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Acute Dermatological Toxicity of Hypofractionated Radiotherapy after Breast Conservative Surgery in Early Breast Cancer Patients

Omnia Yousef Thabet*, Eman Ismail Ibrahim, Alaa Abd El Hamid Fayed, Mona Salah Fattahalla
Department of Clinical Oncology& Nuclear Medicine, Faculty of Medicine, Zagazig University, Egypt
***Corresponding author:** Omnia Yousef Thabet, **Mobile:** (+20) 01020866805, **E-Mail:** oncoomnia2019@gmail.com

ABSTRACT

Background: Breast cancer patients treated with chemotherapy and whole breast hypofractionated radiation may experience acute and delayed cutaneous damage depending on a number of factors.
Objective: Evaluation of acute skin toxicity of hypofractionated radiotherapy (HF Rth) in early breast cancer patients.
Subjects and methods: We included 300 patients in a retrospective study at Clinical Oncology & Nuclear Medicine Department, Zagazig University Hospitals. Our patients received radiotherapy 40 Gray /15 fractions (40Gy/15Fr) in 3weeks, 5 days a week by use of opposed tangential fields to the whole Breast +/- regional lymph nodes followed by Boost of 10Gy/5Fr given to the tumor bed. Tumor bed was delineated using preoperative clinical data, cavity seroma or scar. Acute skin toxicity was assessed in all patients.
Results: About 27% of patients (81 patients) had G0 acute skin toxicity 48.7% had G1 (146 patients), 13.3% (40 patients) had G2 and only 11% had G3. The results demonstrate a strong association between breast and boost volume, body mass index, bolus use, and acute skin toxicity. No significant correlation was found in patients between age, diabetes mellitus, hypertension and acute toxicity. Moreover, adjuvant chemotherapy is not linked to acute skin toxicity.
Conclusion: Hypofractionated whole breast irradiation (HF-WBI) is feasible as well as safe, because of the low rate of moderate-high scores toxicity. Obesity and increase breast size makes acute skin toxicity more pronounced.
Keywords: Hypofractionated Radiotherapy, Breast Conservative Surgery, Breast cancer.

INTRODUCTION

Cancer of the breast is the most frequent malignancy in women, accounts for 29% of all malignancies in women. After lung cancer, breast cancer is the leading cause of cancer death among women [(1)].

According to the statistics of Egypt's National Population-Based Registry Program from 2008-2011, breast cancer is the most common malignancy among Egyptian women. Adjuvant systemic chemotherapy and radiation therapy have drastically reduced the death rate from breast cancer because of their documented benefit in local management of cancer (radiotherapy) and prevention of distant metastases (chemotherapy) [(2)].

Standard loco-regional treatment for early-stage breast cancer nowadays typically consists of breast-conserving surgery (BCS) and radiation therapy. Several prospective and randomised investigations and a large number of clinical trials have concluded that it is a safe and preferred therapeutic option in early breast cancers, with similar overall survival and survival rates to those seen in patients treated with mastectomy [(3)]. In addition, the cosmetic results from BCS are superior to those of more invasive procedures [(4)]. For effective local disease control, radiation must be administered after breast-conserving surgery [(5)].

Whole-brain radion therapy (WBRT) alone decreases the risk of death from breast cancer by 4% over 15 years and the risk of any recurrence (both local and distant) by 15% over 10 years.

Most patients with unfavorable risk factors for local control, such as age less than 50 years, grade 3 tumors, presence of lymphovascular invasion, hormone receptor negativity, or extensive intraductal component and non-radical tumor excision (focally—otherwise further surgery should be advocated), will benefit from a radiation boost that provides an additional 50% (RR)? reduction [(6)].

Conventional radiotherapy given in 6-7 weeks consisting of 45–50Gy in 25 fractions of 1.8 or 2Gy/day, 5 days a week then boost 10-16Gy over 5-8 days. Many randomized trials have confirmed that hypo-fractioned whole breast irradiation 3-4 weeks 40 GY in 15 fractions of 2.67 GY/ day is equivalent to more conventional whole-breast irradiation with respect to local recurrence, toxicity and cosmetic outcome [(7)].

The majority of patients undergoing radiation therapy for early-stage breast cancer will develop acute skin damage. Within 1–4 weeks of starting treatment, they may experience erythema, dry or wet desquamation, and in rare situations, ulceration. Women may experience skin toxicity along after treatment has ended. The majority of breast cancer patients receiving adjuvant radiotherapy (RT) have RT-induced skin toxicity, which can result in temporary or permanent treatment interruption. Swelling, redness, itching, and discomfort are all symptoms of a severe skin reaction, as it is the risk of localized or even systemic infection and lasting scarring. Improvements in radiation procedures, such as boosting dose conformity and dosage uniformity within the irradiated area, may help lower the rate of RT-related toxicity [(7)].

This study aim was evaluation of acute skin toxicity of adjuvant hypofractionated radiotherapy in management of early breast cancer.

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SUBJECTS AND METHODS

We included 300 patients in a retrospective study at Clinical Oncology & Nuclear Medicine Department, Zagazig University Hospitals. Our patients received radiotherapy (2018 -2021) 40Gy/15Fr in 3weeks, 5 days a week by use of opposed tangential fields to the whole Breast +/- regional lymph nodes followed by Boost of 10Gy/5Fr given to the tumor bed. Clinical information obtained before surgery, cavity seroma, or scarring were used to define the tumor bed.

Inclusion criteria:

Histologically confirmed invasive duct carcinoma early breast carcinoma (Stages I-IIB).

- Underwent breast conservative surgery.
- Margin of loss (no tumor on ink).
- No previous radiotherapy.
- Chemotherapy and hormone therapy was allowed.

Exclusion criteria:

- If the patient has received previous RT for the affected breast, or if they have a history of contralateral or synchronous breast cancer
- Synchronous second primary tumor.
- Distant metastases.
- Pregnancy.
- Comorbid conditions: Paget's disease, collagen vascular disease, life expectancy <2 years secondary to comorbidities.

Methods:

All patients in the sample with early breast cancer who underwent breast-conserving surgery and HF Rth between 2018 and 2021 were evaluated for acute skin toxicity. From Patient Follow-Up Toxicity Sheets, where weekly exams were conducted during radiotherapy treatment.

Personal & medical history, pathology data, and treatment details were recorded for all patients in the study (chemotherapy & radiotherapy).

Radiotherapy:

Dose of radiotherapy 40Gy/15Fr in 3weeks, 5 days a week by use of opposed tangential fields to the whole breast +/- regional lymph nodes followed by boost of 10Gy/5Fr given to the tumor bed.

Treatment plan of radiotherapy:

All patients were immobilized with a breast board before undergoing CT scans, which were taken at 5 mm intervals starting at the top of the thyroid notch and ending 5 cm below the contralateral inframammary fold. The CT scan data is subsequently sent to the treatment planning software. Using radiation therapy oncology group (RTOG) guidelines, we carefully outlined the gross tumour volume (GTV) and any nearby critical structures, known as organs at risk (OARs) [8].

Plans for the target volumes informed the creation of tangential fields. A dose-volume histogram was created to aid in planning optimization, and better dose homogeneity was achieved, with dosage in the target volume falling within the range of -5% to +7% as per ICRU-50 guidelines. A total of 40 Gy was delivered in 15 fractions over the course of 5 weeks to the breast, with an additional 10 Gy delivered in 5 fractions to the tumor bed (figures 1-4).

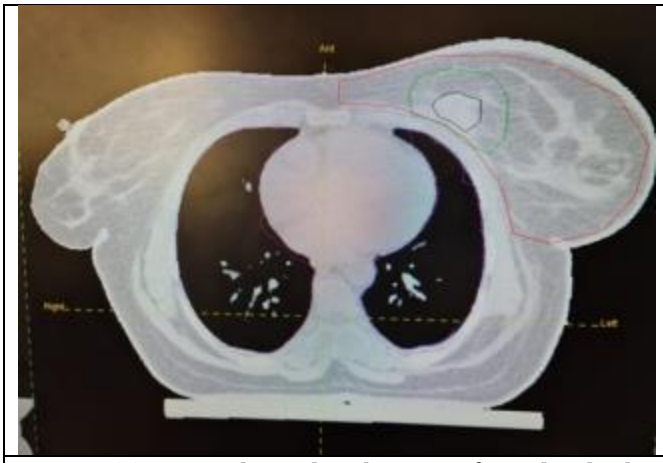

Figure (1): Case planned with 3D conformal radiotherapy (Axial view)

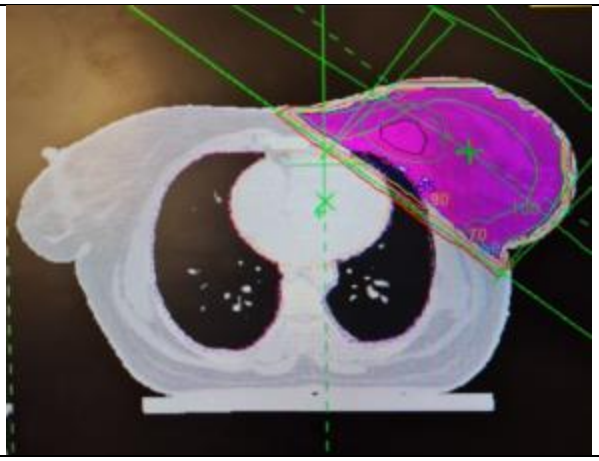

Figure (2): Illustrating dose distribution of a case

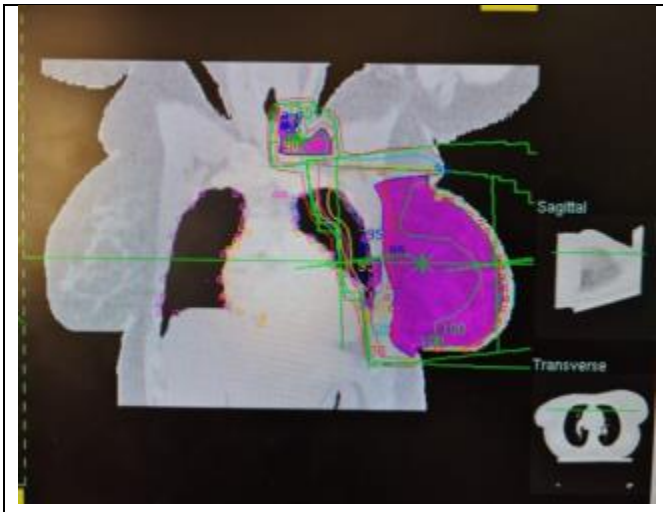

Figure (3): Beam eye view of case planned with three-dimensional conformal radiotherapy (3DCRT).

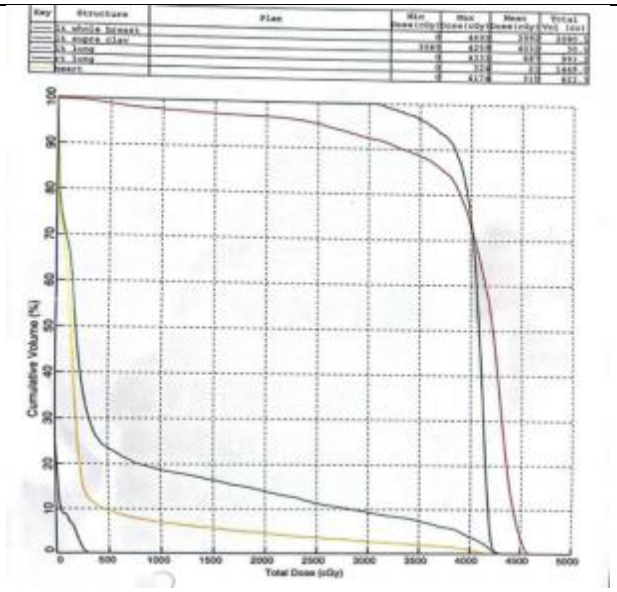

Figure (4): Dose-volume histogram (DVH) of Case planned with 3DCR.

Treatment evaluation:

Each patient's level of toxicity and tolerance to radiotherapy was recorded weekly, at the conclusion of therapy, and at 3 and 6 month intervals as per the breast cancer follow-up protocol.

The RTOG guidlines evaluated cosmetic outcomes in breast surgery [(9)], and Harvard criteria [(10)] respectively. Before beginning radiation therapy, after each week of treatment, after radiation therapy was completed, and at 3 and 6 months, the patient's cosmetic appearance was evaluated. Both the patient (subjective) and the doctor (objective) evaluated the results by contrasting the treated breast with the unaffected side. There was a meticulous charting of breast characteristics such as size, shape, texture, and scar.

Ethical approval:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee (IRB Approval No.: #8051/14-9-2021). After explaining our research objectives, written informed consent was obtained from all study participants. This study was conducted in compliance with the code of ethics of the world medical association (Declaration of Helsinki) for human subjects.

Statistical analysis

IBM SPSS was used, namely version 22.0. The range of values, from minimum to maximum, as well as the central and quartile values, were employed to describe numerical information. The acquired results were deemed statistically significant at the 5% level. This study made use of a Chi-square test.

RESULTS

Clinico pathological features in patients in our study : (Table 1 & 2)

The age ranged between 31 and 74 years and the median age of patients was 52 years. 78% of patients (234 patients) were obese, 11.7% (35 patients) are over weight and only 9% (27 patients) are average weight, 36% of patients (108 patients) were diabetic and 28.3 % (85 patients) were hypertensive, 62% (186) patients had right breast cancer while 38% (114) patients had left sided cancer. 57.7% (173 patients) of breast cancer lesions detected were in upper outer quadrant. The majority of patients 233 patients (77.7%) were invasive duct carcinoma (IDC) and 67 patients (22.3%) were invasive lobular carcinoma (ILC).

Grade I tumours were 9.7 % (29 patients), Grade II tumors were the predominant representing 66.7% (200 patients) and Grade III were 23.7% (71 patients). The number of patients had T1 tumor was 170 patients (56.7%),T2 were 97 patients (32.3%) and the remaining 33 patients (11%) had T3, 57.7% of patients (173 patients) had stage II breast cancer while the remaining 42.3% (127 patients) had stage I .

(ER) Hormonal positive patients in our study represented 54.7% (164 patients) and remaining 45.3 % (136 patients) were ER negative .PR hormonal positive patients were 123 patients (41%) while the remaining 59% (177 patients) were PR negative. Lymph node positive patients were 93 patients (31%), while Lymph node negative patients were 207 patients (69%).

Table (1): Breast cancer patients' basic characters (N=300).

Basic characteristics		All studied patients (N=300)	
		No.	%
Age (years)	Mean±SD	51.28	±11.85
	Median (Range)	52	(31 – 74)
BMI	Underweight	4	1.30%
	Average weight	27	9%
	Overweight	35	11.70%
	Obese	234	78%
Hypertension	Absent	215	71.70%
	Present	85	28.30%
Diabetes	Absent	192	64%
	Present	108	36%
Laterality	Right	186	62%
	Left	114	38%
Site of tumor	UOQ	173	57.70%
	UIQ	44	14.70%
	LOQ	26	8.70%
	LIQ	55	18.30%
	Central	2	0.70%

Table (2): Pathology and IHC staining of the studied breast cancer cases (N=300).

Pathological findings and IHC staining		All studied patients (N=300)	
		No.	%
Pathology	IDC NOS	233	77.7%
	ILC	67	22.3%
Grade	Grade I	29	9.7%
	Grade II	200	66.7%
	Grade III	71	23.7%
LVI	Absent	201	67%
	Present	99	33%
EIC	Absent	229	76.3%
	Present	71	23.7%
pT	pT1	170	56.7%
	pT2	97	32.3%
	pT3	33	11%
pN	pN0	207	69%
	pN1	93	31%
Pathological AJCC stage	Stage I	127	42.3%
	Stage IA	127	42.3%
	Stage IB	0	0%
	Stage II	173	57.7%
	Stage IIA	93	31%
	Stage IIB	80	26.7%
ER	Negative	136	45.3%
	Positive	164	54.7%
PR	Negative	177	59%
	Positive	123	41%

The majority of patients 80.7% (242 patients) received chemotherapy, 43.7% of them was on AC-Taxol regimen, while 19.3 % (58 patients) didn't receive chemotherapy **(Table 3).**

Table (3): Adjuvant chemotherapy among the studied breast cancer cases (N=300).

Adjuvant chemotherapy	All studied patients (N=300)	
	No.	%
Chemotherapy		
No	58	19.3%
Yes	242	80.7%
Regimen		
No	58	19.3%
CAF	21	7%
AC-Taxol	131	43.7%
AC-Docetaxel	39	13%
EC-Taxol	35	11.7%
EC-Docetaxel	16	5.3%

All patients in this study received 40 Gy / 15 Fr, 90.3% of them (271 patients) were treated by energy 15 MV while 5% (15 patients) were treated by Cobalt -60 machine. All patients received boost 10Gy/5 Fr. Most of them, 85.3% (256 patients) received boost dose by electron. The mean breast volume among the studied patients was 1433.47 cc, ranged between (125.6 and 3001.1 cc) while the mean boost volume was 110.09 cc (range between 15.9 and 199.5cc), bolus was used in treatment of 9.7% (29 patients). 33.3 % of patients (200 patients) had LNs irradiation **(Table 4).**

Table (4): Adjuvant radiotherapy among the studied breast cancer cases (N=300).

	Adjuvant Radiotherapy	All studied patients (N=300)	
		No.	%
Energy	Cobalt-60	15	5%
	6MV	6	2%
	15MV	271	90.3%
	6 & 15MV	8	2.7%
Breast volume (cc)	Mean±SD	1433.47	±496.35
	Median	1412.60	
	(Range)	(125.60-3001.10)	
Boost volume (cc)	Mean±SD	110.09	±45.20
	Median	105.60	
	(Range)	(15.90 – 199.50)	
Boost type	Photon	256	85.3%
	Electron	44	14.7%
Bolus use	No	271	90.3%
	Yes	29	9.7%
Lymph node irradiation	No	200	66.7%
	Yes	100	33.3%

Acute skin toxicity was assessed as illustrated in **table (5):** 27% of patients (81 patients) had G0 acute skin toxicity, 48.7% had G1 (146 patients), 13.3% (40 patients) had G2 and only 11% had G3.

Table (5): Radiotherapy induced acute skin toxicity among the studied breast cancer cases (N=300).

Radiotherapy induced skin toxicity	All studied patients (N=300)	
	No.	%
Acute skin toxicity		
G0	81	27%
G1	146	48.7%
G2	40	13.3%
G3	33	11%

A statistical analysis of the data reveals a highly significant link between body mass index and acute skin toxicity (p value 0.001), but there was no correlation between age, diabetes, or hypertension and acute toxicity. Neither the sex of the patients nor the location of the tumour was significantly related to the severity of the initial cutaneous toxicity **(Table 6)**.

Table (6): Relationship between basic characters and acute skin toxicity.

Basic charactertics	N	Acute skin toxicity								Test	p-value (Sig.)
		G0 (N=81)		G1 (N=146)		G2 (N=40)		G3 (N=33)			
		No.	%	No.	%	No.	%	No.	%		
Age (years)											
Mean±SD		51.41	±12.78	51.26	±11.74	50.97	±12.55	51.42	±9.29	0.222[a]	0.974
Median (Range)		51	(31 – 73	53	(31 – 74	50.50	(31 – 70)	55	(31 - 66)		(NS)
BMI											
Underweight	4	4	100%	0	0%	0	0%	0	0%	58.565[c]	<0.001
Average weight	27	25	92.9%	0	0%	2	7.4%	0	0%		(HS)
Overweight	35	25	71.4%	3	8.6%	7	20%	0	0%		
Obese	234	27	11.5%	143	61.1%	31	13.2%	33	14.1%		
Hypertension											
Absent	215	55	25.6%	102	47.4%	33	15.3%	25	11.6%	3.383[b]	0.336
Present	85	26	30.6%	44	51.8%	7	8.2%	8	9.4%		(NS)
Diabetes											
Absent	192	54	28.1%	90	46.9%	29	15.1%	19	9.9%	2.447[b]	0.485
Present	108	27	25%	56	51.9%	11	10.2%	14	13%		(NS)
Laterality											
Right	186	58	31.2%	84	45.2%	25	13.4%	19	10.2%	4.686[b]	0.196
Left	114	23	20.2%	61	54.4%	15	13.2%	14	12.3%		(NS)
Site of tumor											
UOQ	173	44	25.4%	82	47.4%	20	11.6%	27	15.6%	41.720[b]	<0.001
UIQ	44	7	15.9%	27	61.4%	9	20.5%	1	2.3%		(HS)
LOQ	26	2	7.7%	20	76.9%	2	7.7%	2	7.7%		
LIQ	55	28	50.9%	15	27.3%	9	16.4%	3	5.5%		
Central	2	0	0%	2	100%	0	0%	0	0%		

a: Kruskal Wallis H test; b: Chi-square test; c: Chi-square test for trend

Results also revealed that Adjuvant chemotherapy has no significant correlation with acute skin toxicity (p-value=0.24) **(Table 7).**

Table (7): Relationship between adjuvant chemotherapy and acute skin toxicity.

Adjuvant chemotherapy	N	Acute skin toxicity								Test	p-value (Sig.)
		G0 (N=81)		G1 (N=146)		G2 (N=40)		G3 (N=33)			
		No.	%	No.	%	No.	%	No.	%		
Chemotherapy											
No	58	20	34.5%	24	41.4%	10	17.2%	4	6.9%	4.200[b]	0.241
Yes	242	61	25.2%	122	50.4%	30	12.4%	29	12%		(NS)
Regimen											
No	58	20	34.5%	24	41.4%	10	17.2%	4	6.9%	18.485[b]	0.238
CAF	21	4	19%	13	61.9%	3	14.3%	1	4.8%		(NS)
AC-Taxol	131	34	26%	71	54.2%	13	9.9%	13	9.9%		
AC-Docetaxel	39	12	30.8%	14	35.9%	5	12.8%	8	20.5%		
EC-Taxol	35	7	20%	19	54.3%	4	11.4%	5	14.3%		
EC-Docetaxel	16	4	25%	5	31.2%	5	31.2%	2	12.5%		

b: Chi-square test

A strong association was also seen between the usage of boluses and acute skin toxicity (P 0.001), and between breast and boost volume and acute skin toxicity (P 0.01). (P value 0.015). There was no correlation between lymph node (LN) irradiation and skin toxicity (P value 0.061) **(Table 8).**

Table (8): Relationship between adjuvant radiotherapy and acute skin toxicity.

Adjuvant radiotherapy	N	Acute skin toxicity								Test	p-value (Sig.)
		G0 (N=81)		G1 (N=146)		G2 (N=40)		G3 (N=33)			
		No.	%	No.	%	No.	%	No.	%		
Energy											
Cobalt-60	15	4	26.7%	8	53.3%	2	13.3%	1	6.7%	11.932[b]	0.217
6MV	6	4	66.7%	1	16.7%	1	16.7%	0	0%		(NS)
15MV	271	68	25.1%	135	49.8%	36	13.3%	32	11.8%		
6 & 15MV	8	5	62.5%	2	25%	1	12.5%	0	0%		
Breast volume (cc)											
Mean±SD		978.85	±255.94	1441.83	±356.07	1740.61	±319.95	2140.14	±531.56	162.291[a]	<0.001
Median (Range)		985.60 (125.60-1478.90)		1412.60 (690.90-2906.60)		1770.60 (690.90-2906.60)		2232.30 (1122.10-3001.10)			(HS)
Boost volume (cc)											
Mean±SD		74.39	±35.57	111.25	±36.97	139.78	±39.73	156.56	±35.38	101.286[a]	<0.001
Median (Range)		71.60 (15.90-187.60)		105.60 (15.90-198.60)		141.65 (75.50-198.60)		168.90 (72.70-199.50)			(HS)
Boost type											
Photon	256	59	23%	132	51.6%	37	14.5%	28	10.9%	14.758[b]	0.002
Electron	44	22	50%	14	31.8%	3	6.8%	5	11.4%		(S)
Bolus use											
No	271	79	29.2%	127	46.9%	38	14%	27	10%	10.416[b]	0.015
Yes	29	2	6.9%	19	65.5%	2	6.9%	6	20.7%		(S)
LN irradiation											
No	200	63	31.5%	89	44.5%	28	14%	20	10%	7.386[b]	0.061
Yes	100	18	18%	57	57%	12	12%	13	13%		(NS)

a: Kruskal Wallis H test; b: Chi-square test

DISCUSSION

Treatment for early-stage breast cancer typically combines local methods (such as surgery or radiation therapy) with systemic anticancer therapies (such as chemotherapy, hormone therapy, or targeted therapies). Nowadays, most women with early breast cancer Opt for breast conservative surgery (BCS) with radiotherapy since it allows for effective local disease control and cosmetic outcomes [(11)].

Conventional radiotherapy given in 6-7 weeks consisting of 45–50Gy in 25 fractions of 1.8 or 2Gy/day, 5 days a week then boost 10-16Gy over 5-8 days, many randomized trials have confirmed that hypo-fractioned whole breast irradiation 3-4 weeks 40 GY in 15 fractions of 2.67 GY/ day is equivalent to more conventional whole-breast irradiation with respect to local recurrence, toxicity and cosmetic outcome [(12)].

Radiation therapy for breast cancer frequently causes a skin response. Over ninety percent of women undergoing radiation therapy for breast cancer will experience some form of skin alteration [(13)].

The current study included 300 patients, their median age was 52 years (range 31 – 74 years), which is nearly similar to **Kumbhaj *et al.*** [(14)] study in which median age was 50, **El-Sayed *et al.*** [(15)] study in which median age was 51 years and **Ali and Al Mageed** [(16)] study in which mean age was 49.4 years and median 46.6.

In our study 36% of patients were diabetic and 28.3 % were hypertensive. In **Ciammella *et al.*** [(17)] and **De Santia *et al.*** [(18)] study 11% were diabetics and 12 % and 47% were hypertensive respectively.

In this study 62% patients had right breast cancer while 38% patients had left sided cancer. 57.7% of breast cancer lesions detected were in upper outer quadrant and the least common was central lesion, nearly the same result was in **Ciammella *et al.*** [(17)] study, the most common tumor site was the UOQ (46.7%) and (26.7%), while the least common were the central location. In the present study, the majority of patients (77.7%) were IDC, as in **Ciammella *et al.*** [(17)] **and Santia *et al.*** [(18)] the most common pathological type was also invasive duct carcinoma (86.7%) % (47 %) respectively.

Most of patients in our study had T1 tumor (56.7%),this is in accordance with the results of both **Santia *et al.*** [(18)] **study and Ciammella *et al.*** [(17)] as the majority of patients had stage T1 tumor (89.2 %) and (64 %) respectively. In the present study 31% of patients are nodal positive. While nodal positive patients in **Santia *et al.*** [(18)] **study and Ciammella *et al.*** [(17)] were 19% and 16 % respectively. The majority of patients had grade II tumor (67%). **In Ciammella *et al.*** [(17)] **and Santia *et al.*** [(18)] (65%) nearly the same finding as our study, grade II tumors were the predominant representing 66.7%.

The mean breast volume among the currently studied patients was 1433.47 cc, ranged between (125.6 and 3001.1 cc) while the mean boost volume was 110.09 cc (range between 15.9 and 199.5cc), while the average beast volume and boost volume in **Santia *et al.*** [(18)] 722.1cc and 54.1 cc respectively and in **Ciammella *et al.*** [(17)] 813.8 and 138.75 respectively**.**

In our study, Acute toxicity was assessed as the followings 27% of patients had G0 acute skin toxicity, 48.7% had G1, 13.3% had G2 and 11% had G3 acute skin toxicity. The current investigation found a strong correlation between body mass index and acute skin toxicity, as well as a substantial association with breast and boost volume and this toxicity.

Similar results was recorded by **Ciammella *et al.*** [(17)] when examining the correlation between boost volume and the occurrence of acute cutaneous response.

Vrieling *et al.* [(18)] found a similar pattern, showing that the severity of acute cutaneous responses rises with breast size. **Ciammella *et al.*** [(17)] results also showed that there was statical significance between acute skin toxicity and boost administration which wasn't found in the current study as all patients received boost dose.

Our results revealed that in the patients, there was no significant correlation between age, DM, HTN and acute toxicity and there was also no significant correlation between acute skin toxicity and laterality nor site of tumor. Lymph node irradiation had no statistical significance with acute skin toxicity, this was confirmed also by **Ciammella *et al.*** [(17)] **and Morsy *et al.*** [(19)]**.**

CONCLUSION

Our study's findings corroborated those of major randomised trials showing that hypofractionated whole breast irradiation can be successfully implemented with a negligibly high risk of adverse events. Acute skin toxicity is exacerbated in obese people and women who have their breast sizes increased. Acute skin toxicity was not affected by either chemotherapy or diabetes mellitus.

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Competing interests: Nil.

REFERENCES

1. **Siegel R, DeSantis C, Virgo K *et al.* (2012):** Cancer treatment and survivorship statistics, 2012. CA: A Cancer Journal for Clinicians, 62(4): 220-241.
2. **Ragaz J, Olivotto I, Spinelli J *et al.* (2005):** Locoregional radiation therapy in patients with high-risk breast cancer receiving adjuvant chemotherapy: 20-year results of the British Columbia randomized trial. Journal of the National Cancer Institute, 97(2): 116-126.
3. **Veronesi U, Cascinelli N, Mariani L *et al.* (2002):** Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. The New England Journal of Medicine, 347(16): 1227–1232.
4. **Newman L (2005):** Breast cancer in African-American women. The Oncologist, 10(1): 1-14.
5. **Fisher B, Anderson S, Bryant J *et al.* (2002):** Twenty-year follow-up of a randomized trial comparing total

mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. The New England Journal of Medicine, 347(16): 1233–1241.

6. **van Werkhoven E, Hart G, Tinteren H *et al.* (2011):** Nomogram to predict ipsilateral breast relapse based on pathology review from the EORTC 22881-10882 boost versus no boost trial. Radiotherapy and Oncology, 100(1): 101–107.
7. **Whelan T, Pignol J, Levine M *et al.* (2010):** Long-term results of hypofractionated radiation therapy for breast cancer. The New England Journal of Medicine, 362(6): 513–520.
8. **Chen G, Liu F, White J *et al.* (2015):** A planning comparison of 7 irradiation options allowed in RTOG 1005 for early-stage breast cancer. Medical Dosimetry, 40(1): 21–25l.
9. **Cox J, Stetz J, Pajak T (1995):** Toxicity Criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys., 31(5):1341-6.
10. **Rose M, Olivotto I, Cady B *et al.* (1989):** Conservative Surgery And Radiation Therapy For Early Breast Cancer. LongTerm Cosmetic Results. Arch Surg., 124: 153-157.
11. **Harbeck N, Penault-Llorca F, Cortes J *et al.* (2019):** Breast cancer. Nature reviews Disease Primers, 5(1): 1-31.
12. **Whelan T, MacKenzie R, Julian J *et al.* (2012):** Randomized trial of breast irradiation schedules after lumpectomy for women with lymph node-negative breast cancer. J Natl Cancer Inst., 94:1143-1150.
13. **Podrock D, Kristjanson L (2018):** Skin reactions during radiotherapy for breast cancer: the use and impact of topical agents and dressings. Eur J Cancer Care, 8:143–153.
14. **Kumbhaj P, Sharma R, Saini P *et al.* (2013):** A study of two different dose fractionation schedules of post mastectomy chest wall irradiation in carcinoma breast patients. International Journal of Medical Science and Public Health, 2(4): 1001-1005.
15. **El-Sayed M, Abdel-Wanis M (2012):** Comparison of hypofractionated and conventional radiotherapy protocols in breast cancer patients: A retrospective study. J Sci Ther., 4(6): 158-163.
16. **Ali E, Al Mageed M (2014):** Post-mastectomy hypofractionation radiotherapy in breast cancer patients. Cancer Oncol Res., 2:87–93.
17. **Ciammella P, Podgornii A, Galeandro M *et al.* (2014):** Toxicity and cosmetic outcome of hypofractionated whole-breast radiotherapy: predictive clinical and dosimetric factors. Radiat Oncol., 9: 97. doi: 10.1186/1748-717X-9-97
18. **Vrieling C, Collette L, Fourquet A *et al.* (2017):** The influence of patient, tumor and treatment factors on the cosmetic results after breast-conserving therapy in the EORTC 'boost vs. no boost' trial. Radio Oncol., 55: 219-232.
19. **Morsy A, Sara H, Shehata S *et al.* (2019):** Toxicity of Hypofractionated Radiotherapy Following Breast Conservative Surgery in Breast Cancer. Journal of Cancer Therapy, 10: 371-381.