TOXICITY ANALYSIS IN CARCINOMA BREAST PATIENTS TREATED WITH CONVENTIONAL AND HYPOFRACTIONATED RADIOTHERAPY

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ABSTRACT

Background: The aim is Toxicity Analysis in Carcinoma Breast Patients Treated with Conventional and Hypofractionated Radiotherapy.

Materials and Methods: A Longitudinal observation study was carried out at the Department of Radiation Oncology, Gandhi Medical College, along with the associated Hamidia Hospital (GMC & HH), Bhopal (M.P), and Jawaharlal Nehru Cancer Hospital (JNCH), Bhopal (M.P) from 1st July 2022 to 30th Dec 2023.This study involved a cohort of 68 patients diagnosed with breast cancer.

Results: In our study, comparable rates of cardiac toxicity, assessed using RTOG criteria, were observed among breast carcinoma patients treated with either conventional or hypofractionation radiotherapy across various intervals. At 0 months, both treatment arms reported Grade 1 cardiac toxicity in 1 patient (2.94%) and no toxicity in 33 patients (97.06%), showing no significant difference (P = 1.0000).

Conclusion: We conclude that hypofractionated radiotherapy is comparable to conventional radiotherapy in terms of adverse effects and locoregional tumor control, making it a safe and effective alternative for postmastectomy breast cancer patients in adjuvant settings. Hypofractionated radiotherapy results in similar cardiac and pulmonary toxicities as conventional fractionation and is a viable alternative for breast cancer patients.

Keywords: Breast cancer, hypofractionated radiotherapy, late skin toxicity, survival.

INTRODUCTION

Globally, breast carcinoma (BC) is the most prevalent malignancy among women.[1] According to a WHO report from 2021, in 2020, there were 2.3 million new cases of breast cancer and 685,000 deaths worldwide. By the end of 2020, there were 7.8 million women alive who had been diagnosed with breast cancer in the past five years, making it the most prevalent cancer globally.[2]

In Asia, breast cancer is the most common cancer and the second leading cause of cancer-related deaths among women, with the continent accounting for 39% of all global breast cancer cases.[3] In India, breast carcinoma has recently surpassed cervical carcinoma to become the most common cancer among Indian women, a change attributed to the evolving lifestyle of Indian women.[4]

There is a growing interest in shortening the duration of radiation treatment by using larger fraction sizes, termed hypofractionation. Recently, hypofractionated radiation therapy (HFRT) has emerged as a promising alternative to conventional radiation therapy for breast cancer patients.. Long-term randomized trials, such as the START A and START B trials, have further affirmed that hypofractionated radiotherapy yields outcomes comparable to those of conventionally fractionated radiotherapy.[6]

MATERIALS AND METHODS

A Longitudinal observation study was carried out at the Department of Radiation Oncology, Gandhi Medical College, along with the associated Hamidia Hospital (GMC & HH), Bhopal (M.P), and Jawaharlal Nehru Cancer Hospital (JNCH), Bhopal (M.P) from 1st July 2022 to 30th Dec 2023.This study involved a cohort of 68 patients diagnosed with breast cancer.

Sample Size: Sample The sample size was determined using the formula

N = z2 pq/d2

With a prevalence rate of 0.0258 percent, the estimated sample size was approximately 62. Including an additional 10% to account for non-responsive patients, the total sample size reached 68 individuals. These participants were comprised of 34 patients each undergoing hypofractionated and conventional radiotherapy for breast cancer.

Inclusion Criteria

- Histopathologically confirmed case of carcinoma breast (DCIS)
- KPS score ≥ 70
- Patient not received any radiotherapy previously
- Age group between 18 to 70 year.
- Patient giving consent for study.
- Confirmed cases of ca breast who have not underwent previous radiotherapy treatment.

Exclusion criteria

- Patients who had previously underwent radiotherapy treatment Patients who do not give consent for the study
- KPS score < 70
- Patients below 18 yr age and above 70 yr age

Study Methodology

Following approval from the Institute's ethical Committee, the study commenced. Patients meeting the inclusion and exclusion criteria were enrolled, and sociodemographic information including age, gender, and place of residence was collected and recorded in an MS Excel spreadsheet. Comprehensive data regarding the tumor, its stage, and the presence of metastasis were also gathered and documented. Subsequently, all 68 participants were randomly allocated to treatment groups using simple randomization, with participants assigned to either the treated with conventional Radiotherapy or Hypofractionated Radiotherapy group. The patients in two groups. All patients were randomly distributed into two treatment groups : CF group = 34 (34 Gy [25 fractions, 2 Gy per fraction, one fraction per day, 5 fractions per week, for 5-6 weeks)and HF group = 34 patients (40 GY/15 fractions, 2.67 Gy per fraction, 1 fraction per day, 5 fractions per week, for 3-3.5 weeks.)

Dosimetric Analysis: All patients were planned on Varian dual energy, linear accelerator CLINAC 2300 machine with IMRT on ECLIPSE Planning System. The treatment was planned with a goal of 100% volume of planning target volume (PTV) to be included by 95% isodose line. Data collected included the volume of PTV receiving at least 95% and 90% of prescribed dose (V95 and V90) and also dose delivered to 90% of the volume of PTV (D90%) from the dose-volume histograms. The acceptable hot spot limit was 107%. The treatment plan was accepted if the volume of heart receiving 25 Gy was < 10% and volume of ipsilateral lung receicing 20 Gy was < 35%.

Toxicity Analysis: The Baseline pretreatment ECG, Echocardiogram and PFT were recorded and patients were kept on follow up at 3 and 6 months with further 2D Echo and PFT at Department of Cardiology, GMC, Bhopal and department of Respiratory Medicine, GMC, Bhopal respectively. Cardio Toxicity and pulmonary toxicity assessment was done according to RTOG and CTCAE toxicity criteria and graded accordingly. Post radiation skin changes at completion of radiation (0) months and subsequent follow up at (3)months and (6) months was assessed using CTCAE criteria and graded accordingly.

RESULTS

[Table 1] presents the distribution of the study population diagnosed with breast carcinoma, categorized by age groups. A total of 68 patients were analyzed. The data is segmented into five age groups: less than 30 years, 31-40 years, 41-50 years, 51-60 years, and older than 60 years. The majority of patients fell within the 41-50-year age group, comprising 33.82% (n=23) of the total population. The second largest group was those aged 51-60 years, accounting for 30.88% (n=21). Patients aged 31-40 years represented 17.65% (n=12) of the cohort. The smallest groups were those under 30 years, constituting 5.88% (n=4), and those over 60 years, making up 11.76% (n=8) of the study population. Overall, the distribution highlights that the majority of breast carcinoma cases in this study occurred in the middle-aged groups (41-60 years), with fewer cases in the youngest and oldest age brackets.

Table 1: Distribution of Study Population of Breast Carcinoma Between Two Arm According to Age Groups

Age Group (year)	N	Column %
<30 year	4	5.88%
31-40 year	12	17.65%
41-50 year	23	33.82%
51-60 year	21	30.88%
>60 year	8	11.76%
All	68	100.00%

Table 2: Distribution of Study Population of Breast Carcinoma Between Two Arm According to Religion

Religion	N	%
Hindu	54	79.41%
Muslim	14	20.59%
All	68	100.00%

[Table 2] illustrates the distribution of the study population diagnosed with breast carcinoma, categorized by religion. Out of a total of 68 patients, the majority identified as Hindu, comprising 79.41% (n=54) of the population. The remaining 20.59% (n=14) identified as Muslim. This distribution indicates that the Hindu patients constituted the predominant group in this study.

Table 3: Distribution of Study Population of Breast Carcinoma Between Two Arm According to Residence

Residence	N	%
Rural	44	64.71%
Urban	24	35.29%
All	68	100.00%

[Table 3] presents the distribution of breast carcinoma patients based on their place of residence. Among the 68 patients included in the study, 64.71% (n=44) resided in rural areas, while 35.29% (n=24) lived in urban areas. This data suggests a higher prevalence of breast carcinoma cases among the rural population in this study.

Table 4: Distribution of Study Population of Breast Carcinoma Between Two Arm According to Side of Carcinoma

Side	N	%
Left	43	63.24%
Right	25	36.76%
All	68	100.00%

Table 4 shows the distribution of breast carcinoma cases based on the side of the carcinoma. Among the 68 patients studied, 63.24% (n=43) had carcinoma on the left side, while 36.76% (n=25) had carcinoma on the right side. This indicates a higher occurrence of left-sided breast carcinoma in the study population.

Table 5: Distribution of Study Population of Breast Carcinoma Between Two Arm According to Stage

	Arm				
Stage	Hypofractionation		Conventional		P Value
Stage	N	%	N	%	
IA	5	7.35%	3	4.41%	
IIA	10	14.71%	8	11.76%	
IIB	11	16.18%	7	10.29%	0.4436
IIIA	5	7.35%	10	14.71%	
IIIB	0	0.00%	1	1.47%	
IIIC	3	4.41%	5	7.35%	
All	34	50.00%	34	50.00%	

[Table 5] shows the distribution of the study population of breast carcinoma between two Arms, according to stage. In the Hypofractionation group, the most common stages were IIB (11 patients, 16.18%) and IIA (10 patients, 14.71%). In the Conventional group, the most common stages were IIIA (10 patients, 14.71%) and IIA (8 patients, 11.76%). The p-value of 0.4436 indicates no statistically significant difference in stage distribution between the two Arms.

Table 6: Distribution of Study Population of Breast Carcinoma Between Two Arm According to HPR

	Arm				
	Hypofractionation		Conventional		P Value
HPR	N	%	N	%	
DCIS	0	0.00%	2	2.94%	
IDC	32	47.06%	26	38.24%	0.2810
IDC-Nos	0	0.00%	2	2.94%	
I-NOS	0	0.00%	1	1.47%	
Malignant Phyllodes	1	1.47%	0	0.00%	
Mucinous	0	0.00%	1	1.47%	
Phyllodes	1	1.47%	2	2.94%	

[Table 6] shows the distribution of the study population of breast carcinoma between two Arms according to histopathological report (HPR). In the Hypofractionation group, invasive ductal carcinoma (IDC) was the most common type, observed in 32 patients (47.06%). The Conventional group also had a majority with IDC, seen in 26 patients (38.24%). Other types observed in the Conventional group include ductal carcinoma in situ (DCIS) in 2 patients (2.94%), IDC-Nos in 2 patients (2.94%), I-NOS in 1 patient (1.47%), mucinous carcinoma in 1 patient (1.47%), and Phyllodes tumor in 2 patients (2.94%). In the Hypofractionation group, malignant Phyllodes was seen in 1 patient (1.47%) and Phyllodes tumor in 1 patient (1.47%). The p-value of 0.2810 indicates no statistically significant difference in HPR distribution between the two Arms.

Table 7: Distribution of Study Population of Breast Carcinoma Between Two Arm According to dose parameters

Variable		Hypofractionation			Conventional					
	Side	n	Mean	SD	n	Mean	SD	Difference	95% CI	P a
Dose (Gy)	Both	34	48.823529	11.172126	34	46.794118	11.661331	-2.029412	-7.559094 to 3.500271	<0.0001
Rt-Lung-Min (Gy)	Both	34	82.941176	5.239368	34	85.588235	5.039947	2.647059	0.157773 to 5.136345	0.0297
Rt-Lung-Max (Gy)	Both	34	40.000000	0.000000	34	50.000000	0.000000	10.000000	10.000000 to 10.000000	0.1592
Rt-Lung-Mean (Gy)	Both	34	0.426471	0.535587	34	0.179412	0.364965	-0.247059	-0.46897 to -0.0251390	0.7337
Lt-Lung-Min (Gy)	Both	34	24.133235	15.481090	34	17.955882	20.004002	-6.177353	-14.838476 to 2.483770	0.6689
Lt-Lung-Max (Gy)	Both	34	4.161765	4.278984	34	3.752941	5.512478	-0.408824	-2.798260 to 1.980613	0.0322
Lt-Lung-Mean (Gy)	Both	34	0.314706	0.356865	34	0.352941	0.376777	0.0382353	-0.139459 to 0.215929	0.0037
Heart-Min (Gy)	Both	34	26.511765	16.014534	34	35.770588	18.773620	9.258824	0.809501 to 17.708146	0.5683
Heart-Max (Gy)	Both	34	4.667647	4.217260	34	7.985294	4.839555	3.317647	1.119650 to 5.515644	0.0002
Heart-Mean (Gy)	Both	34	0.308824	0.410740	34	0.258824	0.299614	-0.050000	-0.224082 to 0.124082	<0.0001
Spinal Cord-Min (Gy)	Both	34	20.252059	13.421036	34	34.302941	15.515574	14.050882	7.026450 to 21.075315	0.2387
Spinal Cord -Max (Gy)	Both	34	2.700000	2.155050	34	6.352941	3.661779	3.652941	2.198095 to 5.107787	0.0005
Spinal Cord-Mean (Gy)	Both	34	0.1000000	0.147710	34	0.138235	0.115509	0.0382353	-0.0259700 to 0.102441	0.0162
Rt-Lung-Mean (Gy)	Right	15	7.400000	4.268155	10	11.540000	3.984470	4.140000	0.627235 to 7.652765	0.0229
Lt-Lung-Mean (Gy)	Left	19	7.447368	3.673685	24	10.750000	2.383640	3.302632	1.430569 to 5.174694	0.0009
Heart-Mean (Gy)	Left	19	4.052632	1.654075	24	7.975000	2.564007	3.922368	2.551114 to 5.293623	<0.0001

a T-test

In [Table 7], the distribution of the study population with breast carcinoma between two Arms is presented based on dose parameters. The dose (Gy) delivered to the tumor (Dose (Gy)) was significantly higher in the hypofractionation group (48.82 ± 11.17) compared to the conventional group (46.79 ± 11.66) ($p < 0.0001$). Regarding radiation doses to organs at risk, the minimum dose to the right lung (Rt-Lung-Min (Gy)) was lower in the hypofractionation group (82.94 ± 5.24) compared to the conventional group (85.59 ± 5.04), with a statistically significant difference ($p = 0.0297$). However, the maximum dose to the right lung (Rt-Lung-Max (Gy)) did not show a statistically significant difference between the two groups ($p = 0.1592$). For the left lung, the hypofractionation group had a significantly higher mean dose (Lt-Lung-Mean (Gy)) of 0.31 ± 0.36 compared to the conventional group (0.35 ± 0.38) ($p = 0.0037$). Similarly, the maximum dose to the left lung (Lt-Lung-Max (Gy)) was significantly higher in the hypofractionation group (4.16 ± 4.28) compared to the conventional group (3.75 ± 5.51) ($p = 0.0322$). Regarding the heart, both the maximum dose (Heart-Max (Gy)) and mean dose (Heart-Mean (Gy)) were significantly lower in the hypofractionation group (4.67 ± 4.22 and 0.31 ± 0.41) compared to the conventional group (7.99 ± 4.84 and 0.26 ± 0.30) ($p = 0.0002$ and $p < 0.0001$, respectively). In terms of the spinal cord, the maximum dose (Spinal Cord-Max (Gy)) was significantly lower in the hypofractionation group (2.70 ± 2.16) compared to the conventional group (6.35 ± 3.66) ($p = 0.0005$), whereas the mean dose (Spinal Cord-Mean (Gy)) did not show a statistically significant difference ($p = 0.0162$).

Dosimetry comparison between same side of two comparable arms

Ipsilateral Lung dose Parameters: The mean dose to the right lung (Rt-Lung-Mean) was significantly lower in the hypofractionation group (7.40 Gy ± 4.27) compared to the conventional group (11.54 Gy ± 3.98). The mean difference was 4.14 Gy, with a 95% confidence interval (CI) of 0.63 to 7.65, and a p-value of 0.0229.

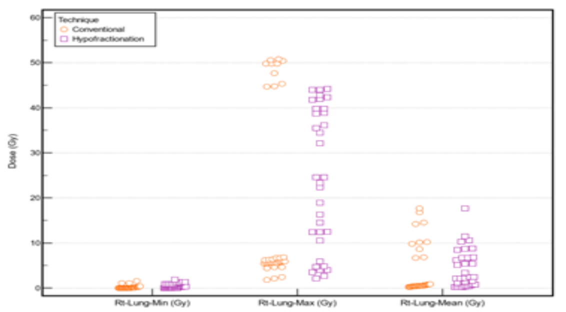

Figure 1: Comparison of dosimetric analysis of Rt Lung between two Arms

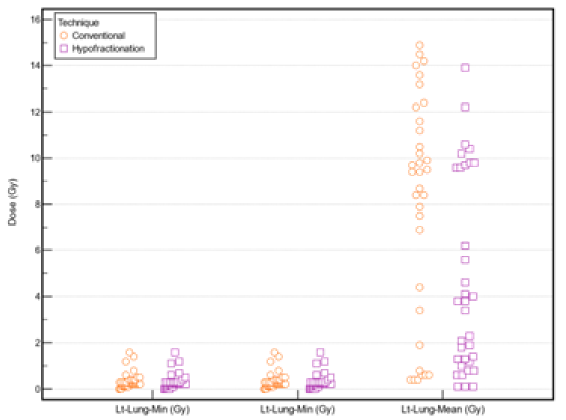

Figure 2: Comparison of dosimetric analysis of Lt Lung between two Arms

The mean dose to the left lung (Lt-Lung-Mean) was also significantly lower in the hypofractionation group (7.45 Gy ± 3.67) compared to the conventional group (10.75 Gy ± 2.38). The mean difference was 3.30 Gy, with a 95% CI of 1.43 to 5.17, and a p-value of 0.0009.

Heart Dose Parameters (Left Side): The mean dose to the heart (Heart-Mean) was significantly lower in the hypofractionation group (4.05 Gy ± 1.65) compared to the conventional group (7.98 Gy ± 2.56). The mean difference was 3.92 Gy, with a 95% CI of 2.55 to 5.29, and a p-value of <0.0001.

These results indicate that hypofractionation radiotherapy delivers significantly lower mean doses to the lungs and heart compared to conventional radiotherapy, which could imply potential benefits in reducing radiation-related toxicity in these organs.

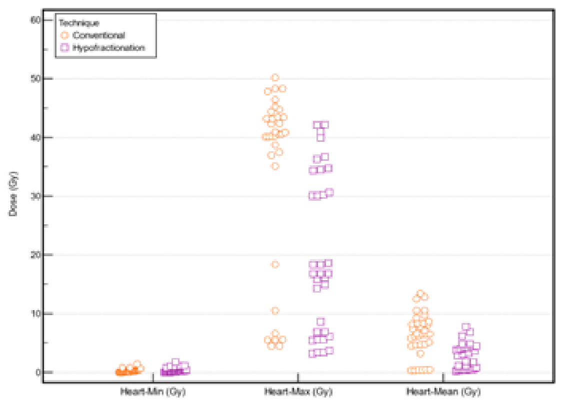

Figure 3: Comparison of dosimetric analysis of heart between two Arms

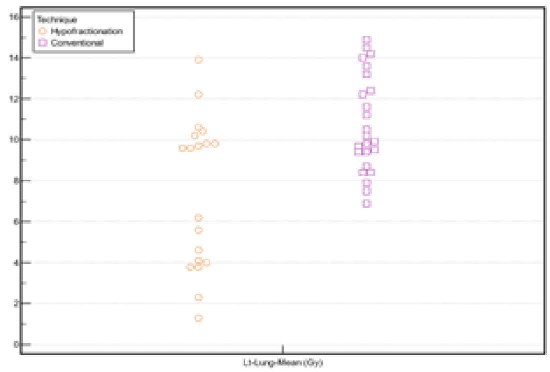

Figure 4: Comparison of dosimetric analysis of Lt Lung between two Arms (Left Side only)

Table 8: Comparison of Study Population of Breast Carcinoma Between Two Arm According to Toxicity Analysis

Variable at baseline(0), 3 ,6 months	**Side**	**Hypofractionation**			**Conventional**					
		n	**Mean**	**SD**	**n**	**Mean**	**SD**	**Difference**	**95% CI**	**P a**
Heart (LVEF) - Baseline (%)	Both	34	63.352941	3.445527	34	63.264706	2.573864	-0.0882353	-1.560846 to 1.384375	0.9051
Heart (LVEF) - 3 (%)	Both	34	61.764706	3.312591	34	60.970588	3.511758	-0.794118	-2.447126 to 0.858890	0.3410
Heart (LVEF) - 6 (%)	Both	34	60.558824	3.173672	34	59.617647	3.533517	-0.941176	-2.567450 to 0.685097	0.2521
Lung (FEV1)-Baseline	Both	34	2.404412	0.308655	34	2.285882	0.219905	-0.118529	-0.248295 to 0.0112365	0.0727
Lung (FEV1)- 3	Both	34	2.330882	0.247477	33	2.203333	0.201101	-0.127549	-0.237766 to -0.0173323	0.0240
Lung (FEV1)- 6	Both	34	2.285588	0.252036	34	2.187941	0.199936	-0.0976471	-0.207803 to 0.0125087	0.0814
Lung (FEV1/FVC)-Baseline	Both	26	80.625000	2.705005	1	79.800000	0.000000	-0.825000	-6.502186 to 4.852186	0.7672
Lung (FEV1/FVC)-3	Both	26	81.007692	2.530917	1	80.200000	0.000000	-0.807692	-6.119507 to 4.504123	0.7568

Lung (FEV1/FVC)- 6	Both	26	80.919231	2.703482	1	80.000000	0.000000	-0.919231	-6.593222 to 4.754760	0.7414
Lung (FEV1)- Baseline	Right	15	2.319333	0.317321	10	2.137000	0.185056	-0.182333	-0.413140 to 0.0484734	0.1158
Lung (FEV1)- 3	Right	15	2.264000	0.257233	10	2.090000	0.200111	-0.174000	-0.373755 to 0.0257551	0.0847
Lung (FEV1)- 6	Right	15	2.202000	0.274726	10	2.098000	0.222301	-0.104000	-0.319773 to 0.111773	0.3291
Lung (FEV1/FVC)- Baseline	Right	15	79.773333	2.778352	10	82.890000	1.521293	3.116667	1.117391 to 5.115943	0.0037
Lung (FEV1/FVC)- 3	Right	15	79.986667	2.745611	10	83.080000	1.323967	3.093333	1.153773 to 5.032894	0.0031
Lung (FEV1/FVC)- 6	Right	15	80.233333	2.771453	10	82.930000	1.406374	2.696667	0.725224 to 4.668109	0.0095
Heart (LVEF) - 0 (%)	Left	19	63.894737	2.469699	24	63.583333	2.124734	-0.311404	-1.726990 to 1.104183	0.6592
Heart (LVEF) - 3 (%)	Left	19	62.000000	2.768875	24	61.083333	3.133503	-0.916667	-2.764079 to 0.930745	0.3222
Heart (LVEF) - 6 (%)	Left	19	60.368421	2.564946	24	59.416667	3.374027	-0.951754	-2.840396 to 0.936888	0.3148
Lung (FEV1)- Baseline	Left	19	2.471579	0.292485	24	2.347917	0.205743	-0.123662	-0.277211 to 0.0298869	0.1115
Lung (FEV1)- 3	Left	19	2.383684	0.232695	24	2.250833	0.180721	-0.132851	-0.260087 to -0.00561459	0.0411
Lung (FEV1)- 6	Left	19	2.351579	0.217569	24	2.225417	0.181754	-0.126162	-0.249125 to -0.00319922	0.0446
Lung (FEV1/FVC)- Baseline	Left	19	80.534211	2.453911	24	83.866667	0.946236	3.332456	2.232489 to 4.432423	<0.0001
Lung (FEV1/FVC)- 3	Left	19	81.047368	2.186415	24	83.804167	1.032717	2.756798	1.738336 to 3.775260	<0.0001
Lung (FEV1/FVC)- 6	Left	19	80.894737	2.421770	24	84.020833	1.087070	3.126096	2.010189 to 4.242004	<0.0001

In [Table 8], the comparison of toxicity parameters observed in patients with breast carcinoma treated using either hypofractionation or conventional Arms presented. The study evaluated several variables related to cardiac and pulmonary function across both treatment groups. Firstly, regarding cardiac function assessed through left ventricular ejection fraction (LVEF), there were no statistically significant differences observed between the hypofractionation and conventional groups at baseline (0 months), 3 months, or 6 months ($p > 0.05$ for all comparisons). Specifically, at baseline, the mean LVEF was 63.35% ± 3.45% in the hypofractionation group and 63.26% ± 2.57% in the conventional group. At 3 months, these values were 61.76% ± 3.31% and 60.97% ± 3.51%, respectively. By 6 months, the mean LVEF was 60.56% ± 3.17% in the hypofractionation group and 59.62% ± 3.53% in the conventional group. These findings indicate that both treatment approaches had comparable effects on cardiac function over the monitored period.In terms of pulmonary function, assessed by forced expiratory volume in one second (FEV1) and the ratio of FEV1 to forced vital capacity (FVC), some differences were noted. At 0 months, FEV1 was slightly higher in the hypofractionation group (2.40 ± 0.31 L) compared to the conventional group (2.29 ± 0.22 L), although this difference did not reach statistical significance ($p = 0.0727$). At 3 months, FEV1 was significantly higher in the hypofractionation group (2.33 ± 0.25 L) compared to the conventional group (2.20 ± 0.20 L) ($p = 0.0240$). Overall, while there were subtle differences in pulmonary function parameters between the hypofractionation and conventional groups, the study suggests that both treatment modalities were generally well-tolerated with respect to cardiac and pulmonary toxicities.

Toxicity Analysis

Table 9: Distribution of Study Population of Breast Carcinoma Between Two Arm According to Skin Toxicity

		Arm				
		Hypofractionation		**Conventional**		**P Value**
Skin Toxicity		**N**	**%**	**N**	**%**	
0 month	Grade 1	2	5.88%	2	5.88%	1.0000
	None	32	94.12%	32	94.12%	
3 months	None	34	100.00%	34	100.00%	--
6 months	None	34	100.00%	34	100.00%	--

[Table 9] presents the distribution of skin toxicity among breast carcinoma patients, comparing those receiving hypofractionation and conventional radiotherapy at different time intervals. At the 0-month, Grade 1 skin toxicity was observed in 2 patients (5.88%) in both the hypofractionation and conventional arms, with no significant difference (P = 1.0000). The remaining 32 patients (94.12%) in each arm showed no skin toxicity. At 3 and 6 months, no skin toxicity (Grade 0) was reported in any patients across both treatment arms.

Ipsilateral Lung Toxicity

Right Lung Toxicity:

- The Forced Expiratory Volume in 1 second (FEV1) at baseline (0 months), 3 months, and 6 months did not show statistically significant differences in toxicity between the hypofractionation and conventional arms, with p-values of 0.1158, 0.0847, and 0.3291, respectively.
- Conversely, the FEV1/FVC ratio, which is an indicator of lung toxicity, at baseline, 3 months, and 6 months was significantly lower in the hypofractionation group compared to the conventional group. The respective p-values were 0.0037, 0.0031, and 0.0095.

Left Lung Toxicity:

- The FEV1 at baseline, 3 months, and 6 months did not exhibit significant differences in lung toxicity between the hypofractionation and conventional groups, with p-values of 0.1115, 0.0411, and 0.0446, respectively.
- However, the FEV1/FVC ratio at baseline, 3 months, and 6 months was significantly lower in the hypofractionation group compared to the conventional group, indicating higher lung toxicity. The corresponding p-values were all <0.0001.

Heart Toxicity:

- The Left Ventricular Ejection Fraction (LVEF) at baseline, 3 months, and 6 months did not differ significantly in terms of heart toxicity between the hypofractionation and conventional arms, with p-values of 0.6592, 0.3222, and 0.3148, respectively.

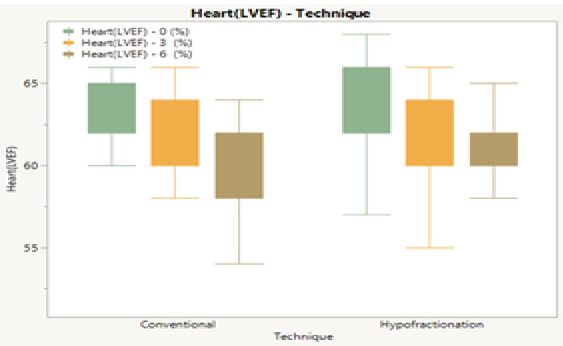

Figure 5: The comparison of toxicity parameter- Heart (LVEF) Between Two Arm in Study Population of Breast Carcinoma (Both Side)

These findings indicate that while there were no significant differences in FEV1 between the two treatment groups, the FEV1/FVC ratio was significantly lower in the hypofractionation group for both lungs at all assessed time points, suggesting increased lung toxicity. Heart function, as measured by LVEF, did not demonstrate significant differences in toxicity between the hypofractionation and conventional groups.

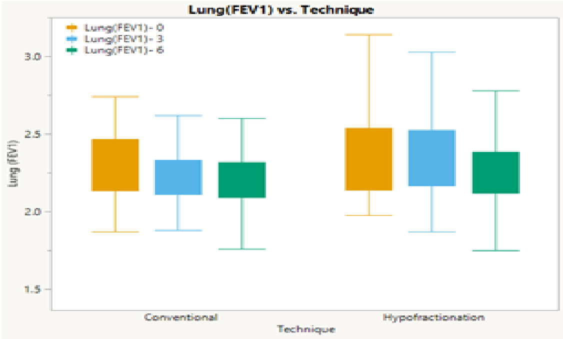

Figure 6: The comparison of toxicity parameter- Lung (FEV1) Between Two Arm in Study Population of Breast Carcinoma (Both Side)

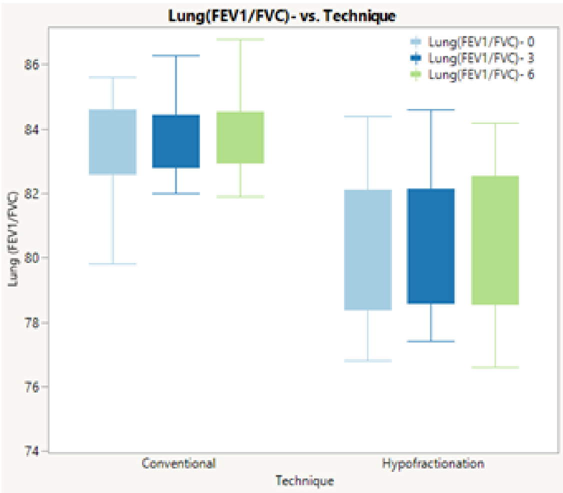

Figure 7: The comparison of toxicity parameter- Lung (FEV1/FVC) Between Two Arm in Study Population of Breast Carcinoma (Both Side)

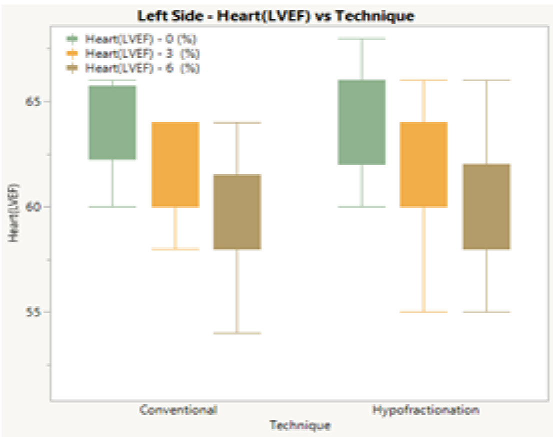

Figure 8: The comparison of toxicity parameter- Heart (LVEF) Between Two Arm in Study Population of Breast Carcinoma (Left Side)

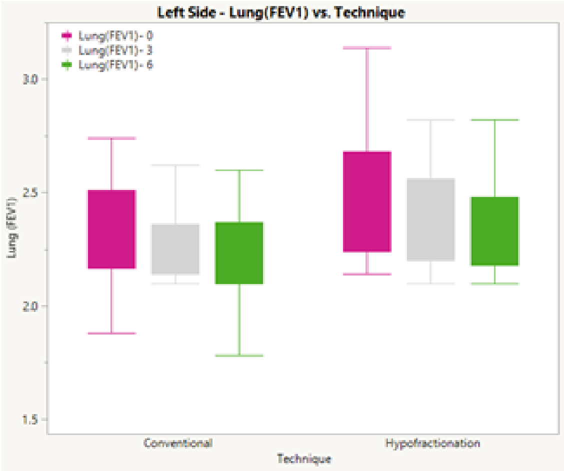

Figure 9: The comparison of toxicity parameter- Lung (FEV1) Between Two Arm in Study Population of Breast Carcinoma (Left Side)

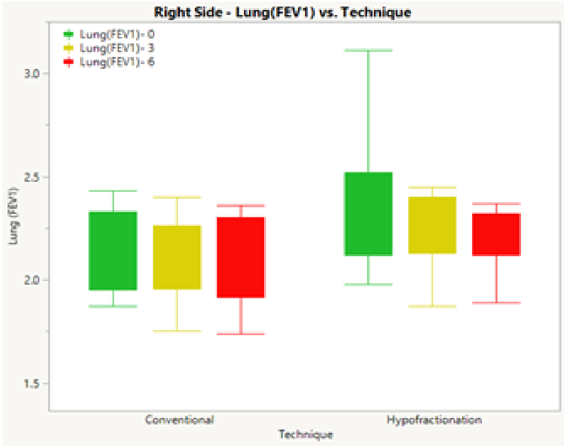

Figure 10: The comparison of toxicity parameter- Lung (FEV1) Between Two Arm in Study Population of Breast Carcinoma (Right Side)

Table 10: Comparison of Cardiac Toxicity Among Study Population of Breast Carcinoma Between Two Arm According to RTOG Criteria

		Arm				
Cardiac toxicity at baseline (0), 3,6 months		**Conventional**		**Hypofractionation**		**P value**
		N	**%**	**N**	**%**	
CT- 0 Months	Grade 1	1	2.94%	1	2.94%	1.0000
	None	33	97.06%	33	97.06%	
CT- 3 Months	Grade 1	2	5.88%	0	0.00%	0.1542
	None	32	94.12%	34	100.00%	
CT- 3 Months	Grade 1	4	11.76%	2	5.88%	0.3960
	None	30	88.24%	32	94.12%	

This table presents a comparison of cardiac toxicity, measured using RTOG criteria, among breast carcinoma patients treated with either conventional or hypofractionation radiotherapy at various time points.

- 0 Months: Both treatment arms reported 1 patient (2.94%) with Grade 1 cardiac toxicity, and 33 patients (97.06%) with no cardiac toxicity, showing no significant difference (P = 1.0000).
- 3 Months: In the conventional arm, 2 patients (5.88%) exhibited Grade 1 cardiac toxicity, whereas no cases were reported in the hypofractionation arm, with 32 patients (94.12%) in the conventional arm and 34 patients (100.00%) in the hypofractionation arm showing no cardiac toxicity as well as no significant difference (P = 0.1542).
- 6 Months: Grade 1 cardiac toxicity was observed in 4 patients (11.76%) in the conventional arm and 2 patients (5.88%) in the hypofractionation arm, with 30 patients (88.24%) and 32 patients (94.12%) showing no toxicity, as well as no significant difference (P = 0.3960).

Table 11: Comparison of Lung Toxicity Among Study Population of Breast Carcinoma Between Two Arm According to CTCAE Criteria

		Arm				
Lung toxicity		**Conventional**		**Hypofractionation**		**P value**
		N	**%**	**N**	**%**	
LT- 0 Months	Grade 1	0	0.00%	1	2.94%	0.3173
	None	34	100.00%	33	97.06%	
LT- 3 Months	Grade 1	2	5.88%	0	0.00%	0.1542
	None	32	94.12%	34	100.00%	
LT- 6 Months	Grade 1	3	8.82%	1	2.94%	0.3062
	None	31	91.18%	33	97.06%	

The [Table 11] compares lung toxicity, as assessed by RTOG criteria, between breast carcinoma patients treated with conventional radiotherapy and hypofractionation at various time points.

- 0 Months: In the conventional arm, no patients (0.00%) experienced Grade 1 lung toxicity, whereas 1 patient (2.94%) in the hypofractionation arm did. All 34 patients (100.00%) in the conventional arm and 33 patients (97.06%) in the hypofractionation arm had no lung toxicity (P = 0.3173).
- 3 Months: At this interval, 2 patients (5.88%) in the conventional arm showed Grade 1 lung toxicity, while no such cases were reported in the hypofractionation arm. The remaining 32 patients (94.12%) in the conventional arm and all 34

- patients (100.00%) in the hypofractionation arm exhibited no lung toxicity and no statistically significant difference was observed (P = 0.1542).
- 6 Months: By the 6-month mark, 3 patients (8.82%) in the conventional arm experienced Grade 1 lung toxicity compared to 1 patient (2.94%) in the hypofractionation arm. No lung toxicity was observed in 31 patients (91.18%) in the conventional arm and 33 patients (97.06%) in the hypofractionation arm and no statistically significant difference was observed (P = 0.3062).

DISCUSSION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related deaths in women worldwide.[7] This collaborative approach ensures comprehensive and personalized care, aimed at achieving the best possible treatment outcomes for each patient. In the context of breast-conserving surgery, whole breast radiotherapy (WBRT) is routinely administered to most patients.

In this study, the largest proportion of patients fell within the 41-50-year age group, comprising 33.82% (n=23) of the total population. The next largest group consisted of individuals aged 51-60 years, accounting for 30.88% (n=21). Patients aged 31-40 years constituted 17.65% (n=12) of the cohort.

Our study encompassed patients with breast carcinoma affecting both sides, with a higher incidence observed on the left side. Among the 68 patients evaluated, 63.24% (n=43) had carcinoma on the left breast, compared to 36.76% (n=25) on the right side. In contrast, Saha et al. specifically included patients with left-sided breast carcinoma only in their study.[8]

In terms of radiation doses to organs at risk, the hypofractionation group in our study exhibited a statistically lower minimum dose to the right lung (Rt-Lung-Min (Gy)) at 82.94 ± 5.24, compared to the conventional group's 85.59 ± 5.04 (p = 0.0297). However, there was no statistically significant difference in the maximum dose to the right lung (Rt-Lung-Max (Gy)) between the two groups (p = 0.1592). Conversely, for the left lung, the hypofractionation group showed a significantly higher mean dose (Lt-Lung-Mean (Gy)) of 0.31 ± 0.36 compared to the conventional group's 0.35 ± 0.38 (p = 0.0037). Similarly, the maximum dose to the left lung (Lt-Lung-Max (Gy)) was significantly higher in the hypofractionation group (4.16 ± 4.28) compared to the conventional group (3.75 ± 5.51) (p = 0.0322).

Similar to our study, previous research did by Wang et al,[9,10] has shown no significant difference between groups regarding the incidence of acute or late toxicities such as symptomatic radiation pneumonitis, lymphedema, ischemic heart disease, late skin toxicity, lung fibrosis, or shoulder dysfunction.

In our study, comparable rates of cardiac toxicity, assessed using RTOG criteria, were observed among breast carcinoma patients treated with either conventional or hypofractionation radiotherapy across various intervals. At 0 months, both treatment arms reported Grade 1 cardiac toxicity in 1 patient (2.94%) and no toxicity in 33 patients (97.06%), showing no significant difference (P = 1.0000). By 3 months, Grade 1 cardiac toxicity was noted in 2 patients (5.88%) in the conventional arm, while no cases were reported in the hypofractionation arm; 94.12% of patients in the conventional arm and 100.00% in the hypofractionation arm remained free of cardiac toxicity, with no significant difference observed (P = 0.1542). At 6 months, Grade 1 cardiac toxicity was observed in 4 patients (11.76%) in the conventional arm and 2 patients (5.88%) in the hypofractionation arm; 88.24% and 94.12% of patients in the conventional and hypofractionation arms, respectively, did not experience cardiac toxicity, with no significant difference noted (P = 0.3960). Our findings regarding functional cardiac toxicities align with existing evidence. Alagizy et al,[11] reported no additional cardiac toxicity associated with hypofractionated radiotherapy compared to conventional fractionation in the adjuvant treatment of breast cancer.

CONCLUSION

We conclude that hypofractionated radiotherapy is comparable to conventional radiotherapy in terms of adverse effects and locoregional tumor control, making it a safe and effective alternative for postmastectomy breast cancer patients in adjuvant settings. Hypofractionated radiotherapy results in similar cardiac and pulmonary toxicities as conventional fractionation and is a viable alternative for breast cancer patients. hypofractionation in breast has shown its efficacy in terms of safety profile and comparable adverse effects with advantages of improved patient convenience due to shorter overall treatment time, decreased dropout rates and potentially lower health care costs. In India, given the challenges with patient compliance to the prolonged conventional schedule and the need for optimal resource utilization, hypofractionated radiotherapy protocols have evolved and may become the standard practice in the future.

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