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One-week Accelerated Hypo-Fractionation Adjuvant Radiotherapy in High-Risk Breast Cancer Patients

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ABSTRACT

Background: Radiation therapy is an important part of the multimodal management of breast cancer, including early stage, locally progressed, and metastatic cases.

Objectives: this work aims to compare a 2-year locoregional disease control between 1-week and 3-weeks course adjuvant radiotherapy in high-risk breast cancer patients, and to compare disease-free survival (DFS), overall survival, and radiation-related adverse events, both early and late events.

Methods: This study was carried out on 160 female patients 45 years of age or older, who had Oncoplastic Breast Surgery or total mastectomy with adequate axillary clearance and a negative margin, breast carcinomas that is invasive (TXN1-3M0, T0N2-3 M0, T1N2- 3M0, T2N2-3M0, T3N0-3M0, T4N0-3M0). Patients were divided in to two groups: patients were assigned to the 40 Gy over 3 weeks schedule and patients to the 26 Gy over 1 week schedule.

Results: There were significant differences between both groups regarding all postoperative data with P value < 0.05 except post operative pathology. one week radiation in advanced breast cancer patients were efficient in locoregional control and disease-free survival that was comparable with moderate hypofractionation. DFS for all studied population after 24 months were 91.91%. DFS in one week arm were 92.88% but in control arm DFS were 90.85%. There was a statistically significant difference regarding radiation dermatitis P value 0.0001.

Conclusions: One week radiation therapy (26 GY/5 fractions/1 week) can save time, effort, overload in radiotherapy machines, improve our patient compliance with efficient disease control.

Keywords: Prospective study, Adjuvant radiotherapy, Hypo-fractionation, High-risk, Breast cancer.

INTRODUCTION

Cancer ranks as a leading cause of death and it is an important barrier in increasing life expectancy in every country of the world [1]. According to the World Health Organization in 2019, cancer is the first or second leading cause of death before the age of 70 years in 112 of 183 countries [1]. Worldwide, Breast cancer is the most common cancer in women and the 5th leading cause of cancer related deaths that comes after lung cancer, colorectal cancer, liver cancer and gastric cancer [2]. More than half of all breast cancer cases in the world occur in developing countries. Egypt has a high mortality rate from breast cancer, with a rate of 21.3 per 100,000 cases. Breast cancer is diagnosed at an advanced stage in 60 to 70% of cases in Egypt. Median age at diagnosis in Egypt is 48.5 years, which seems to be a decade younger than in Europe and North America [3]. About 49% occurred in the left and right breasts, respectively, with 2% occurring bilateral, 3% of the patients presented with Stage I, 11% with Stage IIA, 14% with Stage IIB, 32% with Stage IIIA, 36% with Stage IIIB, and 4% with distant metastases in Stage IV [4].

Nonmetastatic early invasive stages (I, IIa, IIb) and locally progressed stages (IIIa, IIIb, IIIc) have three types of therapies. When tumours express oestrogen, progesterone or ERBB2 receptors, systemic endocrine, chemotherapy or immunotherapies are used in the preoperative phase [5].

Systemic treatment is initiated prior to local-regional management in neo-adjuvant therapy. It is also known as preoperative chemotherapy or primary systemic therapy. While, previously reserved for patients with inoperable disease, today's breast cancer management includes a neoadjuvant approach for patients with inflammatory breast cancer, locally advanced breast cancer (ABC), metastatic breast cancer (MBC), and some patients with early-stage, operable breast cancer (TNBC, HER2\NEU positive) [6]. Neo-adjuvant chemotherapy has emerged as a powerful treatment modality with individualized prognostic significance based on response to therapy [7].

Radiation therapy is an important part of the multimodal management of breast cancer, including early stage, locally progressed, and metastatic cases. Breast cancer radiation therapy has come a long way in the last 20 years [8]. The role of adjuvant radiotherapy as the standard of care for breast cancer after breast-conserving surgery, the role of partial-breast irradiation and hypo fractionated whole-breast irradiation, and the evolving indications for postmastectomy radiation therapy and extent of nodal coverage [9]. The cornerstone of systemic adjuvant treatment for estrogenic receptor (ER) in positive breast cancer is hormonal therapy. Long-term adherence is required to get the full benefits of this medication. Adjuvant endocrine therapy substantially reduces tumour recurrence and mortality in pre- and post-menopausal women with hormone receptor-positive early breast cancer but is ineffective in women with hormone receptor-negative tumours [10]. Immunotherapy emerged as a new treatment modality for breast cancer in early and advanced stages and its use is approved in combination with chemotherapy for in MBC [11].

The aim of this work was to compare a 2-year locoregional disease control between 1-week and 3-

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week course adjuvant radiotherapy in high-risk patients, and to compare disease-free survival (DFS), overall survival, and radiation-related adverse events.

PATIENTS AND METHODS

This prospective study was carried out on 160 female patients 45 years of age or older, who had Oncoplastic Breast Surgery (OBS) or total mastectomy with adequate axillary clearance and a negative margin, breast carcinomas that is invasive (TXN1-3M0, T0N2-3 M0, T1N2- 3M0, T2N2-3M0, T3N0-3M0, T4N0-3M0) whatever type of tumours biology, and with locally ABC who received neoadjuvant chemotherapy and underwent either OBS or modified radical mastectomy (MRM).

Exclusion criteria: MBC at the time of diagnosis proved clinically or radiologically, postoperative positive margin., carcinomas in situ, mesenchymal breast lesions, locoregional recurrent breast cancer, synchronous bilateral breast cancer, and very early breast cancer (T1-2N0M0, T1N1M0).

Patients were further divided into two groups: 75 patients were assigned to the 40 Gy schedule and 85 patients to the 26 Gy schedule. All patients were subjected to history taking, usual investigations, and clinical examinations.

Interventions: Control Arm: Patients received 40 GY in 15 fractions to the entire breast or chest wall over a three-week period. Patients undergoing OBS (OBS received an additional boost to the tumour site if indicated and will receive sequential dose 12GY\4 fractions or SIB 8 GY 15 fractions. The supraclavicular fossa (SCF) and internal mammary were treated in patients with the node-positive disease or those receiving neoadjuvant chemotherapy. If indicated, the IMLN were irradiated. Experimental Arm: Patients received 26 GY in 5 fractions to the entire breast or chest wall over the course of one week. The volume of the treatment arm was the same as the volume of the control arm. Patients who had oncoplastic resection given a boost (if indicated). If a boost is given, SIB of 6 GY in 5 fractions will be used (or a sequential boost of 12GY\4 fractions) (Table 1).

Radiotherapy details: Within 12 weeks of the date of surgery or the final cycle of scheduled adjuvant chemotherapy therapy, radiotherapy began. All patients were treated in a linear accelerator (ranging from 6 to 15 MV). Radiotherapy preparation was carried out using volumetric planning CT scans using a pre-defined simulation protocol. A predefined simulation technique was used to plan radiotherapy using volumetric planning CT scans. While, our approach enables for Deep Inspiration Breath Hold (DIBH) treatment. The organs at risk were the ipsilateral and contralateral lungs, the heart, and the contralateral breast. All patients undergoing regional nodal radiotherapy had thyroid, and spinal cord defined. Unless IMN coverage was necessary, a field-based 3D planning technique based on pre-specified anatomical landmarks was used.

(Table 1): Dosimetry planning of 3 weeks versus one week protocol of breast cancer radiotherapy

Arm A **40 Gy /15 fx/ 3 weeks**		**Arm B** **26 GY /5 fx/1 week**	
PTV	V90 % (36 Gy) ≤ 90 %.	**PTV**	V90 % (23.4Gray) ≤ 90%.
	V105 % (42 Gy) ≥ 5%		V105 % (27.3Gy) ≥ 5%
	V107% (42.8 Gy) ≥3 %. D98 %≥ 43.2 Gy		V107% (27.82Gy) ≥ 2% D98 %≥ 28.8 Gy
Ipsilateral lung	V16 less than 15 - 20%	**Ipsilateral lung**	V30% (7.8Gy) ≥ 15-30%
	V 8 less than 35%		V15% (4Gy) ≥ 30-35%
	V12 (18%-30%)		V5 % (1.3Gy) ≥ 5-55% V8 (18%-30%)
Contra lateral	V4 ≥ 10 %.	**Contra lateral**	V5 % (1.3Gy) ≥ 5 %.
Heart	Mean (2 GY-2.5 GY).	**Heart**	Mean (1.3Gy -1.6 Gy)
	V10 (3%-5%)		V7 (3%-5%)
	V2 (20%-30%)		V1.2 (20%-30)
Contra lateral breast	D mean≥ 5 Gy.	**Contra lateral breast**	V3 % (0.78Gy) less than 5 %.
SCV	V90 (%36 G) ≤ 90%.	**SCV**	V90 % (23.4 Gy) ≤ 90 %.
Thyroid	D-max Less than 2 % (0.8 Gy)	**Thyroid**	
Spinal cord	D max < 45 Gy.	**Spinal cord**	V23 Gy< 0.35CC orV14.5 Gy <1.2cc.
Brachial plexus	D max <66 Gy (RTOG 0619)	**Brachial plexus**	D-max < 30.5 Gy
Oesophagus	Mean dose < 30 Gy (D-max <50 GY	**Oesophagus**	D max < 30 Gy

Ethical approval

Informed written consent was obtained from the patients or relatives of the patients. The study was done after approval from the Ethical Committee of Sohag University Hospitals. The Helsinki Declaration was followed throughout the course of the investigation.

Statistical analysis

Statistical analysis was done by SPSS V26 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD) and it is compared between the two groups utilizing unpaired Student's t- test.

Qualitative variables were presented as frequency and percentage (%) and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. The Kaplan–Meier survival method with the log rank test was used to assess different categories on survival. Cox-regression was used to calculate hazards ratio in different subgroup. Graphs were produced by using Excel or STATA program. A two tailed P value < 0.05 was considered statistically significant.

RESULTS

There was statistically significant difference regarding mean age, menopausal status, preoperative biology between both groups, and significant difference between both groups regarding NAC, target therapy, adjuvant target therapy, adjuvant hormonal, and internal mammary irradiation (P<0.05).

while, insignificant difference was observed regarding preoperative pathology, grade, clinical T, clinical N, clinical stage, laterality treatment, adjuvant chemotherapy treatment, boost, radiotherapy target Breast with regional radiation treatment, and Chest wall with regional radiation (Table 2).

(Table 2): Comparison between the two radiation groups as regards age, and menopausal status, preoperative data, and treatment (n=160)

		Test arm (n=85)	Control arm (n=75)	P value
Age	**Mean ± SD**	55.88±7.90	52.96±7.49	**0.02***
	≤60 year	61 (71.76%)	62 (82.67%)	0.10
	>60 year	24 (28.24%)	13 (17.33%)	
Menopausal status	**Premenopausal**	18 (21.18%)	30 (40.00%)	**0.01***
	Postmenopausal	67 (78.82%)	45 (60.00%)	
Preoperative data				
Pathology	**IDC ILC**	81 (95.29%)	72 (96.00%)	0.57
	IDC\ILC	2 (2.35%)	2 (2.67%)	
	Medullary Papillary	1 (1.18%)	0	
	IDC ILC	1 (1.18%)	0	
	IDC\ILC	0	1 (1.33%)	
Grade	**GII**	74 (87.06%)	70 (93.33%)	0.19
	GIII	11 (12.94%)	5 (6.67%)	
Biology	**Luminal A**	14 (16.47%)	24 (32.00%)	**0.048***
	Luminal B	21 (24.71%)	23 (30.67%)	
	Luminal B Her2/ neu over expression	14 (16.47%)	9 (12.00%)	
	HER2 over expression	17 (20.00%)	6 (8.00%)	
	Triple negative	19 (22.35%)	13 (17.33%)	
Clinical T	**T0**	0	2 (2.67%)	0.30
	T1	3 (3.53%)	2 (2.67%)	
	T2	15 (17.65%)	18 (24.00%)	
	T3	32 (37.65%)	23 (30.67%)	
	T4	35 (41.18%)	28 (37.33%)	
	Tx	0	2 (2.67%)	
Clinical N	**N0**	3 (3.23%)	2 (2.67%)	0.054
	N1	41 (48.24%)	23 (30.67%)	
	N2	39 (45.88%)	43 (57.33%)	
	N3	2 (2.35%)	7 (9.33%)	
Clinical stage	**Stage IIB**	2 (2.35%)	0	0.18
	Stage IIIA	47 (55.2%)	41 (54.67%)	
	Stage IIIB	34 (40.00%)	27 (36.00%)	
	Stage IIIC	2 (2.35%)	7 (9.33%)	
Treatment				
NAC	**Single agent**	29 (34.12%)	10 (13.33%)	**0.01***
	Two agents	34 (40.00%)	41 (54.67%)	
Target therapy	**Single agent**	5 (5.88%)	0	**0.02***
	Two agents	19 (22.35%)	9 (12.00%)	
Laterality	**Left**	48 (56.47%)	42 (56.00%)	0.95
	Right	37 (43.53%)	33 (44.00%)	
Adjuvant chemotherapy	**Taxol**	9 (10.59%)	2 (2.67%)	0.12
	Xeloda	4 (4.71%)	6 (8.00%)	
	Two agents	18 (21.18%)	23 (30.67%)	
Adjuvant target therapy	**Herceptin**	7 (8.24%)	0	**0.02***
	TDM	2 (2.35%)	1 (1.33%)	
	Two agents	23 (27.06%)	13 (17.33%)	
Adjuvant hormonal		50 (58.82%)	57 (76.00%)	**0.02***
Radiotherapy		85 (100%)	75 (100%)	-
BOOST	**Omit**	17 (20.00%)	9 (12.00%)	0.45
	Sequential	8 (9.41%)	10 (13.33%)	
	SIB	9 (10.59%)	11 (14.67%)	
Radiotherapy target Breast with regional radiation		34 (40.00%)	30 (40.00%)	1.00
Chest wall with regional radiation		51 (60.00%)	45 (60.00%)	
Internal mammary irradiation		19 (22.35%)	34 (45.33%)	**0.002***

Data are presented as mean ±SD or number (%). IDC: Invasive duct carcinoma, ILC: Invasive lobular carcinoma, HER2: human epidermal growth factor receptor 2, NAC: Neoadjuvant chemotherapy, PCR: Pathological complete response. *: significant as P value <0.05.

(Table 3) shows that there were significant differences between both groups regarding all postoperative data (Grade, biology, clinical T, clinical N, and clinical stage) with P value < 0.05. Post-operative pathology shows insignificant difference regarding site of recurrence, death and all side effects of treatment except radiation dermatitis was significantly less in test arm with P value 0.0001.

(Table 3): Comparison between the two radiation groups as regards postoperative data, and side effects (n=160)

		Test arm (n=85)	Control arm (n=75)	P value
Postoperative				
Pathology	**PCR**	17 (20.00%)	6 (8.00%)	0.16
	IDC	65 (76.47%)	66 (88.00%)	
	ILC	1 (1.18%)	2 (2.67%)	
	IDC\ILC	1 (1.18%)	0	
	Medullary	1 (1.18%)	0	
	Papillary	0	1 (1.33%)	
Grade	**PCR**	17 (20.00%)	6 (8.00%)	**0.03***
	GII	62 (72.94%)	67 (89.33%)	
	GIII	6 (7.06%)	2 (2.67%)	
Biology	**PCR**	17 (20.00%)	6 (8.00%)	**0.045***
	Luminal A	13 (15.29%)	24 (32.00%)	
	Luminal B	21 (24.71%)	23 (30.67%)	
	Luminal B Her2/ neu over expression	11 (12.94%)	6 (8.00%)	
	HER2 over expression	10 (11.76%)	5 (6.67%)	
	Triple negative	13 (15.29%)	11 (14.67%)	
Clinical T	**PCR**	2 (2.35%)	0	**0.02***
	T0	20 (23.53%)	12 (16.00%)	
	T1	22 (25.88%)	8 (10.67%)	
	T2	25 (29.41%)	31 (41.33%)	
	T3	13 (15.29%)	15 (20.00%)	
	T4	3 (3.53%)	9 (12.00%)	
Clinical N	**PCR**	2 (2.35%)	0	**0.02***
	N0	43 (50.59%)	25 (33.33%)	
	N1	24 (28.24%)	16 (21.33%)	
	N2	14 (16.47%)	22 (29.33%)	
	N3	2 (2.35%)	12 (16.00%)	
Clinical stage	**Stage 0**	20 (23.53%)	8 (10.67%)	**0.003***
	Stage IA	12 (14.12%)	4 (5.33%)	
	Stage IIA	18 (21.18%)	15 (20.00%)	
	Stage IIB	7 (8.24%)	8 (10.67%)	
	Stage IIIA	23 (27.06%)	19 (25.33%)	
	Stage IIIB	3 (3.53%)	9 (12.00%)	
	Stage IIIC	2 (2.35%)	12 (16.00%)	
Side effect				
Radiation dermatitis	**G0**	24 (28.24%)	5 (6.67%)	**0.0001***
	G1	58 (68.24%)	61 (81.33%)	
	G2	2 (2.35%)	8 (10.67%)	
	G3	1 (1.18%)	1 (1.33%)	
Dysphagia	**G0**	83 (97.65%)	71 (94.67%)	0.52
	G1	1 (1.18%)	3 (4.00%)	
	G2	1 (1.18%)	1 (1.33%)	
Laryngitis	**G0**	81 (95.29%)	68 (90.67%)	0.52
	G1	0	1 (1.33%)	
	G2	4 (4.71%)	6 (8.00%)	
Breast distortion		5 (5.88%)	3 (4.00%)	0.72
Breast shrinkage		6 (7.06%)	4 (5.33%)	0.75
Breast induration		2 (2.35%)	0	0.50
Telangiectasia		2 (2.35%)	1 (1.33%)	1.00
Cardiac toxicity	**G0**	83 (97.65%)	74 (98.67%)	1.00
	G1	2 (2.35%)	1 (1.33%)	
Pulmonary	**G0**	81 (95.29%)	71 (94.67%)	0.55

		Test arm (n=85)	Control arm (n=75)	P value
toxicity	**G1**	3 (3.53%)	4 (5.33%)	
	G2	1 (1.18%)	0	
Site of recurrence				
Locoregional recurrence		2 (2.35%)	2 (2.67%)	1.00
Distant recurrence		4 (4.71%)	3 (4.00%)	1.00
Site of distant recurrence	**Skin nodules**	2 (33.33%)	2 (40.00%)	0.42
	Bone metastasis	1 (16.67%)	1 (20.00%)	
	Lung metastasis	2 (33.33%)	0	
	Liver metastasis	1 (16.67%)	0	
	Brain metastasis	0	1 (20.00%)	
	Liver and bone metastasis	0	1 (20.00%)	
Death		1 (1.18%)	0	1.00

Data are presented as frequency (%). IDC: Invasive duct carcinoma, ILC: Invasive lobular carcinoma, HER2: human epidermal growth factor receptor 2, NAC: Neoadjuvant chemotherapy, PCR: Pathological complete response. *: significant as P value <0.05.

(Table 4) presents survival outcomes (overall, disease-free, locoregional recurrence-free, and distant recurrence-free) over time among different groups, including one-week, three-week, MRM, and OBS. Across all outcomes, survival rate was consistently high, ranging from 92.26% to 100%, with the OBS group achieving perfect locoregional recurrence-free survival (100%). Statistical analysis shows no significant differences between groups for any outcome, (P = 0.22 for overall survival, P = 0.40 for disease-free survival, P = 0.10 for locoregional recurrence-free survival, and P = 0.84 for distant recurrence-free survival). These findings suggest that the interventions, including timing and surgical techniques, were not significantly impact survival or recurrence-free outcomes in the studied population (Table 4 and figures 1 & 2).

(Table 4): Overall, disease, locoregional recurrence, and distant recurrence free survival function over time in studied population

	12 months	At the end (rate %)	P value
One week (n=85)	98.82%	98.82%)	0.35
Three weeks (n=75)	100%	(100%)	
MRM (n=96)	100%	(100%)	0.22
OBS (n=64)	98.44%	(99.44%)	
Disease free survival function			
One week (n=85)	95.27%	(92.88%)	0.89
Three weeks (n=75)	97.33%	(90.85%)	
MRM (n=96)	95.83%	(91.42%)	0.40
OBS (n=64)	96.88 %	(92.26%)	
Locoregional recurrence free survival			
One week (n=85)	98.81%	(97.62%)	0.90
Three weeks (n=75)	98.67%	(97.02%)	
MRM (n=96)	97.92%	(95.60%)	0.10
OBS (n=64)	100%	100%	
Distant recurrence free			
One week (n=85)	96.46%	(95.27%)	0.81
Three weeks (n=75)	98.67%	(93.86%)	
MRM (n=96)	97.92%	(95.83%)	0.84
OBS (n=64)	96.88%	(92.26%)	

Data are presented as %. OBS: Oncoplastic breast surgery, MRM: modified radical mastectomy

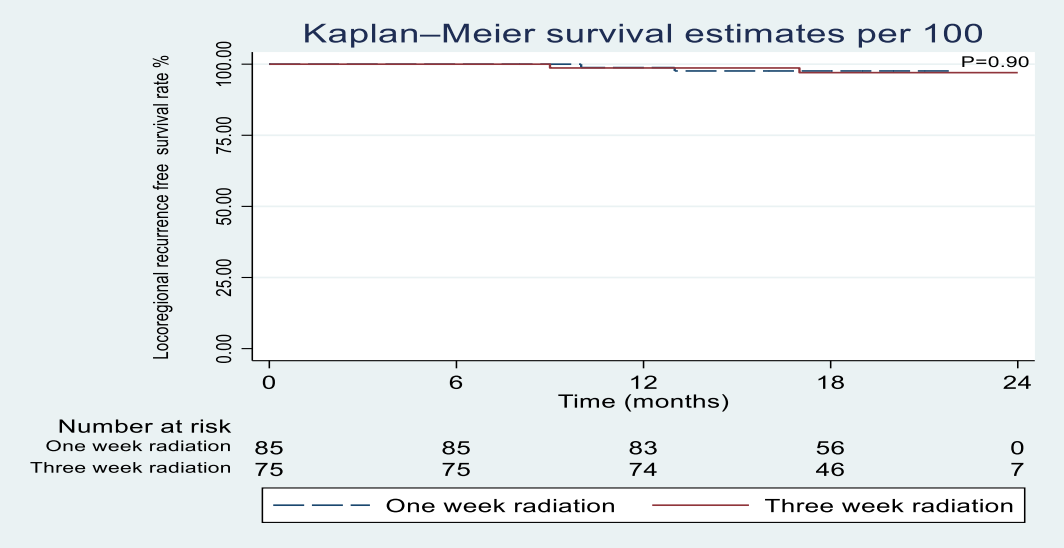

Figure 1: Locoregional recurrence free survival rate in all patients

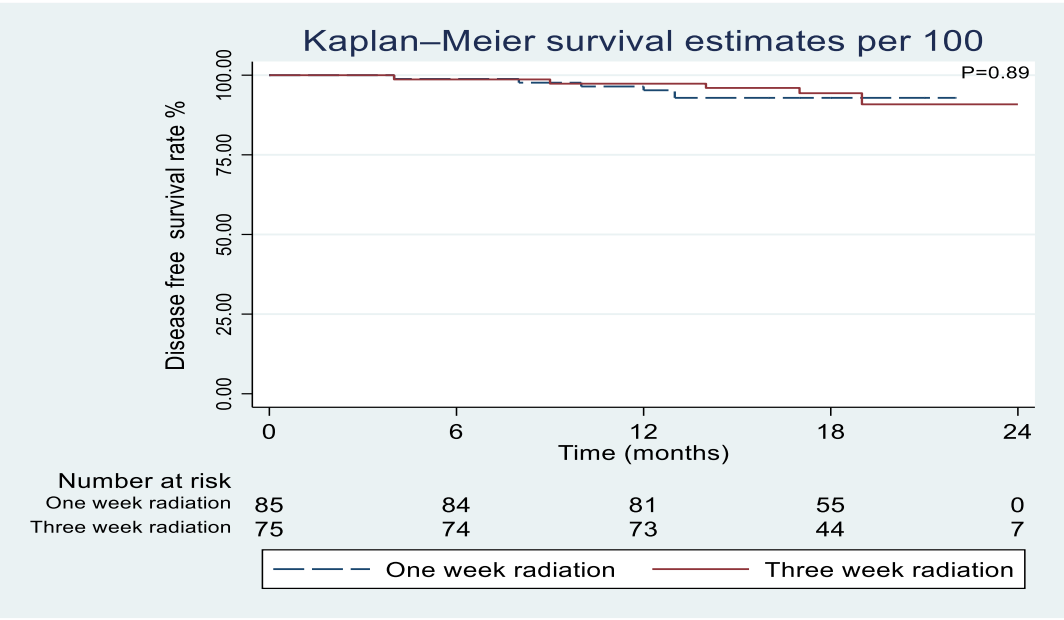

Figure 2: Disease free survival rate in all patients by (groups).

DISCUSSION

In our study, as regard radiation dermatitis in test arm, there were 24 (28.24%) cases were G0, 58 (68.24%) cases were G1, 2 (2.35%) cases were G2 and1 (1.18%) case was G3, but in control arm, there were 5 (6.67%) cases were G0, 61 (81.33%) cases were G1, 8 (10.67%) cases were G2 and1 (1.33%) case were G3 (p-value 0.0001), So much less radiation toxicity in one week arm radiotherapy.

Patients aged 65 years were treated in 5 fractions with a total dose of 28.5 Gy/5 fractions to the breast or thoracic wall and, if indicated, 27 Gy/5.4 Gy to the lymph node regions and 32.5 Gy/6.5 Gy to 34.5 Gy/6.9 Gy to the tumour bed (52.6% of grade 1 dermatitis for whole breast irradiation and chest wall irradiation combined), shorter delivery time may have impacted toxicity. However, toxicity scales differed, with possibly an upward shift of faint erythema toward grade 1 with the CTCAE toxicity scale [12]. While, in our study, late toxicity appeared through 24 months follow up breast distortion that occurs only in 8 (5.00%) cases, breast shrinkage appeared in 10 (6.23%) cases, breast induration appeared in 2 (1.25%) cases and telangiectasia occurred in 3 (1.88%) cases.

In test arm, breast distortion occurs only in 5 (5.88%) cases, breast shrinkage appears in 6 (7.06%) cases, breast induration appeared in 2 (2.35%) cases and telangiectasia occurred in 2 (2.35%) cases. In control arm, breast distortion appeared only in 3 (4.00%) cases, breast shrinkage appeared in 4 (5.33%) cases, breast induration appeared in 0 (0%) case and telangiectasia occurred in 1 (1.33%) case, which is statistically insignificant between two arms. The START-B study found that induration rates were 11.8% in the 50 Gy group and 9.0% (95% confidence interval 7.2 e 11.1%) in the 40 Gy group [13].

In our study as regard acute dysphagia, 154 (96.25%) cases were G0, 4 (2.50%) cases were G1, 2

(1.25%) cases were G2 and no G3. But acute laryngitis occurs in 10 (6.25%) cases were G3, 1 (0.63%) were G1 and 149 (93.13%) cases were G0. In test arm, 83 (97.65%) cases were G0 acute dysphagia, 1 (1.18%) case were G1 and 1 (1.18%) case were G2. In control arm, 71 (94.67%) cases were G0, 3 (4.00%) cases were G1, and 1 (1.18%) case was G2, which were statistically insignificant.

Test arm acute laryngitis occurred in 81 (95.29%) cases were G0, 0 (0%) cases were G1 and 4 (4.71%) cases were G2. But, control arm, 68 (90.67%) cases were G0, 1 (1.33%) case was G1, and 6 (8.00%) cases were G2, which were statistically insignificant with slight increase in laryngitis G1 and G2 in control arm.

Despite the significant proportion of patients undergoing regional nodal irradiation in the HYPORT Adjuvant study (70% in each arm), no patients had grade 2 or higher dysphagia [14].

Our study, Cardiac toxicity appears only in 3 (1.88%) cases with G1 (decreased EF from 13-15%, which was reversible and did not disrupt continuation of systemic therapy). Cardiac toxicity appears only in 2 (2.35%) cases with G1 in test arm but it occurred in 1 (1.33%) case in control arm, which were statistically insignificant.

The heart often requires a very long follow-up to assess the full risk, although there is no specific reason to expect an increased cardiac sensitivity to hypofractionation. there is no safe dose to the heart and therefore the effort is to reduce or eliminate cardiac dose. At this early stage, after imaging and further investigation, excluding cases confirmed not to be radiotherapy-related. Left-sided breast cancer radiotherapy, there were six cases of ischemic heart disease in the 40 Gy group and three cases in the 26 Gy group [15].

Pulmonary toxicity occurred in 7 (4.38%) cases in form of G1pulmonary fibrosis and 1 (0.63%) case was G2. Pulmonary toxicity in test arm occurred in 3 (3.53%) cases in form of G1pulmonary fibrosis and 1 (1.18%) case was G2, but in control arm, it occurred in 4 (5.33%) cases in form of G1pulmonary fibrosis and 0 (0%) case was G2, which were statistically insignificant. Clinically significant radiation pneumonitis develops in <1% of patients, which received local RT with a mean central long distance <2 cm or a mean ipsilateral V20 of <7%. However, if loco-regional RT is administered with template techniques and without 3-D planning aimed at reducing dose to lung. Short-term pulmonary toxicity of grade 2 was detected in roughly 10% of patients and predominantly in cases where the ipsilateral V20 is ≥30% [16].

Locoregional recurrence occurred in 4 (2.50%) cases in form of skin nodules no regional lymph node recurrence. Locoregional recurrence occurred in 2 (2.35%) cases in form of skin nodules no regional lymph node recurrence in test arm. In control arm, it occurred also in 2 (2.67%) cases in form of skin nodules which were statistically insignificant. Distant recurrence occurred in 7 (4.38%) cases, bone metastasis occurred in 2 (18.18%) cases, pulmonary metastasis occurred also in 2 (18.18%) cases, liver metastasis occurred in 1 (9.09%) case, brain metastasis occurred in 1 (9.09%) case and both liver and bone metastasis occurred in 1 (9.09%) case. One case died after 8 months due to cerebrovascular accidents.

In test arm, distant recurrence occurred in 4 (4.71%) cases and meanwhile bone metastasis occurred in 1 (16.67%) case, pulmonary metastasis occurred also in 2 (33.33%) cases and liver metastasis occurred in 1 (16.67%) case. but, control arm, it occurred in 3 (4.00%) cases, bone metastasis occurred in 1 (20.00%) case, brain metastasis occurred in 1 (20.00%) case and both liver and bone metastasis occurred in 1 (20.00%) case. one case died after 8 months due to cerebrovascular accidents in test arm which is statistically insignificant.

In advanced cases, all 103 patients in the group were assessed for locoregional recurrence. Our findings imply that NAC followed by surgery and RT for breast cancer is linked with low rates of LRR (about 10% at 5 years) and relatively good OS (more than 75% at 5 years). Distant recurrence (15 patients) was twice as common as LRR (9.7%,7 patients), which was consistent with previously published outcomes of RT after NAC and surgery [17].

The Ontario Clinical Oncology Group reported IBTR rates of 3.2%/6.7% and 2.8%/6.2% after 50 Gy in 25 fractions versus 42.5 Gy in 16 fractions respectively, with an absolute difference of 0.4% (95% confidence interval e1.5e2.4%) and 0.5% (95% confidence interval e2.5e3.5%) at 5- and 10-year time points [18].

According to retrospective studies, adjuvant RT helps individuals treated with NAC for ABC. comparing 542 patients who underwent NAC, surgery, and adjuvant radiation therapy against 134 patients who did not receive radiation therapy. The RT cohort had more advanced disease (73% were pre-treatment stage III and 10% were stage IV) than the control group (46% were stage III and 4% were stage IV). LRR was still significantly lower in RT patients (11% versus 22%; p = 0.0001), and RT increased specific survival in patients with stage IIIB or IV illness, clinical T4 tumours, and four or more positive lymph nodes [19].

Overall survival for all studied population after 24 months were 99.38%. Overall survival in one week arm patients were 98.82% but in control arm overall survival were 100%, which were statistically insignificant (p-value =0.35). Disease free survival for all studied population after 24 months were 91.91%. Disease free survival for test arm were 92.88%. In control arm disease free survival were 90.85%, which were statistically insignificant (p-value=0.89).

Disease free survival in patients with MRM were 91.42%. In OBS patients, disease free survival was 92.26% which were statistically insignificant (p-value =0.40).

Locoregional recurrence free survival for all studied population after 24 months were 97.35%.

Locoregional recurrence free survival for test arm were 97.62%, in control arm disease free survival were 97.02%, which were statistically insignificant (p-value =0.90). Distant recurrence free survival for all studied population after 24 months were 94.58%. Distant recurrence free survival for test arm were 95.27%. In control arm distant recurrence free survival were 93.86%, which were statistically insignificant (p-value =0.81).

Another study, the clinical and pathologic predictors of LRR after neoadjuvant chemotherapy, mastectomy, and radiation therapy. Although the overall rate of LRR was low (11% after 10 years), we were able to detect numerous risk variables for LRR, including skin/nipple involvement, SCV nodal involvement, no tamoxifen treatment, extracapsular extension, and ER-negative illness. According to recent research, achieving locoregional control is a major predictor of survival [20].

Limitations: Detecting acute toxicities one or two weeks after radiation is difficult in our setting because patients frequently travel long distances. Furthermore, the lack of planned assessments in the first six weeks after radiation due to the second wave COVID-19 pandemic. The acute toxicity of hypo-fractionated radiation is anticipated to peak within the first few weeks following treatment completion.

CONCLUSION

Ultra-hypo fractioned radiotherapy (26 Gy over five fractions in one week) approved its safety and efficacy in comparison with moderate hypofractionation (40 Gy /15 fractions over three weeks) in advanced high risk breast cancer patients with comparable acute and late toxicities and less radiation dermatitis through 24 month follow up. One week radiation in advanced breast cancer patients were efficient in locoregional control and disease-free survival that were comparable with standard moderate hypofractionation. It is suitable for all patient characteristics with better results for patients with age more than 60 years, clinically N2, Her2/neu overexpression, MRM and patients who receiving adjuvant hormonal therapy.

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