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Evaluating Loco-Regional Hypofractionated versus Conventional Radiotherapy in Post-Mastectomy Breast Cancer

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ABSTRACT

Background :Hypofractionated radiotherapy (HFRT) has emerged as a cost-effective and logistically favorable alternative to conventional fractionated radiotherapy (CFRT) in the treatment of breast cancer, particularly in resource-limited settings. This study aimed to compare loco-regional toxicities and treatment outcomes between HFRT and CFRT in post-mastectomy breast cancer patients in Bangladesh.

Methods:A quasi-experimental, comparative study was conducted among 60 post-mastectomy breast cancer patients, divided equally into Arm A (CFRT) and Arm B (HFRT). Socio-demographic, clinical, tumor-related, treatment-related characteristics, and radiotherapy-induced toxicities were assessed and compared. Data were analyzed using appropriate

statistical tests, with a p-value < 0.05 considered significant.

Results:The mean age of participants was similar across both groups. Significant differences were observed in monthly income, BMI, ECOG performance status, tumor grade, and pathological staging ($p < 0.05$). Acute skin toxicity (Grade II/III) was more frequent in CFRT (23.3%) compared to HFRT (10%), though not statistically significant ($p > 0.05$). Chronic dermatitis and esophageal toxicities were also higher in CFRT. Lymphedema, pulmonary, and cardiac toxicities were mild and comparable. Besides, HFRT displayed a substantial cost reduction (86,900 BDT compared to 1,33,250 BDT in CFRT). Lastly, no Grade IV toxicities were reported in either group.

Conclusion:HFRT offers equivalent safety and tolerability to CFRT with the added advantages of shorter treatment duration, improved compliance, and reduced cost. In high-patient-load, low-resource settings like Bangladesh, HFRT can be an effective alternative to CFRT in post-mastectomy breast cancer treatment. Long-term, multicenter studies are recommended to assess survival and loco-regional control outcomes

Keywords: *Breast cancer, Hypofractionated radiotherapy, Conventional fractionated radiotherapy, Post-mastectomy, Toxicity, Cost-effectiveness, Radiotherapy outcomes*

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1. INTRODUCTION

Breast cancer remains one of the most common malignancies among women worldwide. For patients undergoing mastectomy, loco-regional radiotherapy (RT) has been acclaimed as a key component of adjuvant therapy in order to reduce chances of locoregional recurrence and to improve overall survival, particularly in those patients with stage IIB to III disease or high-risk features. [1]

Conventional fractionated radiotherapy (CFRT), typically delivered at doses of 45-50 Gy in 25-28 fractions over 5 weeks, remains as the established modality of management. However, in Bangladesh and similar low- and middle-income countries (LMICs), long treatment duration, high resource utilization, patient travel, accommodation, and lost wages contribute to substantial direct and indirect cost burdens. [2]

In this regard, hypofractionated RT (HFRT), which delivers larger fraction sizes over fewer treatments (e.g., 40–42.5 Gy in 15-16 fractions over three weeks), can be considered as an alternative. The rationale includes logistical convenience, reduced travel burden for patients, faster completion, and potential cost savings without compromising efficacy. [3]

Several studies are present where HFRT has been compared CFRT to evaluate outcomes in post-mastectomy breast cancer cases. For instance, a recently conducted meta-analysis covering 25 trials (consisting of 3871 postmastectomy breast cancer patients) demonstrated no significant differences between HFRT and CFRT in overall survival, disease-free survival, locoregional recurrence, or major acute or late side effects. [4] In addition, another huge cohort study of over 1600 patients reported that HF-PMRT was feasible, with comparable 5-year locoregional recurrence-free survival, disease-free survival, as well as overall survival. [5]

Moreover, HFRT has demonstrated preferable toxicity profiles, compared to CFRT. Prospective and retrospective reports suggest that, acute skin toxicity (dermatitis) and late normal tissue effects are comparable, or sometimes even lower, in HFRT vs CFRT, especially when modern RT techniques (3D-conformal, IMRT) and careful planning to reduce dose inhomogeneity are applied. [6]

From an economic standpoint, HFRT has reported favorable cost-effectiveness. An analysis based on the phase III trial NCT00793962 demonstrated that, HFRT resulted in lower overall treatment costs compared to CFRT across various healthcare systems, including those in China, France, and the United States. The study found that, CFRT incurred substantially higher additional costs while offering only minimal improvement in quality-adjusted life years (QALYs), thereby positioning HFRT as a more economically efficient option. [7]

Despite existing global evidence, data from Bangladesh remain limited. This study was conducted to compare toxicity, tolerability, and loco-regional control in post-mastectomy breast cancer patients treated with CFRT versus HFRT. We hypothesized that HFRT would be more cost-effective than CFRT while maintaining comparable loco-regional control and manageable toxicity.

2. METHODS

This quasi-experimental study was conducted at Khwaja Yunus Ali Medical College & Hospital, Enayetpur, Sirajganj,

Bangladesh. The total duration of the study was 1.5 years, from October 2017 to March 2019.

Patients with histologically confirmed breast cancer who underwent mastectomy followed by adjuvant or neoadjuvant chemotherapy and subsequently received either CFRT or HFRT between October 2017 and September 2018 were enrolled as participants of the study.

Sample size was calculated using the following formula:

$n = [(p_1 \times (1 - p_1)) + (p_2 \times (1 - p_2))] / (p_1 - p_2)^2 \times (Z\alpha + Z\beta)^2$

Where:

p_1 = Proportion of toxicity in CFRT arm = 0.528

p_2 = Proportion of toxicity in HFRT arm = 0.12

$Z\alpha$ = 1.96 (at 5% level of significance, two-tailed)

$Z\beta$ = 1.64 (at 95% power)

Substituting the values:

$n=[(0.528\times0.472)+(0.12\times0.88)]/(0.528-0.12)^2\times(1.96+1.64)^2$
$n=(0.249+0.106)/(0.408)^2\times(3.6)^2$
$n=0.355/0.166\times12.96$
$n = 27.63$

Adding 10% to account for potential loss to follow-up:

Final sample size per group = 27.63 + 2.76 = 30. [8]

Therefore, 30 patients were included in each arm, making a total of 60 patients.

Written informed consent was obtained from all participants prior to enrollment, and ethical standards were strictly maintained throughout the study.

After obtaining written informed consent, eligible patients were assigned to one of two study arms. Arm A included 30 patients who received CFRT at a dose of 50.4 Gy in 28 fractions over 5½ weeks; Arm B comprised of 30 patients treated with HFRT at a dose of 42.56 Gy in 16 fractions over approximately 3.1 weeks.

Convenient and purposive sampling was employed. The first patient was assigned to Arm A (CFRT) by lottery, the second to Arm B (HFRT), and alternately thereafter.

Selection criteria

Inclusion criteria

Histologically confirmed carcinoma of the breast.

Post-mastectomy status.

Clinical stage II and III.

Primary tumor <5 cm with high-risk features such as lymphovascular invasion or close deep resection margins.

Exclusion criteria

Evidence of distant metastasis.

Patients with no positive lymph nodes or with ≥10 nodes examined negative for fixation.

Uncontrolled diabetes mellitus or hypertension.

Active uncontrolled infection.

Severe pre-existing cardiac or pulmonary disease.

Pregnant or lactating women.

Age <18 years or >75 years.

ECOG performance status 3 or 4.

Unwillingness to participate.

Data were collected using a structured data collection sheet and included patient demographics and clinical characteristics (age, occupation, educational status, ECOG performance score, BMI, family history of cancer), tumor-related variables (site, laterality, histological type, tumor grade, pathological stage, lympho-vascular invasion, and margin status), and

treatment details (type of surgery, chemotherapy regimen—adjuvant or neoadjuvant—radiotherapy protocol including dose and fractionation, and use of hormonal therapy). Toxicity assessments included both acute (e.g., skin toxicity and mucositis) and chronic toxicities (e.g., subcutaneous fibrosis, lymphedema, radiation pneumonitis, and cardiac effects), evaluated using standard grading criteria.

Prior to treatment, all patients underwent comprehensive clinical evaluation, including detailed history, physical examination, ECOG performance status assessment and tumor site documentation. Histopathological confirmation was obtained from biopsy or surgical specimens. Baseline investigations included complete blood counts, liver and renal function tests, chest X-ray or CT thorax, abdominal ultrasound or CT, and bone scan in selected cases. Cardiac and pulmonary evaluations were performed using ECG, echocardiography and imaging as appropriate. Patients were registered upon completion of pretreatment evaluation and after fulfilling all eligibility criteria.

Radiotherapy was delivered using 3D conformal technique on an Elekta Oncor Expression linear accelerator with 6 MV photons. Treatment planning ensured ≥95% of the prescribed dose covered 100% of the planning target volume (PTV), with a maximum hot spot of 107%. Constraints included V30 ≤46% for heart and V20 ≤30% for the ipsilateral lung.

All patients underwent CT-based simulation for treatment planning. Radiotherapy was delivered using a linear accelerator (LINAC) with a three-dimensional conformal radiotherapy (3D-CRT) technique. In both Arm A and Arm B, chest wall irradiation was performed using 6 MV photons with tangential (medial and lateral) wedged fields. The supraclavicular, infraclavicular, and axillary nodal regions were treated using an anterior–posterior (AP) field with 6 MV photons, half-beam matched to the superior border of the tangential chest wall fields.

Patients were assessed weekly during treatment for toxicity and tolerability. Toxicities were graded using RTOG, CTC, and SOMA/LENT criteria. Quality of life was monitored using ECOG scale. Post-treatment follow-up was conducted at 6 weeks, then every 3 months, and later every 6 months, including physical exams and imaging as needed. Pulmonary and cardiac toxicities, lymphedema, and late skin changes were assessed at 6 weeks, 3 months, and 6 months after radiotherapy.

Data from both Arm A and Arm B were entered into separate tables, checked for consistency, manually coded, and entered into a computer for analysis. Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) version 23.0. Differences between means were analyzed using the independent samples t-test, while Z-tests were used to compare proportions in patient characteristics. Chi-square tests were applied to assess associations between categorical variables, and Fisher's exact test was used when more than 20% of cells had an expected frequency of less than 5. A p-value of <0.05 (two-tailed) was considered statistically significant.

Ethics

Prior to the commencement of the study, the research protocol was reviewed and approved by the institutional ethical committee of KYAMC&H. Permission was also obtained from the relevant departmental authority. All patients were informed about the nature and purpose of the study, including its aims, procedures, potential risks, and benefits. Informed consent was obtained in a language easily understood by the participants before enrollment.

3. RESULTS

Table 1: Socio-demographic and clinical characteristics of the participants (n=60).

Characteristics	Arm A [CFRT] (n=30)	Arm B [HFRT] (n=30)	Total (n=60)	p-value
Age (in years)				
Mean age ± SD	45.26 ± 10.49	44.1 ± 10.49		0.611
Monthly income (in BDT) (n/%)				
<15,000	1 (3.3)	8 (26.7)	9 (15.0)	0.001*
15,000-40,000	17 (56.7)	22 (73.3)	39 (65.0)	
>40,000	12 (40.0)	0 (0.0)	12 (20.0)	
Level of education (n/%)				
Below SSC	11 (36.7)	16 (53.3)	27 (45.0)	0.441
SSC	5 (16.7)	1 (3.3)	6 (10.0)	
HSC	15 (16.7)	4 (13.3)	9 (15.0)	

Graduate	3 (10.0)	3 (10.0)	6 (10.0)	
Occupation				
Housewife	26 (86.7)	28 (93.3)	54 (90.0)	0.529
Service holder	3 (10.0)	2 (6.7)	5 (8.3)	
Others	1 (3.3)	0 (0.0)	1 (1.7)	
BMI (in kg/m^2) (n/%)				
<25	9 (30.0)	19 (63.3)	28 (46.7)	0.010*
>25	21 (70.0)	11 (36.7)	32 (53.3)	
ECOG performance scale (n/%)				
0	12 (40.0)	9 (30.0)	21 (35.0)	0.035*
1	18 (60.0)	15 (50.0)	33 (55.0)	
2	0 (0.0)	6 (20.0)	6 (10.0)	
Family history (n/%)				
Present	2 (6.7)	2 (6.7)	4 (6.7)	1.00
Absent	28 (93.3)	28 (93.3)	28 (93.3)	

p-value estimated by unpaired t-test for age; Fisher's exact test for income, education, occupation and ECOG; Chi-squared test for BMI and family history. *: statistically significant. SD: Standard deviation; BMI: Body mass index; ECOG: Eastern Cooperative Oncology Group; BDT: Bangladeshi Taka.

Table 1 describes the socio-demographic and clinical characteristics of the participants. The mean age of the participants was similar in both groups (45.26 ± 10.49 years in Arm A vs. 44.1 ± 10.49 years in Arm B; p = 0.611). However, significant differences were observed in monthly income, BMI, and ECOG performance status. A greater proportion of participants in Arm B had a monthly income below 15,000 BDT (26.7% vs. 3.3%), while all high-income participants (>40,000 BDT) were in Arm A (p = 0.001). Regarding BMI, a higher percentage of participants in Arm A had a BMI >25 (70.0%) compared to Arm B (36.7%), which was statistically significant (p = 0.010). ECOG performance status also showed significant variation between groups, with 20.0% of participants in Arm B having an ECOG score of 2, while none in Arm A fell into this category (p = 0.035). Meanwhile, most participants were below SSC in both arms (36.7% vs. 53.3%) and majority were housewives (86.7% vs. 93.3%). Regarding family history, only 6.7% had a family history of cancer in both arms. These associations were not statistically significant.

Table 2: Tumor-related characteristics of the participants (n=60)

Characteristics	**Arm A [CFRT] (n=30)**	**Arm B [HFRT] (n=30)**	**Total (n=60)**	**p-value**
Histopathological classification (n/%)				
Ductal carcinoma	27 (90.0)	28 (93.3)	55 (91.7)	0.839
Lobular carcinoma	2 (6.7)	1 (3.3)	3 (5.0)	
Others	1 (3.3)	1 (3.3)	2 (3.3)	
Pathological staging (n/%)				
II	21 (70.0)	29 (96.7)	50 (83.3)	0.006*
III	9 (30.0)	1 (3.3)	10 (16.7)	
Tumor size (in cm) (n/%)				
Upto 2	5 (16.7)	8 (26.7)	13 (21.7)	

>2-<5	21 (70.0)	20 (66.7)	41 (68.3)	0.501
>5	4 (13.3)	2 (6.7)	6 (10.0)	
Tumor grade (n/%)				
I	1 (3.3)	8 (26.7)	9 (15.0)	0.040*
II	23 (76.7)	17 (56.7)	40 (66.7)	
III	6 (20.0)	5 (16.7)	11 (18.3)	

p-value for pathological staging estimated by Chi-squared test; for the rest by Fisher's exact test. *: statistically significant.

Table 2 illustrates the tumor-related attributes of the participants. Ductal carcinoma was the predominant histological type in both the groups: 90.0% in CFRT and 93.3% in HFRT; with no significant difference (p = 0.839). Meanwhile, pathological staging showed a significantly higher proportion of Stage II tumors in the HFRT group (96.7%) compared to the CFRT group (70.0%) (p = 0.006). Furthermore, we found that, tumor size was similar across groups, with the majority falling in the 2–5 cm range (70.0% in CFRT vs. 66.7% in HFRT; p = 0.501). Lastly, tumor grade differed significantly (p = 0.040), with more well-differentiated (Grade I) tumors observed in the HFRT group (26.7%) compared to CFRT (3.3%).

Table 3: Treatment-related characteristics of the participants (n=60).

Characteristics	Arm A [CFRT] (n=30)	Arm B [HFRT] (n=30)	Total (n=60)	p-value
Neoadjuvant therapy (n/%)				
Yes	11 (36.7)	4 (13.3)	15 (25.0)	0.072
No	19 (63.3)	26 (86.7)	45 (75.0)	
Adjuvant therapy (n/%)				
Yes	26 (86.7)	25 (83.3)	51 (85.0)	0.718
No	4 (13.3)	5 (16.7)	9 (15.0)	
Hormone therapy (n/%)				
Yes	14 (46.7)	17 (56.7)	31 (51.7)	0.438
No	16 (53.3)	13 (43.3)	29 (48.3)	
Chemotherapy history (n/%)				
FEC	3 (10.0)	0 (0.0)	3 (5.0)	0.001*
FAC	2 (6.7)	17 (56.7)	19 (31.7)	
TAC	7 (23.3)	5 (16.7)	12 (20.0)	
AC-T	16 (53.3)	6 (20.0)	22 (36.7)	
mCME	2 (6.7)	2 (6.7)	4 (6.7)	

p-values for chemotherapy history were estimated by Fisher's exact test and the rest by Chi-squared tests; *statistically significant; FAC: Fluorouracil (5-FU), Doxorubicin (Adriamycin), and Cyclophosphamide; FEC: Fluorouracil, Epirubicin, and Cyclophosphamide; TAC: Docetaxel (Taxotere), Doxorubicin, and Cyclophosphamide; AC-T: Doxorubicin and Cyclophosphamide followed by Paclitaxel (Taxol); mCME: Modified Cyclophosphamide, Methotrexate, and 5-FU (CMF)

Table 3 highlights the treatment-based variables in the study. It was clearly evident that, neoadjuvant therapy was more commonly administered in the CFRT group (36.7%) compared to the HFRT group (13.3%), although this difference was not statistically significant (p = 0.072). Besides, the distribution of adjuvant therapy (86.7% in CFRT vs. 83.3% in HFRT; p = 0.718) and hormone therapy (46.7% vs. 56.7%, respectively; p = 0.438) was similar between the two groups. On the contrary, a significant difference was documented in the types of chemotherapy regimens used (p = 0.001). The FAC

regimen was predominantly used in the HFRT group (56.7%), whereas the AC-T regimen was more frequently administered in the CFRT group (53.3%). The FEC regimen was used exclusively in the CFRT group (10.0%). Lastly, TAC and mCME regimens were distributed relatively evenly across both the arms.

Table 4: Dermatological toxicities experienced by the participants (n=60).

Toxicities	Arm A [CFRT] (n=30)	Arm B [HRCT] (n=30)	Total (n=60)	p-value
Acute dermatitis (n/%)				
Nil	5 (16.7)	11 (36.7)	16 (26.7)	0.138
<Grade II	18 (60.0)	16 (53.5)	34 (56.7)	
Grade II	4 (13.3)	2 (6.7)	6 (10.0)	
Grade III	3 (10.0)	1 (3.3)	4 (6.6)	
Chronic dermatitis (n/%)				
Nil	22 (73.7)	28 (93.5)	50 (83.3)	0.08
≤Grade II	8 (26.7)	2 (6.7)	10 (16.7)	
Skin retraction (n/%)				
Nil	29 (96.7)	28 (93.3)	57 (95.0)	0.554
<Score 2	1 (3.3)	2 (6.7)	3 (5.0)	
Skin atrophy (n/%)				
Nil	28 (93.3)	29 (96.7)	57 (95.0)	0.554
<Score 2	2 (6.7)	1 (3.3)	3 (5.0)	

p-value was estimated by Fisher's exact test for acute dermatitis; and the rest by Chi-squared tests.

Table 4 presents dermatological toxicities observed in both arms. For acute dermatits, Grade I and II reactions were more common in Arm A (60.0% and 13.3%) compared to Arm B (53.3% and 6.7%), while 36.7% of patients in Arm B experienced no toxicity vs. 16.7% in Arm A. Although acute dermatitis was more frequent in Arm A, the difference was not statistically significant ($p > 0.05$). Regarding chronic dermatitis, Grade I was observed in 26.7% of patients in Arm A and 6.7% in Arm B. Again, the difference was not statistically significant ($p > 0.05$). Furthermore, In Arm A, 29 patients (96.7%) experienced no skin retraction, while 1 patient (3.3%) developed a skin retraction score of 2; in Arm B, 28 patients (93.3%) had no skin retraction, and 2 patients (6.7%) developed a score of 2. Although skin retraction was slightly more frequent in Arm B, this difference was not statistically significant ($p > 0.05$). No patients in either group developed skin retraction scores above 2. Nearly similar findings were observed in the context of skin atrophy.

Table 5: Various toxicities reported by the participants (n=60).

Toxicity	Arm A [CFRT] (n=30)	Arm B [HFRT] (n=30)	Total (n=60)	p-value
Dysphagia (n/%)				
Nil	7 (23.3)	15 (50.0)	22 (36.7)	0.065
<Grade II	19 (63.4)	14 (46.7)	33 (55.0)	
Grade II-III	4 (13.3)	1 (3.3)	5 (8.3)	
Cardiotoxicity (n/%)				
Nil	29 (96.7)	29 (96.7)	58 (96.7)	

≤Grade II	1 (3.3)	1 (3.3)	2 (3.3)	1.00
Pulmonary toxicity (n/%)				
Nil	29 (96.7)	29 (96.7)	58 (96.7)	1.00
≤Grade II	1 (3.3)	1 (3.3)	2 (3.3)1	
Lymphedema (n/%)				
Nil	26 (86.7)	28 (93.3)	54 (90.0)	0.389
≤Grade II	4 (13.3)	2 (6.7)	6 (10.0)	
Chest wall pain in RT area (n/%)				
Nil	17 (56.7)	20 (60.7)	37 (61.7)	0.426
<Score 2	13 (43.3)	10 (33.3)	23 (38.3)	

p-value for dysphagia estimated by Fisher's exact test; the rest by Chi-squared test.

Table 5 summarizes the various types of delayed toxicities experienced by participants in both the arms. Dysphagia was more common in Arm A, with 76.7% of patients reporting some degree of dysphagia compared to 50.0% in Arm B, though this difference did not reach statistical significance ($p = 0.065$). Cardiotoxicity and pulmonary toxicity were rare and evenly distributed between the groups, with 96.7% of patients in both arms experiencing no toxicity ($p = 1.00$ for both). Besides, lymphedema occurred in 13.3% of patients in Arm A and 6.7% in Arm B, without a significant difference ($p = 0.389$). Similarly, chest wall pain in RT area was reported by 43.3% of patients in Arm A and 33.3% in Arm B ($p = 0.426$). Overall, these toxicities were mild to moderate in severity and did not differ significantly between the treatment arms.

Table 6: Radiotherapy cost distribution for both the groups (n=60).

Cost distribution	Arm A [CFRT] (n=30)	Arm B [HFRT] (n=30)
Cost of RT/ (in BDT)	1,33,250	86,900

Table 6 shows the cost of radiotherapy for patients in both the treatment arms. It was clearly evident that, all patients in Arm A who received CFRT incurred a cost of 133,250 BDT. On the the other hand, those patients in Arm B who were administered HFRT were charged 86,900 BDT.

4. DISCUSSION

A total of 60 patients with post-mastectomy carcinoma of the breast (Stage II to III) were analyzed, having received either HFRT or CFRT radiotherapy. These patients were followed for up to 6 months after completion of treatment. The primary objective of the study was to compare the tolerability, toxicity profiles, treatment cost, and overall treatment duration between HFRT and CFRT regimens in the post-mastectomy setting.

The two groups were comparable in terms of tumor and clinical characteristics. In both arms, the majority of patients were younger than 50 years, with a mean age of 44.68 ± 10.49 years, and no statistically significant difference was observed between the groups ($p > 0.05$). These findings are consistent with previous studies, including those by Rastogi et al., Das et al., Bhattacharyya et al. (2018), and Banu et al., which also reported similar age distributions among patients receiving hypofractionated and conventional radiotherapy. [2, 9-11]

The majority of patients in both groups were housewives, comprising 86% in the CFRT group and 93% in the HFRT group, with no significant difference between the groups ($p > 0.05$). Additionally, most patients were multiparous, with only 2 patients (6.7%) in Arm B being nulliparous ($p > 0.05$). Moreover, most patients belonged to middle-class families, with a monthly income ranging from 15,000 to 40,000 Taka. Notably, the HFRT group had a higher proportion of patients with lower monthly income, highlighting the potential accessibility benefits of HFRT in resource-constrained populations. Furthermore, most patients in both groups had education levels below SSC pass, followed by those who were illiterate. Besides, the BMI distribution and ECOG scores indicated slightly better general condition in the CFRT group, which could influence treatment tolerability but did not significantly affect toxicity outcomes. Regarding ECOG performance scores, the results aligned with previous studies. [2, 10-11]

In our study, the majority of patients in both treatment arms (93.3%) reported no positive family history of breast cancer, with only 6.7% in each group having a positive family history ($p > 0.05$). This finding aligns with Aich et al., who reported similarly low proportions of positive family history in both control (2.1%) and study groups (2.3%). [12]

Pathological staging revealed a higher proportion of Stage II tumors in the HFRT group, and tumor grading showed more well-differentiated tumors in this arm. Similar findings were reported by Rastogi et al. with 66% and 54%, Das et al. with 79.2% and 80%, Bhattacharyya et al. with 52% and 60%, and Banu et al. reported 86% stage II tumors in their cohorts. [2, 9-11] Despite this, tumor sizes were comparable, supporting the clinical applicability of both treatment regimens across similar disease presentations. Moreover, infiltrating ductal carcinoma was more in both arms (90% in Arm A & 93.3% in Arm B) (p value >0.05). Infiltrating ductal carcinoma was also abundant in previous studies. [10]

Furthermore, our study found a statistically significant difference in tumor grade distribution between the two groups, with 26.7% of patients in the HFRT group having well-differentiated (Grade I) tumors compared to only 3.3% in the CFRT group ($p = 0.040$). Grade II tumors accounted for 56.7% in HFRT and 76.7% in CFRT, reflecting variation in tumor differentiation. These findings are consistent with Deanantonio et al., who reported Grade II tumors in 56% of the HFRT group and 54% in the CFRT group. [13] Similarly, Akl et al. documented Grade II tumors in 78% of HFRT and 82% of CFRT groups, supporting the comparable tumor grade distribution between HF and CF treatments. [14]

Neo-adjuvant chemotherapy (NACT), adjuvant chemotherapy (ACT), and hormonal therapy (HT) were administered to similar proportions of patients in both groups (NACT: 36.7% CFRT vs. 13.3% HFRT; ACT: 87% CFRT vs. 83% HFRT; HT: 46% CFRT vs. 56% HFRT; $p > 0.05$). These findings align with Rastogi et al., who reported comparable rates of NACT (58% CFRT vs. 52% HFRT), ACT (96% CFRT vs. 98% HFRT), and HT (58% CFRT vs. 52% HFRT). Bhattacharyya et al. also observed similar treatment distributions across groups. [2, 10]

In this study, acute skin toxicity of Grade I was observed in 60% of patients in the CFRT group and 53.3% in the HFRT group, with Grade II/III toxicity in 23.3% and 10%, respectively. Although acute skin toxicity was higher in the CF arm, the difference was not statistically significant ($p > 0.05$), and no Grade IV toxicity was observed. These findings are consistent with previous reports showing comparable or lower rates of acute skin toxicity with HFRT. [2, 13] Late skin toxicity was also mild and similar between arms, with Grade I chronic dermatitis in 26% (CFRT) versus 6.7% (HFRT), without significant differences ($p > 0.05$). [13] Besides, esophageal toxicity followed a similar pattern, with Grade I toxicity in 63.3% (CFRT) versus 46.7% (HFRT), and Grade II/III toxicity less common and not statistically different ($p > 0.05$). Lymphedema incidence was low and comparable between groups (13.3% CFRT vs. 6.7% HFRT, $p > 0.05$), consistent with ranges reported in the literature. [15]

Pulmonary and cardiac toxicities were rare and mild, with only 3.3% of patients in each arm developing Grade I toxicity and no higher-grade events. These rates align with previously published data demonstrating low incidence of severe pulmonary and cardiac toxicity following post-mastectomy radiotherapy, regardless of fractionation. [2, 16-17]

Post-radiotherapy pain was slightly more common in the CFRT group, but differences were not statistically significant ($p > 0.05$), echoing findings from Jagsi et al. that reported similar pain profiles across fractionation regimens. [18]

Overall, toxicity profiles between HFRT and CFRT were comparable, with slightly lower but statistically insignificant toxicity in the HFRT group. Importantly, no Grade IV toxicities occurred in either arm, and all toxicities were manageable. Lastly, the total cost of radiotherapy was lower in Arm B (86,900 Tk) compared to Arm A (133,450 Tk). All this cumulatively supports the growing evidence that HF post-mastectomy radiotherapy is a safe and effective alternative to conventional schedules, especially beneficial in resource-limited settings due to shorter treatment duration and lower costs. [2, 10]

This study had several limitations. Firstly, due to its quasi-experimental design, randomization was not feasible, which may have introduced selection bias. Secondly, being a single-institution study, the findings may not be generalizable to the broader population, emphasizing the need for larger, multicenter trials. Thirdly, the short follow-up duration limited the ability to assess long-term outcomes such as loco-regional control and overall survival. Lastly, certain relevant investigations could not be performed due to financial constraints and limited availability of resources, potentially affecting the comprehensiveness of the clinical assessment.

Given the non-randomized design and short-term follow-up, long-term data on loco-regional control and survival remain to be established. However, these results suggest that HF radiotherapy can be confidently adopted in high patient-volume centers like ours, addressing socioeconomic challenges and workforce shortages while maintaining treatment efficacy and tolerability.

5. CONCLUSION

CFRT and HFRT demonstrated comparable results in terms of acute and late toxicities, indicating that HFRT is as effective as CFRT in the post-mastectomy setting. Additionally, HF offers significant advantages—shorter treatment duration, improved patient compliance, reduced interruption, and lower overall treatment cost. In resource-limited settings with high patient volumes, HF schedules can help reduce waiting times, increase patient turnover, and optimize the use of available infrastructure. Therefore, HFRT presents a viable, efficient, and cost-effective alternative for post-mastectomy breast cancer patients, especially in low-resource countries like Bangladesh.

Conflict of interest disclosure

The authors disclose no conflict of interest.

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