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Hypofractionated versus Conventionally Fractionated Radiotherapy in Post-Mastectomy Breast Cancer Patients - A Comparative Study

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Abstract

Background: To assess the efficacy, toxicity, and feasibility of Hypofractionated radiotherapy in post-mastectomy breast cancer patients compared with conventional radiotherapy.

Materials and Methods: A total of 100 post-mastectomy breast cancer patients were randomized into two groups for adjuvant radiotherapy. The control group (CFRT) of 50 patients received conventional radiotherapy of 50 GY in 5 weeks and the Study group (HFRT) of 50 patients received Hypofractionated radiotherapy of 42.62 GY in 3.1 weeks.

Results: Grade I–II acute skin reactions were observed in 19 patients (48%) of the CFRT Group and 22 patients (55%) of the HFRT Group. Grade III skin toxicities were observed in 6 patients (15%) in the CFRT Group and 16 patients (40%) in the HFRT Group, during treatment, the development of dysphagia was equal in both groups, in 7 patients and did not cause much disturbance to the patients in continuation of the treatment, managed with supportive measures. After one year of follow-up, lymphoedema which is a late complication was observed in 3(6%) of the patients in the CFRT Group and 2(4%) in the HFRT Group. No chest wall recurrence and Axillary nodal recurrence were observed in either group. At 1 year of follow-up, two patients presented with lung metastasis, two patients with bone metastasis and one patient with liver metastasis in the CFRT Group while in the HFRT Group, two patients had bone metastasis and one liver metastasis. Local control, toxicity and efficacy were comparable in both groups.

Conclusion: HF PMRT is comparable to conventional RT without evidence of higher adverse effects or inferior locoregional tumour control; hence, it can be offered as a safe and effective alternative to conventional RT for postmastectomy breast cancer patients in adjuvant settings with the advantage of reducing overall treatment time, treatment burden & cost.

Keywords: Breast carcinoma, Conventional fractionation radiotherapy, Hypofractionated radiation therapy (HFRT).

Introduction

Breast cancer is the most commonly diagnosed cancer in women in the majority of countries and a leading cause of cancer death among women worldwide. Breast cancer is ranked the number one cancer among Indian females. [(1)] As per the Globocan data 2020, in India, breast cancer accounted for 13.5% (178361) of all cancer cases and 10.6% (90408) of all deaths with a cumulative risk of 2.81% [(1)]

In India, nearly 60% of Breast cancer cases are diagnosed at stage III or IV of the disease[(2)]. Most of the patients present to the healthcare facility only when there is a large palpable mass or secondary changes like local skin/chest wall changes are visible. Women tend to ignore the minor symptoms and do not show up at the hospital until it is unbearable, owing to their household responsibilities.

Hence, radical mastectomy is more often performed than breast conservative surgeries such as lumpectomy, quadrantectomy in developing countries like India, where people do not give much importance to cosmetic outlook. [(3,4)] Nearly, all of these post-mastectomy patients require adjuvant radiotherapy to prevent locoregional recurrence and distant metastasis. [(5-7)]

Despite the established role of adjuvant radiotherapy, much debate remains about the ideal radiotherapy regimen to use. Several alternative fractionation regimens have recently been assessed and compared with the standard fractionation schedule (25 fractions, 2 Gy each/5 weeks [(8).]

The theoretical advantages of hypofractionation include an improvement in cell killing from the increase in fraction size and a reduction in treatment duration. Furthermore, shortening the treatment duration means that more patients can be treated with a limited number of machines, a concern that arises in many countries in which access to radiation therapy is limited [(9).]

Conventional fractionation modality requires a lengthy hospitalization or commuting to the hospital for radiotherapy for a prolonged period. The probability of missing radiotherapy is higher with older patients and those living farther away from radiotherapy centres

The most tested regimen of adjuvant radiotherapy in carcinoma breast is hypofractionated radiotherapy with a total dose of 42.72 GY, 2.67 GY per fraction in 16 fractions. The other fractionation protocols are 42.9 GY in 13 fractions, 39 GY in 13 fractions, 40 GY in 15 fractions, 28.5 GY in 5 fractions, and 30 GY in 5 fractions. [(10 -13)]

Materials and Methods

This prospective study was carried out in the Department of Radiation Oncology, Government Medical College, Srinagar from June 2021 to August 2022. A total of 100 patients were taken for this study. Post-mastectomy patients were randomized into two groups – the control group and the study group with 50 patients in each group. Control group – Arm A – 50 patients, conventional fractionation radiotherapy regime, 5000 CGY, 200 CGY per fraction, 5 fractions per week, and a total of 25 fractions in 5 weeks.

Study group – Arm B – 50 patients, Hypofractionated radiotherapy regime, 4262 CGY, 266 CGY per fraction,

5 fractions per week, and a total of 16 fractions in 3.1 weeks.

All patients had signed an informed consent form before enrollment.

Inclusion criteria included

1. A pathological proof of breast cancer and surgical intervention by modified radical mastectomy (MRM) and axillary dissection.
2. Radiation started after completion of the last cycle of adjuvant chemotherapy, Histological proof of breast cancer.
3. ECOG performance status 0–2.
4. Unilateral breast cancer

Exclusion criteria included those who had a skin disease that may interfere with radiation toxicity. History of previous irradiation, Recurrent breast cancer, co-morbid conditions such as cardiac disease, diabetes mellitus, hypertension, Pregnancy, Breast conservation surgery such as lumpectomy and quadrantectomy and Evidence of metastasis.

All the patients were clinically evaluated before the treatment.

Radiotherapy

In Arm A of the control group, 50 patients with a conventional fractionation regimen were given a total dose of 50 Gy/2Gy/per fraction/5 days a week/25 fractions/ in 5 weeks. In Arm B of the study group, 50 patients of Hypofractionated radiotherapy were given a total dose of 42.62GY/2.66 GY/per fraction/5 days a week/16 fractions/in 3.1 weeks. The patients were delivered radiation on a telecobalt machine to the chest wall and drainage area. The chest wall received radiation with bilateral tangential fields.

Radiation Toxicity and Its Grading.

During the radiation therapy schedule; patients were weekly observed for acute radiation reactions and it was reported and graded according to the Radiation Therapy Oncology Group (RTOG) toxicity criteria.

Monitoring of Patients during Radiotherapy.

Patients on radiation treatment were regularly examined for Tolerance, Acute toxicities, Dysphagia and oral intake, Pulmonary symptoms, Cardiac symptoms and Arm edema.

After ending the radiation schedule, patients were followed up every 2 weeks for one month and then, every month for a minimum of 1 year for late reactions. Statistical analysis was done using Software SPSS version 26.

Results

The patients, characteristics were matched between the two groups. 100 patients were taken for this study out of which 50 patients were assigned to Group A(CFRT) and were treated conventionally to a dose of 50 Gy /25≠ and another 50 in Group B(HFRT) were treated to a hypofractionated dose of 42.62 Gy/16≠.(Table 1)

The majority of the patients in Group A were in the age of 40-50(90%) while as in Group B majority of patients were also in the age group of40-50 (38%) (Table 2). The majority of the patients in Group A were 20(40%) Perimenopausal and Premenopausal while the majority of patients in Group B were 24(48%) Perimenopausal (Table 3). The majority of the patients in Group A were ER +.PR+ (80%) and while 84% of patients in Group B were also hormone-positive(Table4)

The primary tumour site in Group A was the Right breast30/50(60%) Followed by the left breast 20/50(40%) while the majority of patients in Group B had right-sided tumours 30/50(60%) Followed by left breast 20/50(40%) (Table 5).

The majority of patients in Group A, 30(60%) had stage II while as majority of patients in Group B, 35(70%) also had stage II (Table 5). The majority of patients in Group

A, 30(40%) had Tumour Grade II while 32(64%) in Group B also had tumour Grade II.

All the patients were monitored for toxicities during radiation. All patients tolerated radiotherapy well and completed the treatment protocol in the scheduled duration, with 1–2 days interruption of radiation, which was seen in 8 patients in conventional fractionation radiotherapy (Group A) and 10 patients in Hypofractionated radiation therapy (Group B) due to toxicities (Table 6).

Regarding toxicities, Grade I–II acute skin reactions were observed in 19 patients (48%) of CFRT and 22 patients (55%) of HFRT. Grade III skin toxicities were observed in 6 patients (15%) in CFRT and 16 patients (40%) in HFRT (Table 7).

During treatment, the development of dysphagia was equal in both groups, in 7 patients and did not cause much disturbance to the patients in continuation of the treatment and were managed with supportive measures.

After one year of follow-up, lymphoedema which is a late complication was observed in 3(6%) of the patients in Group A and 2(4%) in Group B. No chest wall recurrence and Axillary nodal recurrence were observed in either group. At 1 year of follow-up, two patients presented with lung metastasis, two patients with bone metastasis and one patient with liver metastasis in the CFRT Group A while in HFRT Group B, two patients had bone metastasis and one liver metastasis (Table 8).

Discussion

Adjuvant local or locoregional radiation treatment improves locoregional control and survival for women treated with breast-conserving surgery and in patients with high-risk disease treated with mastectomy. The results of numerous randomized trials which compared conventional fractioned radiotherapy (50 Gy in 5 weeks/25 fractions) for patients with breast cancer with Hypofractionated radiotherapy (39 - 42.9 Gy/13 - 16 fractions in 3 -5 weeks) indicated that hypofractionation can be safely delivered to most patients [14].

The routine use of HFRT in breast radiotherapy is supported by the results of five large randomized controlled trials (RCTs) in women with early breast cancer. [15-18].

These studies demonstrate that HFRT yields equivalent or improved outcomes in all essential endpoints: Efficacy, toxicity, cosmesis, and cost-effectiveness. HFRT also results in greater patient convenience and resource efficiency. In our study, we also compared CFRT and HFRT for local control and toxicity.

Early and late toxicities observed in our study were comparable to the study conducted by Vijayakumar who also randomized patients in two groups and found that early and late toxicities were comparable in CFRT and HFRT [19]. No local recurrence and Axillary recurrence were observed in both groups which is similar to study done by N jain et al [20]who also found same results.

Lymphedema is an established complication of both ALN dissection (ALND) and axillary Radiotherapy, in our study 6% of patients in CFRT and 4% in HFRT developed lymphoedema which is similar to the study conducted by Rastogi et al [21].

Conclusion

HF PMRT is comparable to conventional RT without evidence of higher adverse effects or inferior locoregional tumour control; hence, it can be offered as a safe and effective alternative to conventional RT for postmastectomy breast cancer patients in adjuvant settings with the advantage of reducing overall treatment time, treatment burden & cost.

Limitations

This study is limited by the relatively small number of patients and short follow-up-Period.

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Legend Tables

Table 1: Treatment Protocol.

	CFRT	HFRT
No of Patients	50	50
Total Dose	50Gy/25≠	42 Gy/16≠.
Fractions	25≠	16≠.
Dose/Fraction	2 GY	2.625 Gy
Treatment Days	5 days/week	5 days/week
Treatment per week	5 weeks	3 weeks/1 day

Table 2: Patient Characteristics.

Characteristics		
Age	CFRT	HFRT
30-40	10(20%)	10(20%)
40-50	45(90%)	34(68%)
50-60	5(10%)	6(12%)
Menopausal Status	CFRT	HFRT
Pre menopausal	20(40%)	16(32%)
Perimenopausal	20(40%)	24(48%)
Post menopausal	10(20%)	10(20%)
ECOG	CFRT	HFRT
0	5(10%)	3(6%)
1	40(80%)	45(90%)
2	5(10%)	2(4%)
Hormone Receptor status		
ER +, PR+	40(80%)	42(84%)
ER -, PR-	8(16%)	5(10%)
ER +.PR-	2(4%)	3(6%)
ER -,PR+	0	0

Table 3: Characteristics of tumor

Anatomical Site	CFRT	HFRT
Left	20(40%)	20(40%)
Right	30(60%)	30(60%)
Tumour stage		
ii	30(60%)	35(70%)

III	20(40%)	15(30%)
Tumour Grade		
I	6(12%)	8(16%)
II	30(40%)	32(64%)
III	14(28%)	10(20%)

Table 4: Aute skin reaction

Acute Skin reaction		
Grade I and II	45(90%)	40(80%)
Grade III	5(10%)	10(20%)

Table 5: Treatment break

	CFRT	HFRT
Yes	8(16%)	10(20%)
NO	42(84%)	40(80%)

Table 6: Late complication after 1 year of follow up

	CFRT	HFRT
Lymphoedema	3(6%)	4(8%)
Chest Wall recurrence	2(4%)	0
Axillary Nodal Recurrence	0	0
Lung mets	3(6%)	0
Bone mets	2(4%)	2(4%)
Liver mets	1(2%)	1(2%)