

## Randomized Prospective Study Comparing Conventional Versus Hypofractionated Adjuvant Radiotherapy in Node-Positive Breast Cancer

Mai Atef, Eman El Sheikh, Mahmoud A. Ellithy, Khaled Naguib, Amr S. Tawfik

Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

**Background:** Hypofractionated radiotherapy in early breast cancer yields equivalent or better outcome in terms of efficacy, toxicity, cosmesis and cost-effectiveness. However, its role in node-positive breast cancer is less clear.

**Aim:** To compare between adjuvant conventional and hypofractionated radiotherapy in node-positive breast cancer.

**Methods:** Prospective pilot study of 66 node-positive breast cancer patients recruited over 1 year in a single institution. Patients were randomized to receive adjuvant conventional radiotherapy 200 cGy x 25 fractions with 200 cGy x 5 fractions boost to the tumor bed in case of breast conservation (control arm) or hypofractionated radiotherapy 266 cGy x 16 fractions with 266 cGy x 4 fractions boost to the tumor bed in case of breast conservation (intervention arm). The end points were disease-free survival, cosmetic outcome, ipsilateral arm lymphedema and acute skin reactions.

**Results:** Disease-free survival did not differ significantly between the two treatment arms ( $p = 0.6$ ) and the 2-year disease-free survival rate was 87% and 89% in the hypofractionated and conventional arms. The rate of excellent/good cosmetic score was higher in the hypofractionated arm than the conventional as rated by patients (71% vs. 46%,  $p = 0.182$ ) and physicians (29% vs. 8%,  $p = 0.32$ ). Hypofractionation, when compared to conventional fractionation, was associated with less arm lymphedema (22% vs. 40%,  $p = 0.149$ ), dry desquamation (28% vs. 53%,  $p = 0.04$ ), skin darkness (0% vs. 15%,  $p = 0.054$ ) and wet desquamation (16% vs. 21%,  $p = 0.601$ ).

**Conclusion:** Hypofractionated adjuvant radiotherapy in node-positive breast cancer patients is equivalent to conventional fractionation as regards disease-free survival, cosmetic outcome and arm lymphedema with less early skin reactions.

**Keywords:** Breast Cancer, Node-positive, Adjuvant, Hypofractionated radiotherapy

**Corresponding Author:** Mai Atef Ali El-Din, MD; Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt; Email: [dr.mai.atef@hotmail.com](mailto:dr.mai.atef@hotmail.com)

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### INTRODUCTION

Breast cancer is the most common cancer among United States women, representing 30% of all newly diagnosed cancer cases<sup>1</sup>. It has been estimated that 93% of breast cancer cases are diagnosed with localized and regional stage with 31 % node-positive cases<sup>2</sup>. In Egypt, the estimated incidence rates of breast cancer among females in Lower, Middle, and Upper Egypt were 53/100000 (33.2%) in 2009-2011, 35.6/100000 (26.8%) in 2009 and 64.5/100000 (38.7%) in 2008, respectively<sup>3</sup>. In a single Egyptian institutional epidemiological study that included 1906 breast cancer patients treated over a 5-year period, 74% of them were diagnosed with localized and regional disease, including 57% with node-positive disease<sup>4</sup>.

Randomized clinical trials have confirmed that adjuvant irradiation not only spares patients the morbidity and distress of local recurrence by improving local control, but it also improves overall survival by preventing distant metastases from remaining reservoirs of loco-regional disease<sup>5</sup>. Based on the historical hypothesis that breast cancer cells are less sensitive to changes in the dose per fraction than the dose limiting normal tissues; a daily fraction equal to 2 Gy for 25

fractions over 5-7 weeks for total dose of 50-60 Gy was delivered in most of the original studies, therefore it was suggested to be the standard fractionation schedule<sup>6</sup>.

Despite the established role of adjuvant conventionally-fractionated radiotherapy in breast cancer, there are some challenges like the cost and time consumed by the daily treatment course for 5-7 weeks<sup>7</sup>. Hypofractionated radiotherapy may offer several advantages including treatment time reduction which is more suitable for patients; especially those from rural areas, the elderly and those caring for dependents. It also reduces the financial burden on patients, with the reduction of transportation and accommodation expenses and radiotherapy fees. From a departmental perspective, adjuvant radiotherapy occupies a considerable percentage of the radiation oncology department's workload. Hypofractionated radiotherapy may free up staff and reduce radiotherapy machine use time allowing better access for radiotherapy services and reducing delays in treatment. Therefore, by utilizing hypofractionated radiotherapy schedules more routinely, there may be significant returns to patients, oncology departments and health expenditure<sup>8</sup>.

Routine utilization of hypofractionated radiotherapy is evidenced by the results of five main randomized

controlled trials in patients with early breast cancer, demonstrating that hypofractionated radiotherapy has comparable or better outcomes in all main end points; effectiveness, toxicity, cosmetic outcome and cost effectiveness<sup>6, 7, 9-11</sup>. The latest American Society for Radiation Oncology (ASTRO) clinical guideline for the adjuvant whole breast radiotherapy recommends a hypofractionated whole breast irradiation regimen (4000 cGy in 15 fractions or 4250 cGy in 16 fractions)<sup>12</sup>.

However, the role of hypofractionated radiotherapy in case of patients with metastatic lymph nodes who require regional lymphatic irradiation is less clear. It was evaluated in retrospective and prospective series studying hypofractionated radiotherapy in the post-mastectomy setting. A retrospective study addressed the effect of hypofractionated regional nodal irradiation in node-positive breast cancer after mastectomy or breast conservative surgery and its results suggested that hypofractionation is an acceptable alternative to conventional fractionation for breast cancer patients requiring regional lymphatic irradiation in terms of effect and toxicity<sup>13</sup>. Also, in the United Kingdom Standardisation of Breast Radiotherapy (START) trials A and B, 13.8% and 6.9 % of patients received adjuvant nodal irradiation to the supraclavicular area or the axillary area or both<sup>14</sup>.

Here, we compared between adjuvant conventional radiotherapy and hypofractionated radiotherapy to the chest wall or whole breast together with regional lymphatics in axillary node-positive breast cancer patients. We hypothesized that hypofractionated radiotherapy would yield local control and survival rates similar to conventional fractionation in this setting without an increase in toxicities.

## METHODS

A prospective open-label randomized pilot study conducted at the Department of Clinical Oncology and Nuclear Medicine, Ain Shams University Hospitals.

### Patients

Patients aged  $\geq 20$  years old were recruited after complete excision of primary breast cancer with free surgical margin (ink free) by modified radical mastectomy or breast conservative surgery with axillary clearance ( $\geq 8$  lymph nodes excised) (pT1-3, N1-2, M0). Patients should have finished adjuvant chemotherapy by at least 2 weeks gap. In patients who received neoadjuvant chemotherapy, pathological examination after definitive surgery should have confirmed pathologic pT1-3, N1-2, M0 disease and/or clinical T1-3, N1-2, M0 with pathologic verification of axillary nodal positivity at presentation (i.e. before neoadjuvant therapy). The surgical wound must have completely healed with no signs of any infection and no immediate surgical reconstruction allowed.

Written informed consent was acquired for every patient. The study was approved by the Research Ethics Committee of the Faculty of Medicine, Ain Shams University.

### Procedures

Sixty-six patients were 1:1 randomized to one of two treatment arms. The control arm received adjuvant conventional radiotherapy 200 cGy x 25 fractions with sequential 200 cGy x 5 fractions boost to the tumor bed for those who underwent breast conservation surgery. The experimental arm received adjuvant hypofractionated radiotherapy 266 cGy x 16 fractions with 266 cGy x 4 fractions sequential boost to the tumor bed for those who underwent breast conservation surgery.

Patients were treated using external beam 3-D conformal radiotherapy technique. They were treated in the supine position with the arm abducted ( $\geq 90$  degrees) utilizing breast tilt boards with the chest wall slope parallel to the table. The planning target volume has been defined according to the Radiation Therapy Oncology Group (RTOG) breast cancer atlas consensus for whole breast irradiation, chest wall irradiation, supraclavicular lymph nodes area, infraclavicular lymph nodes area and with or without internal mammary lymph nodes. Most of the patients received 6 MV X-rays, though treatment with higher energies was allowed.

Dose constraints applied for plan were that to achieve 95% of target volume covered by 95% of the dose, V105 < 10% and Dmax 108%. The dose constraints for organs at risk were as follows: heart (V30 < 1% and mean dose < 2-3 Gy), ipsilateral lung (V20 < 30%), contralateral lung (V5 < 10%) and contralateral breast (Dmax 3 Gy). The dosimetric measurements were checked in a 3-D breast phantom by the quality assurance team, including the matching line between supraclavicular and infraclavicular fossae, and the chest wall / whole breast fields.

The principle end points were disease free survival (DFS), cosmetic outcome, ipsilateral arm lymphedema and acute skin reaction by following up patients for 2 years. Disease free survival has been defined as the time from surgery to any breast cancer related event (locoregional or distant relapse, contralateral breast cancer or death from breast cancer).

Aesthetic evaluation of the irradiated breast was done using the 4-point Harvard / National Surgical Breast and Bowel Project (NSABP) / Radiation Therapy Oncology Group (RTOG) Breast Cosmesis Scale (table 1)<sup>15</sup>. Observer evaluation (physician score) and subjective evaluation (patient score) were obtained. Upon evaluation, each score acquired a point ranging from 1 to 4 (excellent to poor cosmetic outcome). The cumulative incidence of cosmetic changes in the irradiated breast from baseline (before radiotherapy) for each patient had been evaluated yearly for 2 years following the end of radiotherapy in the two study groups using photos which was taken to assess the changes in the breast size, shrinkage, shape and skin color.

To assess the cumulative incidence of lymphedema following radiotherapy; lymphedema was defined as  $\geq 10\%$  increase in arm circumference over baseline circumference compared to the contralateral arm. This was assessed every 6 months from the time of beginning of radiotherapy for 2 years.

Acute skin reactions defined as erythema, dry desquamation, wet desquamation and skin darkness were observed weekly during radiotherapy, at the end of radiotherapy and every 3 months for 2 years following the end of radiotherapy. Toxicities were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03.

**Table 1: Harvard / National Surgical Breast and Bowel Project (NSABP) / Radiation Therapy Oncology Group (RTOG) Breast Cosmesis Scale**

<b>1. Excellent:</b>	When compared with the untreated breast, there is minimal or no difference in the size or shape of the treated breast. The way the breasts feel (its texture) is the same or slightly different. There may be thickening, scar tissue, or fluid accumulation within the breast but not enough to change the appearance.
<b>2. Good:</b>	There is a slight difference in the size or shape of the treated breast as compared with the opposite breast or the original appearance of the treated breast. There may be some mild reddening or darkening of the breast. The thickening or scar tissue within the breast causes only a mild change in the shape or size.
<b>3. Fair:</b>	Obvious difference in the size and shape of the treated breast. This change involves one-quarter or less of the breast. There can be moderate thickening or scar tissue of the skin and the breast, and there may be obvious color changes.
<b>4. Poor:</b>	Marked change in the appearance of the treated breast involving more than one-quarter of the breast tissue. The skin changes may be obvious and detract from the appearance of the breast. Severe scarring and thickening of the breast, which clearly alter the appearance of the breast, may be found.

**Statistical analysis**

Continuous variables were presented as mean with standard deviation ( $\pm$ SD) or median with minimum and maximum values (range). The Kolmogorov–Smirnov test was utilized to test for the normality of distribution of continuous variables. Independent sample *t*-test was utilized to assess the difference in normally-distributed continuous variables between two groups and the Mann-Whitney test for the abnormally-distributed.

Categorical variables were presented as numbers and percentages and the difference in proportions between groups was assessed using Chi-square test.

The median follow up time was estimated by the reverse Kaplan-Meier method. Disease-free survival was calculated by the Kaplan-Meier test and its difference between groups was estimated using the log-rank test.

A p value  $<0.05$  had been considered significant. Statistical analysis was done using the Statistical

Package for the Social Sciences (SPSS) software for Windows.

**RESULTS**

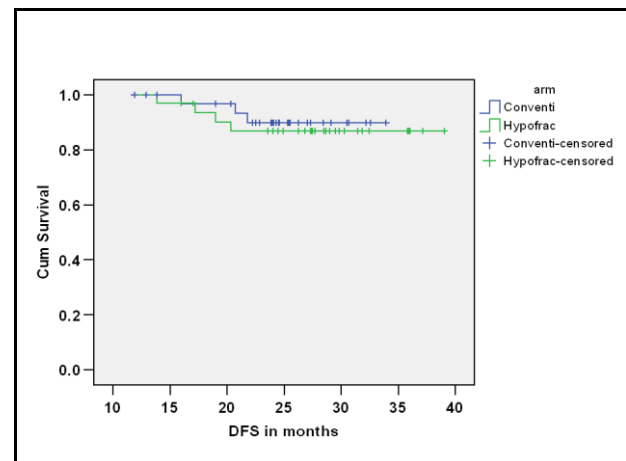
Within one year, 34 and 32 breast cancer female patients were recruited in the conventional fractionation radiotherapy arm and the hypofractionation radiotherapy arm, respectively. Demographic and clinical characteristics were balanced between the two study arms (table 2). The mean age of patients was  $51.1 \pm 8.7$  years in the conventional arm and  $51.3 \pm 11.2$  in the hypofractionation arm.

The estimated median follow up time was 26.8 months (95% confidence interval [CI]: 24.85-28.75).

Three patients out of 31 in the conventional arm developed distant metastasis and one of them developed contralateral breast cancer, while 3 patients out of 32 in the hypofractionation arm developed distant metastasis and only 1 patient developed distant metastasis with axillary regional recurrence.

The estimated mean DFS was 32.48 months (95%CI: 30.9-34.06) in the conventional arm, which was not significantly lower than that in the hypofractionation arm, estimated as 36.22 months (95%CI: 33.64-38.8), ( $p=0.6$ ). The 2-year DFS for the whole group of patients was 88.5%. The 2-year DFS in the conventional arm was 89.9% and in the hypofractionation arm was 86.9% (figure 1).

At the time of analysis performance, the median DFS was not reached yet in both arms.



**Figure 1: Kaplan Meier disease-free survival curves according to treatment arm**

Patient’s rating of cosmetic outcome was done before radiotherapy (baseline) and 2 years after finishing radiotherapy. Out of 16 patients who underwent breast conservative surgery in the conventional fractionation arm, 13 women were involved in the cosmetic outcome analysis with available photographic assessment and 14 patients out of 15 were involved in the hypofractionated radiotherapy arm.

There was no statistically significant difference between the two arms in patients’ cosmetic scores before radiotherapy, where there was no poor scoring in both

**Table 2: Patients' demographic and clinical characteristics**

	Arm		Total n (%)	P value
	Conventional (n=34) n (%)	Hypofractionated (n=32) n (%)		
<b>Menopausal status</b>				
Postmenopausal	14 (41.2)	19 (59.4)	33 (50)	0.139
Premenopausal	20 (58.8)	13 (40.6)	33 (50)	
<b>Side</b>				
Left	13 (38.2)	12 (37.5)	25 (37.9)	0.951
Right	21 (61.8)	20 (62.5)	41 (62.1)	
<b>Surgery</b>				
Breast conservative surgery	16 (47.1)	15 (46.9)	31 (47)	0.988
Modified radical mastectomy	18 (52.9)	17 (53.1)	35 (53)	
<b>Chemotherapy</b>				
Anthracycline + Taxane	28 (82.4)	26 (81.3)	54 (81.8)	0.537
Anthracycline	5 (14.7)	4 (12.5)	9 (13.6)	
Cyclophosphamide, methotrexate, fluorouracil	1 (2.9)	0	1 (1.5)	
Taxane	0	1 (3.1)	1 (1.5)	
None	0	1 (3.1)	1 (1.5)	
<b>T stage</b>				
1	7 (20.6)	7 (21.9)	14 (21.2)	0.803
2	22 (64.7)	22 (68.8)	44 (66.7)	
3	5 (14.7)	3 (9.4)	8 (12.1)	
<b>N stage</b>				
1	16 (47.1)	17 (53.1)	33 (50)	0.622
2	18 (52.9)	15 (46.9)	33 (50)	
<b>Estrogen receptors status</b>				
Negative	6 (17.6)	3 (9.4)	9 (13.6)	0.477
Positive	28 (82.4)	29 (90.6)	57 (86.4)	
<b>Progesterone receptors status</b>				
Negative	9 (26.5)	6 (18.8)	15 (22.7)	0.454
Positive	25 (73.5)	26 (81.3)	51 (77.3)	
<b>Her2neu status</b>				
Negative	22 (66.7)	25 (78.1)	47 (72.3)	0.32
Positive	11 (33.3)	7 (21.9)	18 (27.7)	
<b>Histological grade</b>				
1	1 (2.9)	0	1 (1.5)	0.45
2	30 (88.2)	27 (84.4)	57 (86.4)	
3	3 (8.8)	5 (15.6)	8 (12.1)	
<b>Histological subtype</b>				
Infiltrating duct carcinoma	32 (94.1)	29 (90.6)	61 (92.4)	0.543
infiltrating lobular carcinoma	1 (2.9)	1 (3.1)	2 (3)	
Mixed (infiltrating duct and lobular carcinomas)	0	1 (3.1)	1 (1.5)	
Infiltrating medullary carcinoma	1 (2.9)	0	1 (1.5)	
Invasive mucinous carcinoma	0	1 (3.1)	1 (1.5)	
<b>Extra-capsular invasion</b>				
Negative	15 (46.9)	15 (51.7)	30 (49.2)	0.705
Positive	17 (53.1)	14 (48.3)	31 (50.8)	
<b>Lympho-vascular invasion</b>				
Negative	18 (81.8)	18 (72)	36 (76.6)	0.428
Positive	4 (18.2)	7 (28)	11 (23.4)	
<b>Median (range)</b>				
Age	49 (37-70)	54 (31-78)		0.957
Number of cycles of chemotherapy	6 (6-7)	6 (3-8)		0.918

arms and excellent/good score represented 61.5% and 78.5% in conventional and hypofractionated radiotherapy arms, respectively. The mean patient's score before and after radiotherapy in the conventional arm was  $2.23 \pm 0.73$  and  $2.46 \pm 0.66$  respectively ( $p = 0.083$ ); while, the mean patient's score before and after radiotherapy in the hypofractionation arm was  $2.07 \pm 0.62$  and  $2.21 \pm 0.8$  respectively ( $p = 0.414$ ). The mean

increase in patients' score after radiotherapy in the conventional ( $0.23 \pm 0.43$ ) vs. the hypofractionated radiotherapy ( $0.14 \pm 0.66$ ) arm was not statistically significant ( $p = 0.44$ ). As shown in figure 2, after 2 years from the end of radiotherapy, 46.2% of women in the conventional arm as compared to 71.4% in the hypofractionation arm had an excellent or good cosmetic outcome ( $p = 0.182$ ).

There was no statistically significant difference in physicians' cosmetic scoring before radiotherapy between the two treatment arms ( $p = 0.311$ ). Only 1 patient in each arm had poor cosmetic score. The physicians' cosmetic scores were poorer 2 years after finishing radiotherapy when compared to baseline in both treatment arms. The mean physicians' score for the control arm patients increased from  $2.69 \pm 0.75$  to  $3.31 \pm 0.63$  ( $p = 0.11$ ) and for the hypofractionation arm it increased from  $2.36 \pm 0.75$  to  $2.79 \pm 0.58$  ( $p = 0.14$ ). The mean increase in physicians' cosmetic score from baseline to 2 year post-radiotherapy did not differ significantly between the conventional and hypofractionated arms ( $0.62 \pm 0.65$  and  $0.43 \pm 0.51$ , respectively;  $p = 0.47$ ). Figure 3 shows that after 2 years from the end of radiotherapy, 8% of women in the control arm as compared to 29% in the hypofractionation arm had an excellent or good cosmetic outcome as rated by physicians ( $p = 0.326$ ).

Thirty (88%) patients in the conventional arm and 27 (84%) in the hypofractionated one were followed up for at least 6 months following radiotherapy and were assessed for arm lymphoedema.

Forty percent of patients in the conventional arm suffered from lymphedema in comparison to 22.2% in the hypofractionated radiotherapy arm, but this difference was not statistically significant ( $p = 0.149$ ) (figure 4). In multivariate analysis the occurrence of arm lymphedema did not correlate significantly with radiotherapy fractionation schedule, number of excised lymph nodes or type of surgery (table 3).

Acute skin reactions were observed as erythema, dry desquamation (grade 1), wet desquamation (grade 2-3) and skin darkness. As shown in figure 5, grade 1 dry desquamation was significantly higher in the conventional arm than in the hypofractionated arm (52.9% vs. 28.1%, respectively;  $p = 0.04$ ). Wet desquamation (grade 2-3) rate was higher in the conventional arm (20.6%) as compared to the hypofractionated arm (15.6%), but this difference was not statistically significant ( $p = 0.601$ ). Only one patient suffered from grade 3 wet desquamation and she was in the hypofractionation arm. The rate of skin darkness was higher in the conventional arm than in the hypofractionated arm ( $p=0.054$ ) (figure 6).

## DISCUSSION

Our aim was to determine whether hypofractionation of adjuvant radiotherapy to whole breast / chest wall with regional nodal is comparable to conventional fractionation schedule or not. If proved comparable, several advantages from hypofractionated radiotherapy will be gained in node-positive breast cancer patients without compromising local control and survival benefit or increasing toxicity. The long-term results of the START and the Ontario trials provided strong evidence that hypofractionation is safe and effective in early breast cancer <sup>14</sup>. Based on that, hypofractionated radiotherapy regimen in early breast cancer patients continues to be the United Kingdom

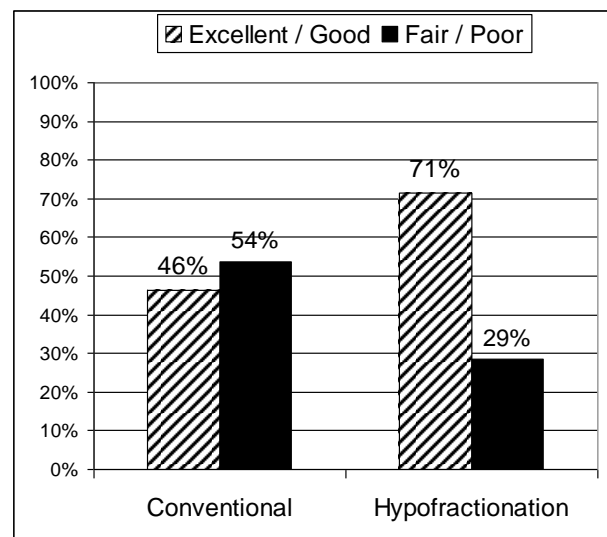


Figure 2: Patients' cosmetic rating two years after finishing radiotherapy

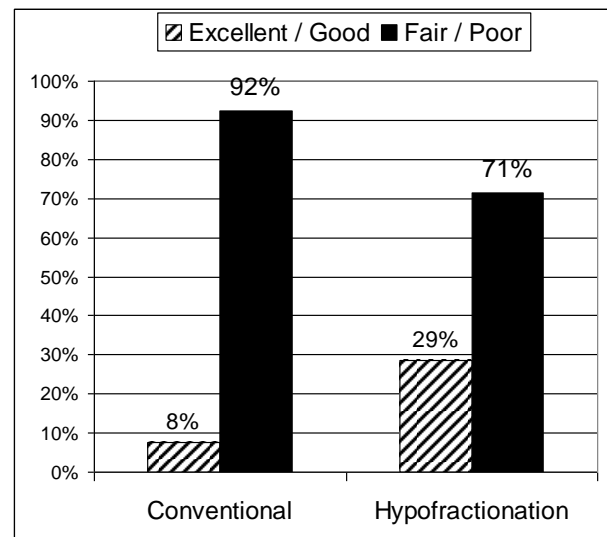


Figure 3: Physicians' cosmetic rating two years after finishing radiotherapy

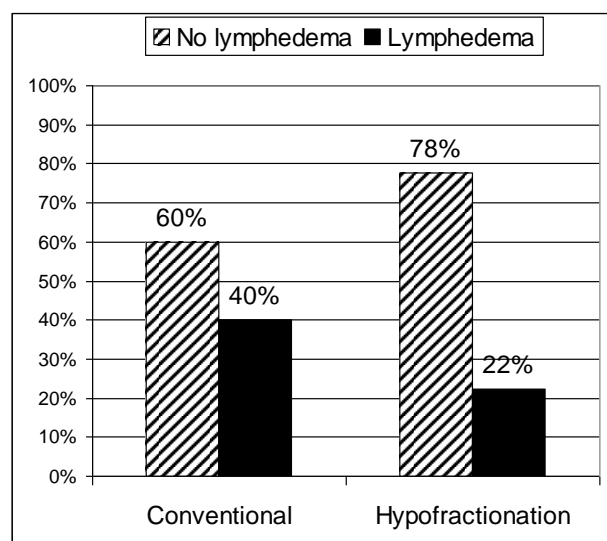
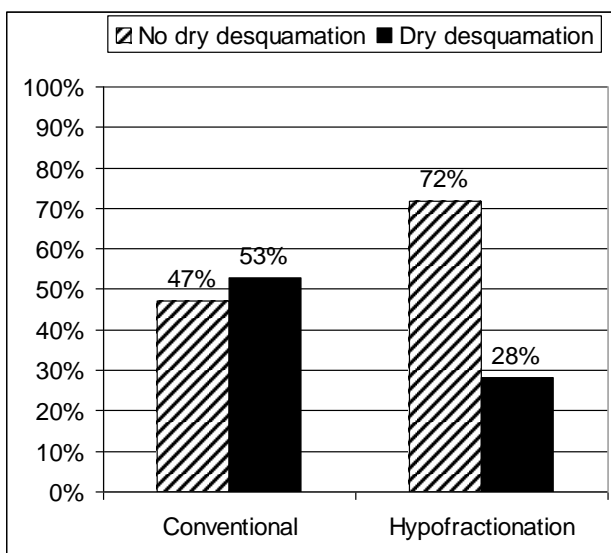


Figure 4: The rate of arm lymphedema (conventional vs. hypofractionated radiotherapy)

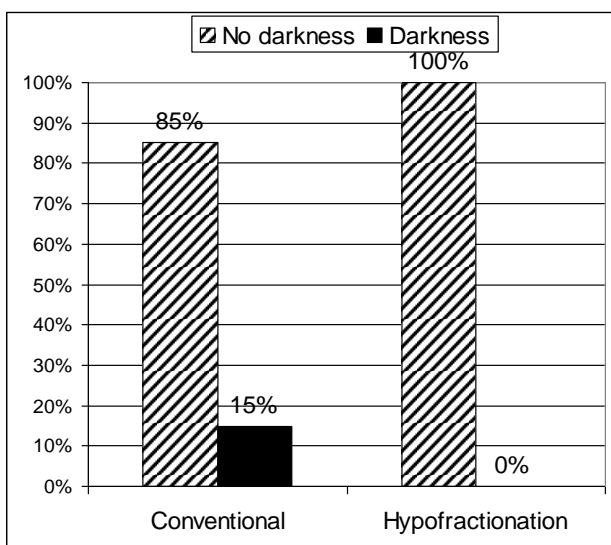
**Table 3: Multivariate analysis for factors associated with lymphedema**

	OR	95% CI	p value
<b>Treatment arm</b>			
Hypofractionated	0.347	0.102 - 1.181	0.09
Conventional	Ref		
<b>Surgery</b>			
Breast conservative surgery	1.604	0.492 - 5.23	0.434
Modified radical mastectomy	Ref		
<b>Number of Excised lymph-nodes</b>			
>20	0.470	0.118 - 1.873	0.285
<20	Ref		

OR: Odds ratio, CI: Confidence interval



**Figure 5: The rate of dry desquamation (conventional vs. hypofractionated radiotherapy)**



**Figure 6: The rate of skin darkness (conventional vs. hypofractionated radiotherapy)**

standard of care as recommended by the National Institute for Health and Care Excellence.

There was no significant difference in the DFS between the conventional arm and the hypofractionation arm ( $p = 0.6$ ). This is consistent with the results of a meta-analysis of 4 studies (including START A, B and Canadian trial)<sup>16-18</sup> that included 5261 patients revealing no significant difference in DFS between the two fractionation schedules ( $p = 0.53$ )<sup>9</sup>.

After 2 years from the end of radiotherapy, there was no statistical difference in the excellent / good cosmetic outcome. Whelan et al found no significant difference in the excellent / good cosmetic outcome between the two groups using the same hypofractionation schedule in early breast cancer patients. The rate of excellent / good cosmetic outcome was 71.3% with conventional fractionation and 69.8% with hypofractionation after 10 years<sup>18</sup>. Also, these results were confirmed in 2015, in a meta-analysis including five trials with a total of 1626 patients comparing conventional fractionation with the 2.5-3 Gy per fraction schedules, showing no significant difference between hypofractionation and conventional fractionation radiotherapy as regards the cosmetic outcome<sup>9</sup>.

There was no significant difference in the rate of lymphedema between the two arms of our study. Hypofractionated radiotherapy doesn't seem to increase the rate of arm lymphoedema<sup>19</sup>. In the START trials, the arm lymphedema rate in 458 women who received nodal irradiation did not differ significantly between conventional and hypofractionated radiotherapy<sup>14</sup>.

Pooled meta-analysis of seven trials including 2170 patients proved that hypofractionated radiotherapy is associated with significantly less grade 2-3 acute skin reactions when compared to conventionally-fractionated radiotherapy<sup>9</sup>. In our study; wet desquamation was higher in the conventional arm as compared with the hypofractionated arm, although, non-significant. While, dry desquamation prevalence was significantly lower in the hypofractionated arm by 24.8%. Similarly, skin darkness prevalence was higher in the conventional arm. This confirms the finding of Taher et al that there is no significant difference between hypofractionation and conventional fractionation radiotherapy as regards the incidence and the grade of acute skin reactions<sup>20</sup>.

Approximately half of the patients in each group of our patients underwent modified radical mastectomy. In a recently published randomized phase III Chinese trial on 820 patients, adjuvant post-mastectomy hypofractionated radiotherapy to the chest wall, supraclavicular and infraclavicular regions in node-positive locally advanced breast cancer cases found to be non-inferior to conventionally-fractionated radiotherapy as regard efficacy and safety<sup>21</sup>. In that study, hypofractionation allowed 40% more women to be treated with the same available resources and therefore increased the number of patients who could receive their radiotherapy on time. This may improve the survival in low- and middle-income countries where resources are limited. Comparable to our results, there was no statistical difference in the DFS between the two

fractionation regimens. The 5-year DFS rate was 70% and 74% for the conventional and hypofractionated radiotherapy groups, respectively. Also, as regards the acute and late toxicities especially in the light of using hypofractionated regional lymphatic irradiation; lymphedema prevalence was not significantly different between the two groups and fewer patients in the hypofractionated radiotherapy arm had suffered from grade 3 acute skin reactions ( $p=0.0001$ )<sup>21</sup>.

The results of trials assessing hypofractionated adjuvant radiotherapy in node-positive breast cancer are comparable to those of large randomized trials comparing hypofractionation radiotherapy vs. conventional fractionation in early breast cancer. The two schedules are equally effective as regard the loco-regional control, systemic metastasis, overall survival, excellent/good cosmetic outcome, radiation induced pneumonitis, ischemic heart disease and rib fracture. However, hypofractionation has the advantage of lower costs and better quality of life, making it a preferred alternative for treatment of early breast cancer<sup>9, 14, 16-18</sup>.

### Conclusion

In conclusion, our results suggest that hypofractionated adjuvant radiotherapy in node-positive breast cancer results in similar DFS, cosmetic outcome and arm lymphedema rate when compared to conventional fractionation. In addition, hypofractionation is associated with decreased early skin reactions. To adopt hypofractionation in node-positive breast cancer, longer follow up period is needed and larger number of patients should be studied.

### CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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