ORIGINAL RESEARCH PAPER

Volume-8 | Issue-8 | August - 2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

HYPOFRACTIONATED ADJUVANT RADIOTHERAPY IN POST MASTECTOMY BREAST CANCER PATIENTS: A SINGLE INSTITUTIONAL RETROSPECTIVE STUDY.

Radiotherapy

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ABSTRACT

Aim of Study: Breast carcinoma is one of the most common cancers in India . Adjuvant hypofractionated radiotherapy has increased local-regional and overall survival rates in breast cancer.

Materials & Methods: Records of patients attending Radiotherapy OPD from December 2016 to May 2018 were analysed retrospectively. Several patient records available in the department were reviewed by census method based on pre-decided inclusion and exclusion criteria.

Results: Hypofractionated radiation schedule was as safe and effective as the standard 5 week fractionation schedule for the treatment of breast cancer.

Discussion: There was no statistically significant difference between the conventional and hypofractionated radiation with respect to both the locoregional failure ,distant failure rates and late skin toxicity. ***Conclusion:*** Hypofractionated radiation therapy is cheaper and more convenient for the patients and also reduces the heavy workload of already overburdened radiotherapy setup in a developing country like ours with scarcity of resources.

KEYWORDS

Breast cancer, Hypofractionation, Post-mastectomy, Radiotherapy

INTRODUCTION

Breast cancer is the most common cancer in women worldwide. Breast cancer represents 12% of all new cases diagnosed and 25% of all cases in women (Statistics, 2007)[1]. Breast cancer incidence has increased in most countries worldwide in the last decades.[2] Data from the International Agency for Research on Cancer (IARC) registry suggest that 45% of newly diagnosed cases of breast cancer and 55% of breast cancer related mortality currently occur in low- and middle income countries. More than 80% of Indian patients are younger than 60 years of age. In India premenopausal patients constitute about 50% of all patients (Agarwal et al., 2007). The average age of breast cancer patients has been reported to be 50-53 years in various population-based studies done in different parts of the country. A significant proportion of Indian breast cancer patients are younger than 35 years of age. Young age has been associated with larger tumour size, higher number of metastatic lymph nodes, poorer tumour grade, low rates of hormone receptor-positive status, earlier and more frequent loco regional recurrences, and poorer overall survival (Shavers, 2003; Mathew et al., 2004). There is a significant difference in the survival rates in developed and developing countries mainly because of a lack of early detection programmes and inadequate resources for treatment.

MATERIALS AND METHODS

A record based descriptive study was conducted at the department of radiotherapy during the month of May and June, 2019. This is an analysis of 60 patients with invasive, previously untreated, non metastatic carcinoma breast that were treated by surgery, chemotherapy (neoadjuvant and/or adjuvant) and adjuvant radiation therapy. Records of patients attending Radiotherapy OPD from December 2016 to May 2018 were considered. Several patient records available in the department were reviewed by census method based on pre-decided inclusion and exclusion criteria.

All patients were treated with a continuous course of radiation therapy with once daily fractionation on Telecobalt 60. The fractionation regime was 34 patients received hypofractionated schedule of 42.5 Gy / 16 # / 3.1 weeks The Overall treatment time ranged from 21 to 24 (mean 22.5) days. The O.T.T. was statistically extremely significant mainly in favour of the shorter treatment time. Statistical analysis was done using statistical tool graph pad software. Two-tailed corrected chi-square test and unpaired t-test were used for p value calculation. The results were studied on an intention-to-treat basis.

RESULTS

From December 2016 to May 2018, 96 breast cancer post-mastectomy patients were registered in our department for adjuvant treatment.46 patients were selected for the study. Out of them, 34 patients gave their consent and they were finally selected for this study. These patients were randomized to receive adjuvant radiotherapy according to our study protocol. 34 patients received hypofractionated schedule of 42.5 Gy / 16 # / 3.1 weeks . 4 patients defaulted during the treatment course. After treatment completion patients were followed according to our study protocol. Any locoregional and distant failure was noted. Maximum duration of follow up in our patients was 12 months, minimum duration was 6 months and mean duration of follow up was 9 months. Final analysis was done on 30 patients.

Results and observations of these patients are as follows:

Patient Related Characteristics:

Table 1. No. & percentage of patients with different characteristics

1. Age distribution	
AGE GROUP	**NO. OF PATIENTS(%)**
20-40	11(36.7)
41-60	19(63.3)
>60	0(0)
2. Tumour size (T)	
T	**NO. OF PATIENTS(%)**
T1	3(10)
T2	12(40)
T3	11(36.7)
T4	4(13.3)
3. Nodal status(N)	
N	**NO. OF PATIENTS(%)**
N0	11(36.7)
N1	6(20)
N2	8(26.7)
N3	0
NX	5(16.7)
4.Response to neoadjuvant chemotherapy	
Response NACT	**NO. OF PATIENTS(%)**
PR	7(58.3)
CR	3(25.0)
NR	2(16.7)
5. Hormone receptor status (ER, PR)	
ER/PR	**NO. OF PATIENTS(%)**
POSITIVE	23(76.7)
NEGATIVE	7(23.3)
6. Hormone receptor status (Her 2/ neu)	
HER2/neu	**NO. OF PATIENTS(%)**
POSITIVE	6(20)
NEGATIVE	24(80)

12 patients (40%) presented with breast cancer which was inoperable at presentation. These patients underwent 2-4 (average 3) cycles of neoadjuvant chemotherapy (FAC, FEC or TAC based) followed by

surgery.

Partial response is found in 7 patients (58.3%), 3 patients (25%) have complete response and 2 patients (16.7%) have no response.

The acute reaction was assessed by R.T.O.G, Acute Radiation Morbidity Scoring Criteria. The late reaction was assessed by RTOG/EORTC Late Radiation Morbidity Scoring Scheme. Arm edema was assessed by taking the mid arm circumference of diseased arm and comparing it with the normal side. Arm edema>2 cm is taken as positive finding. We have assessed pulmonary toxicity on the basis of clinical evaluation, pulmonary function test, chest X-ray and occasional use of CT scan. Echocardiography performed by a single operator was used as a standard procedure for evaluating cardiotoxicity. More than 10% drop in LVEF is taken as positive finding for cardiotoxicity.

Table: 2 ACUTE TOXICITY ASSESSMENT

SUBCUTANEOUS SKIN TOXICITY				
GRADE	G0	G1	G2	G3
NO. OF PATIENT	2(6.6)	15(50)	11(36.7)	2(6.6)

CARDIAC TOXICITY	
	NO. OF PATIENTS
PRESENT	4(13.3)
ABSENT	26(86.7)

PULMONARY TOXICITY	
	NO. OF PATIENTS
PRESENT	5(16.7)
ABSENT	25(83.3)

There were acute subcutaneous skin toxicities (Grade0-3), pulmonary toxicities 5(16.7) , and cardiac toxicity 4(13.3) ,which was assessed by R.T.O.G., Acute Radiation Morbidity Scoring Criteria.

Table3 : Late Toxicity Assessment

SKIN TOXICITY				
GRADE	G0	G1	G2	G3
NO. OF PATIENT	1(3.3)	16(53.3)	11(36.7)	2(6.7)

SUBCUTANEOUS SKIN TOXICITY				
GRADE	G0	G1	G2	G3
NO. OF PATIENT	2(6.6)	15(50)	11(36.7)	2(6.6)

CARDIAC TOXICITY	
	NO. OF PATIENTS
PRESENT	4(13.3)
ABSENT	26(86.7)

PULMONARY TOXICITY	
	NO. OF PATIENTS
PRESENT	5(16.7)
ABSENT	25(83.3)

ARM EDEMA	
ARM EDEMA	**NO. OF PATIENTS**
PRESENT	6(20)
ABSENT	24(80)

There was chronic toxicities including skin toxicity, subcutaneous tissue toxicity, cardiac toxicity, pulmonary toxicity and arm edema were observed significantly .The late reaction was assessed by RTOG/EORTC Late Radiation Morbidity Scoring Scheme.

There were no cases of brachial plexopathy and rib fracture was found in our study.

Figure1. Tumour Size

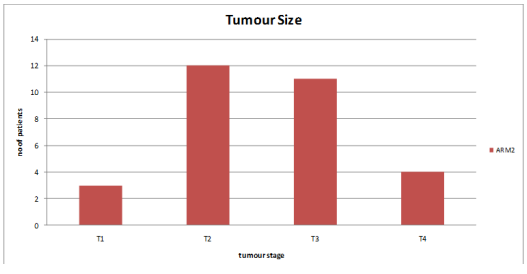


Figure 2 . Stages

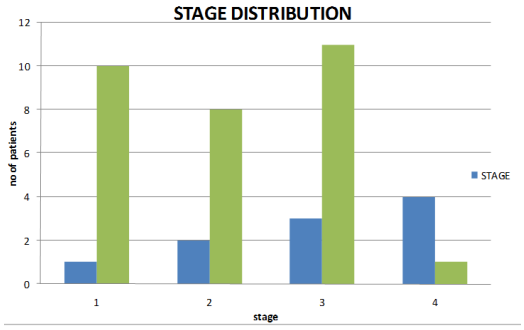


Figure 3. Response of NACT

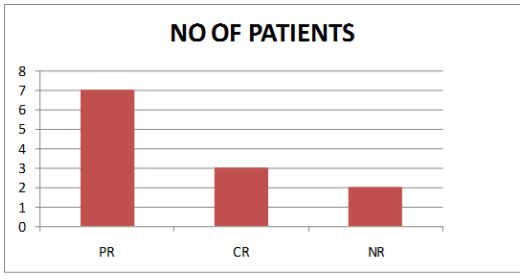


Figure 4. Skin Toxicity

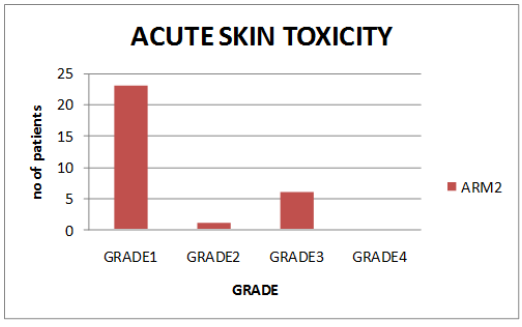
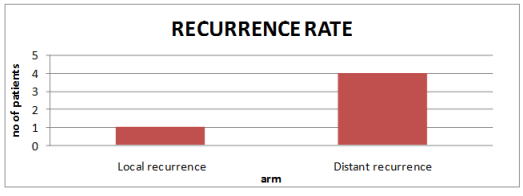


FIGURE15-RESPONSE (RECURRENCE BOTH LOCAL AND DISTANT)



DISCUSSION

The average age of breast cancer patients has been reported to be 50-53years in various population-based studies done in different parts of the country (National Cancer Registry Programme, 2001) In our study the most common age group affected by breast cancer was 40-60 years (63.3%). This age group is in accordance with Indian data. Radiotherapy has an important role in breast cancer treatment, as established from the landmark studies of the British Columbia Cancer Agency, Danish Breast Cancer Cooperative Group, and the Early Breast Cancer Trialists' Collaborative Group.[3-5]

In our study, locally advanced disease is found in 40% of patients, in contrast to more than 50% as shown in many Indian studies.[6,7]

In our study, after a maximum follow up duration of 12 month (mean duration 9 month), local recurrence was found in 1 patient . There was no regional (axillary) failure in our study. Distant failure is found in 4 patients (13.3 %) .

There was no statistically significant difference between other trials, with respect to both the locoregional and distant failure rates (Owen et al., 2006; Whelan et al., 2002; Dewar et al., 2007; Bates, 1988; Goel et al., 2000; Mladenovic, 2001; START A 2008 and Yamada et al., 1999).[8]

In START A, there was no statistical difference in distant relapse, in either of the hypofractionated regimen, compared with the conventional fractionation.[10] START B reported that the 40 Gy study arm had a statistically significant lower rate of distant relapse when compared with conventional fractionation. In Our Study, hypofractionated radiotherapy (13.3%) is insignificant but consistent with available literature in a short follow up period.

Three landmark trials have reported adverse events and toxicity outcomes (Canadian, START A and START B).[9,10,11] These studies reported that there was no difference in adverse events and toxicity in conventional and hypofractionated radiation. There is no significant difference in either conventional and hypofractionated radiation group with regard to late skin toxicity in our study.

CONCLUSION

Radiotherapy is an important component in management of post mastectomy breast cancer patients. Usually it is given after completion of chemotherapy with a gap of 4-6 weeks. Radiation has major advantage in terms of high loco regional and distant control rate leading to improvement in disease free and overall survival. Both conventional and hypofractionated radiation therapies are comparable with respect to loco regional and distant control rates without any significant difference in toxicities. The overall treatment time in hypofractionated radiation therapy is significantly lesser without any significant difference regarding acute and late radiation toxicities of all the normal structures included in the radiation field. It is cheaper and more convenient for the patients and also reduces the heavy workload of already overburdened radiotherapy setup in a developing country like ours with scarcity of resources.

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