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Original Research Article

COMPARISON OF TREATMENT COMPLIANCE AND TOXICITY PROFILE IN PATIENTS UNDERGOING POST-MASTECTOMY IRRADIATION BY HYPOFRACTIONATION VERSUS CONVENTIONAL FRACTIONATION USING CONFORMAL RADIOTHERAPY

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Abstract

Background: Breast cancer remains a significant public health concern, and effective management requires a multimodal approach, including radiotherapy. This study aimed to compare the treatment compliance and toxicity profiles of hypo fractionated and conventional fractionation regimens in breast cancer patients. **Materials and Methods:** This comparative study included 60 patients who underwent post-mastectomy irradiation by hypofractionation versus conventional fractionation using conformal radiotherapy at Rajiv Gandhi Government General Hospital, Chennai, between January 2021 and December 2021. Patients were divided into two treatment ARMS based on the radiotherapy regimen: ARM A received hypofractionation, and ARM B received conventional fractionation. Acute radiation toxicities were assessed and graded using RTOG criteria. **Result:** Most patients were aged 51-60 years 28 (47%), with right-sided involvement in 40 (67%) and postmenopausal status in 39 (65%) patients. The luminal A subtype was the most common 21 (35%), followed by Luminal B 18 (30%). Most of the cancers were stage II B 20 (34%). Estrogen receptor positivity was observed in 39 (65%) patients, progesterone receptor positivity in 30 (50%), and HER-2 positivity in 22 (37%) patients. At 10-12 days post-therapy, radiation dermatitis was higher in Arm B (24 vs. 17 grade 1 cases), while grade 2 and 3 patients were higher in arm A. At 6 weeks, dermatitis and pneumonitis were grade 1. Hypofractionation was preferred by 53% of the patients, with equal treatment in 30 patients (50%). **Conclusion:** Hypo fractionated post-mastectomy radiotherapy is a safe, effective, and well-tolerated alternative to conventional fractionation, with similar toxicity profiles and greater patient preference, and can be used to evaluate late toxicities and survival outcomes.

INTRODUCTION

GLOBOCAN 2020 indicated that female breast cancer is the most common type of cancer worldwide. This condition affects 2.3 million people annually, constituting 11.7% of the global burden of cancer. It also contributes to approximately 0.68 million deaths per year, which translates to 6.9% of global cancer deaths. It ranks fifth among the leading causes of cancer-related deaths worldwide. The incidence rates are more significant in developed regions such as Australia, New Zealand, Western Europe, and North America. The reasons associated with the high rate consist of several hormonal, lifestyle, and reproductive factors, including the delay in pregnancy, shorter breastfeeding periods, more obesity, and hormone replacement therapy.[1]

Breast and cervical cancers are two of the main public health concerns among women in India. Both diseases require urgent measures to promote awareness, the application of preventive measures, early diagnosis, and access to treatment. The management of breast cancer is also needed as a multidisciplinary approach to reduce its incidence and mortality. The anatomical position of the breast lies between the second and sixth ribs with support from Cooper's ligaments, while the axillary and internal mammary lymph nodes primarily provide

lymphatic drainage. These nodes are also important in cancer staging and examine the possibility of the disease progression.[2]

Several risk factors are associated with breast cancer development. This risk factor primarily includes age, and more prominently, in aged women. These factors include reproductive history, long-term exposure to estrogen, genetic makeup, and lifestyle. Mutations in BRCA1 and BRCA2 significantly increase the risk of breast cancer (National Cancer Institute). The occurrence of the disease is also partly due to avoidable risk factors, including obesity, lack of physical activity, alcohol intake, and diets containing high amounts of processed foods.[3]

Breast cancer is diagnosed by imaging and histopathological techniques. Early detection can be accomplished by using mammography as the primary diagnostic modality in any screening program. However, diagnosis using other imaging tools, such as ultrasound, magnetic resonance imaging, or biopsy, provides better details about the characteristics and confirmation of the tumor. Further progress with genetic profiling enhances knowledge regarding different subtypes of cancer to create appropriate and targeted treatments for every individual case.[4]

Breast cancer treatment is generally multimodal and involves surgery, radiotherapy, chemotherapy, targeted therapy, and hormonal therapy. Radiotherapy, especially post-mastectomy irradiation, is crucial for controlling locoregional recurrences. Technological advancements, including 3D conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT), have improved precision, allowing higher doses to the tumor while sparing healthy tissues and minimizing side effects.[5]

The most crucial aspect is the comparison between the hypo fractionated and conventional fractionation regimens. Hypo fractionated radiotherapy is the delivery of larger doses per session, therefore fewer sessions; therefore, it is convenient for patients and economical. However, studies have shown that hypo fractionated regimens do not differ from conventional regimens in terms of the control and survival rates. Indeed, treatment tolerance and tumor stage must dictate the choice of regimen based on the profile of each patient.[6]

Aim

This study aimed to compare treatment compliance and toxicity profiles in breast cancer patients undergoing post-mastectomy irradiation by hypofractionation versus conventional fractionation using conformal radiotherapy.

MATERIALS AND METHODS

This comparative study included 60 patients undergoing post-mastectomy irradiation by hypofractionation versus conventional fractionation using conformal radiotherapy in the Department of Radiation Oncology at Madras Medical College, Rajiv Gandhi Government General Hospital, Chennai, between January 2021 and December 2021. This study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion criteria

Patients who underwent a modified radical mastectomy, who had stage II or III breast cancer, aged between 18 and 70 years, ECOG performance status: 0-2, haemoglobin > 10 g%, total leukocyte count > 4000 cells/cu mm, platelet count > 1,00,000 cells/mm3 were included.

Exclusion criteria

Patients who had undergone breast conservation surgery and those diagnosed with metastatic breast cancer, reduced cardiac reserve, ejection fraction ≤ 30%, a history of interstitial lung disease or active lung infections, hepatic or renal dysfunction, reduced bone marrow reserve, underlying collagen vascular diseases, pregnant or breastfeeding women, a history of chest radiation therapy, or who were unable or unwilling to cooperate at any stage of the treatment process were excluded.

Methods

Patients who underwent mastectomy for breast cancer were divided into two groups. ARM A (n=30) was treated with conformal radiotherapy at a dose of 40.5 Gy in 15 fractions, delivering 270 Gy per fraction daily, five days a week (Monday to Friday) for three weeks. ARM B (n=30) was treated with conformal radiotherapy at a dose of 50 Gy in 25 fractions, delivering 200 Gy per fraction daily, five days a week (Monday to Friday) for five weeks.

In 3D-conformal radiotherapy, patients were immobilized on a breast board, CT images were obtained and transferred to a 3D treatment planning system, and target areas and organs at risk were contoured according to the RTOG guidelines, with specific dose constraints applied to the lungs (volume receiving 20 Gy: <30%), heart (volume receiving 25 Gy: <10% or D mean: <26 Gy), spinal cord (D max: 45 Gy), and contralateral breast (D max: <6 Gy). Beam selection, dose planning, and plan evaluation ensured optimal dose distribution using metrics such as the isodose distribution, conformity index, homogeneity index, and Dose Volume Histogram (DVH).

Treatment was performed after comparing Digitally Reconstructed Radiographs (DRRs) with the portal images. Weekly assessments monitored chest wall dermatitis, graded using RTOG criteria, and treatment was temporarily paused if grade 3 dermatitis occurred, resuming only after regression to grade 1. Post-radiation follow-up was continued for six weeks to assess acute radiation toxicities. Data are presented as frequencies and percentages.

RESULTS

Most patients, aged between 51-60 years were 28 (47%), 41-50 years were 17 (28%), 61-70 years were

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10 (17%), and 35-40 years 5 (8%). In laterality, 40 (67%) and 20 (33%) patients had right- and left-sided involvements, respectively. Regarding menopausal status, 21 (35%) were postmenopausal and 21 (35%) were premenopausal. Among the patients with the Luminal A subtype, 21 (35%) had the luminal A subtype, 18 (30%) had the HER-2-Like subtype, 13 (22%), and 8 (13%) were triple-negative. Most cancer patients were stage II B (34%), III B (20%), III A (18%), II A (15%), or III C (13%) [Table 1].

Table 1: Demographic, clinical characteristics, breast cancer subtype distribution, and cancer stage distribution.

		Frequency (%)
Age (in years)	35-40	5 (8%)
	41-50	17 (28%)
	51-60	28 (47%)
	61-70	10 (17%)
Laterality	Right side	40 (67%)
	Left side	20 (33%)
Menopausal status	Premenopausal	21 (35%)
	postmenopausal	39 (65%)
Subtype	Luminal A	21 (35%)
	Luminal B	18 (30%)
	HER-2-Like	13 (22%)
	Triple-Negative	8 (13%)
Stage	II A	9 (15%)
	II B	20 (34%)
	III A	11 (18%)
	III B	12 (20%)
	IIIC	8 (13%)

In Arm 1 radiation dermatitis, 5 patients were in grade 1, and there were no patients with grade 2, grade 3, or grade 4. In Arm 2, 4 patients were grade 1 and no patients were grade 2, grade 3, or grade 4. In Arm 1 radiation pneumonitis, 7 patients were in grade 1, and there were no patients in grade 2, grade 3, or grade 4. In Arm 2, 5 patients were in grade 1, and no patients were classified as grade 2, grade 3, or grade 4 [Table 2].

Table 2: Incidence of adverse events by grade and treatment ARM

Adverse Event	Arm	Grade 1	Grade 2	Grade 3	Grade 4
Radiation dermatitis	Arm 1	5	0	0	0
	Arm 2	4	0	0	0
Radiation pneumonitis	Arm 1	7	0	0	0
	Arm 2	5	0	0	0

The proportion of patients with estrogen receptor (ER) positivity and negativity was 65% and 35%, respectively. Progesterone receptor (PR) positivity was 50%, and negativity was 50%. HER-2-NEU status positivity and negativity were 37% and 63%, respectively [Table 3].

Table 3: Hormone receptor and her-2-neu status distribution

		Frequency (%)
Estrogen Receptor (ER) Status	ER Positive	39 (65%)
	ER Negative	21 (35%)
Progesterone Receptor (PR) Status	PR Positive	30 (50%)
	PR Negative	30 (50%)
HER-2-NEU Status	HER-2 Positive	22 (37%)
	HER-2 Negative	38 (63%)

At 10-12 days post-therapy, radiation dermatitis was predominantly grade 1, with a higher incidence in Arm B (24 vs. 17 in Arm A). In grades 2 and 3, dermatitis was more common in Arm A (9 and 4 patients, respectively) than in Arm B (5 and 1 patient). No grade 4 dermatitis was observed in either group. At 6 weeks, dermatitis was significant, with only a few remaining grades 1 patients (5 in Arm A and 4 in Arm B) and no higher-grade patients in either group. Regarding radiation pneumonitis at 6 weeks, only grade 1 patients were reported, which was higher in Arm A (7 patients) than in Arm B (5 patients), with no grade 2 or higher pneumonitis observed in either group [Table 4].

Table 4: Comparison of early and late toxic effects of dermatitis and pneumonitis radiation therapy

Post radiation therapy	Radiation dermatitis	ARM A	ARM B
10-12 days	Grade 1	17	24
	Grade 2	9	5
	Grade 3	4	1
	Grade 4	0	0
6 weeks	Grade 1	5	4

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	Grade 2	0	0
	Grade 3	0	0
	Grade 4	0	0
	Radiation pneumonitis		
6 weeks	Grade 1	7	5
	Grade 2	0	0
	Grade 3	0	0
	Grade 4	0	0
	Grade 5	0	0

In the hypofractionation schedule, patient preferences were 53%, those of the conventional group were 7, and 30 (50%) patients were treated in both schedules [Table 5].

Table 5: Patient preferences and treatment allocation by schedule

Schedule	Patients' preference	Patients treated
Hypofractionation	53	30 (50%)
Conventional	7	30 (50%)

DISCUSSION

In our study, the hypofractionation schedule, patient preferences were 53%, those of the conventional group were 7, and 30 (50%) patients were treated in both schedules, and patients in the hypo-fractionation ARM, the majority had only grade 1 dermatitis, and only 4 had grade 1 dermatitis. Patients with grade 3 dermatitis were effectively managed in our OPD, and their reactions subsided to grade 1 within 10 to 12 days. The overall treatment time was 19-21 days in the hypofractionation arm and 33-35 days in the conventional arm. Hence, hypofractionation is cost-effective, and many patients prefer hypofractionation. The late effects of hypo-fractionation on normal tissues require long-term follow-up. Cardiac toxicities can take many years to develop; hence, these patients must be followed-up on a long-term basis.

In a study by Haviland et al., START-A enrolled 2236 women. The median follow-up was 9·3 years (IQR 8·0–10·0), after which 139 local-regional relapses had occurred. 10-year rates of local-regional relapse did not differ significantly between the 41·6 Gy and 50 Gy regimen groups (6·3%, 95% CI 4·7–8·5 vs 7·4%, 5·5–10·0; hazard ratio 0·91, 95% CI 0·59–1·38; p=0·65) or the 39 Gy (8·8%, 95% CI 6·7–11·4) and 50 Gy regimen groups (HR 1·18, 95% CI 0·79–1·76; p=0·41). In START-A, moderate or marked breast induration, telangiectasia, and breast oedema were significantly less common normal tissue effects in the 39 Gy group than in the 50 Gy group. Normal tissue effects did not differ significantly between the 41·6 Gy and 50 Gy groups. START-B enrolled 2215 women. The median follow-up was 9·9 years (IQR 7·5–10·1), after which 95 local-regional relapses had occurred. The proportion of patients with local-regional relapse at 10 years did not differ significantly between the 40 Gy group (4·3%, 95% CI 3·2–5·9) and the 50 Gy group (5·5%, 95% CI 4·2–7·2; HR 0·77, 95% CI 0·51–1·16; p=0·21). In START-B, breast shrinkage, telangiectasia, and breast oedema were significantly less common normal tissue effects in the 40 Gy group than in the 50 Gy group.[7]

In our study, the prevalence of Luminal A (35%) and Luminal B (30%) subtypes was observed, as reported by Perou et al., who found these subtypes to be the most common subtypes in breast cancer cases.[8] O'Brien et al. stated that subtypes usually respond well to hormonal therapy, the importance of endocrine treatment. Additionally, the HER-2-like and triple-negative subtypes accounted for 22% and 13% of cases, respectively.[9] Gupta et al. reported that the stage distribution revealed a predominance of Stage II B (34%) and Stage III B (20%) cases, consistent with findings in low- and middle-income countries where late-stage diagnoses are more prevalent.[10] Further long-term studies are essential to validate these observations in diverse populations and assess survival outcomes.

CONCLUSION

Hypofractionation in patients requiring post-mastectomy radiotherapy is safe and effective and is well tolerated by patients. The rate and severity of acute tissue reactions were comparable to those of conventional fractionation. Patients completed the treatment without any treatment breaks. No significant acute toxicities were observed during follow-up post-radiation therapy. Late normal tissue toxicity must be studied in patients on a long-term basis. Patients found the hypofractionation schedule to be convenient and cost-effective, and many preferred the hypofractionation schedule owing to its reduced overall treatment time.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71:209–49. https://doi.org/10.3322/caac.21660.
2. Kumar A, Abbas AK. Aster: Robbins and Cotran pathologic basis of disease. 2015. https://shop.elsevier.com/books/robbins-and-cotran-pathologic-basis-of disease/kumar/978-0-323-53113-9.
3. Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. J Clin Oncol 2007; 25:1329–33. https://doi.org/10.1200/JCO.2006.09.1066.

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4. Badu-Peprah A, Adu-Sarkodie Y. Accuracy of clinical diagnosis, mammography, and ultrasonography in preoperative assessment of breast cancer. Ghana Med J 2018; 52:133–9. https://doi.org/10.4314/gmj.v52i3.5.
5. Tallet A, Rey D, Casanova C, Lecourtois D, Bergeaud M, Bendiane M-K, et al. Physicians' opinion on intraoperative radiotherapy as a therapeutic DE-escalation option in older women with early breast cancer. Curr Oncol 2023; 30:2812–24. https://doi.org/10.3390/curroncol30030214.
6. Whelan TJ, Pignol JP, Levine MN, Julian JA, Mackenzie R, Parpia S, Shelley W, Grimard L, Bowen J, Lukka H, Perera F. Long-term results of hypo fractionated radiation therapy for breast cancer. N Engl J Med. 2010:11; 362:513-20. https://doi.org/10.1056/NEJMoa0906260.
7. Haviland JS, Owen JR, Dewar JA, Agrawal RK, Barrett J, Barrett-Lee PJ, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. Lancet Oncol 2013; 14:1086-94. https://doi.org/10.1016/S1470-2045(13)70386-3.
8. Perou CM, Sørlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature 2000; 406:747–52. https://doi.org/10.1038/35021093.
9. O'Brien KM, Cole SR, Tse C-K, Perou CM, Carey LA, Foulkes WD, et al. Supplementary figure 1 from intrinsic breast tumor subtypes, race, and long-term survival in the Carolina breast cancer study. AACR 2023. https://doi.org/10.1158/1078-0432.22442892.v1.
10. Gupta A, Shridhar K, Dhillon PK. A review of breast cancer awareness among women in India: Cancer-related practices and survival rates. Indian J Med Res 2015; 142:150–60. https://doi.org/10.1016/j.ejca.2015.07.008.

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