Postmastectomy Radiotherapy Can Decrease Locoregional Recurrence in Triple Negative T1-2N1 Breast Cancer Patients

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Abstract:

Introduction: Postmastectomy RT (PMRT) is the subject of some debate in T1-T2 with one to three involved axillary lymph nodes (N1 disease).

Aim: Our study aims to compare between patients received PMRT and patients didn't receive PMRT regarding locoregional recurrence (LRR) rate and also to define a subgroup of patients at high risk for locoregional recurrence (LRR) who might benefit from postmastectomy radiotherapy.

Patients and Methods: Retrospective study of patients with early stage breast cancer (T1-2) and positive 1- 3 axillary lymph nodes treated in clinical oncology department, Zagazig university during period between 2009 and 2014, we included 124 patients didn't receive postmastectomy radiotherapy (No PMRT, group I) and 124 patients received postmastectomy radiotherapy (PMRT, group II).

Results: The median follow-up duration was 60 months (range; 11-72 months). Patients received PMRT had lower rate of LRR than patients didn't receive PMRT (3.2% versus 35.5% respectively).Among patients didn't receive radiotherapy, we found a significant high rate of locoregional recurrence (LRR) among triple negative patients than non-triple negative patients (61.5% vs 32.4%), also we found the relative risk reduction (RRR) in the LRR rate by PMRT was 81.9% and absolute risk reduction (ARR) was 50.4% (61.5% to 11.1%) among triple negative patients.

Conclusion: PMRT decreases locoregional recurrence rate (LRR) in early breast cancer with T1-2 and positive 1-3 axillary lymph nodes especially in patients had triple negative molecular subtype.

Keywords: Early breast cancer, modified radical mastectomy, postmastectomy radiotherapy, locoregional recurrence, triple negative.

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Introduction:

Breast cancer is the most common malignant tumor that occurs in women worldwide and it is a leading cause of cancer-related deaths.[1] In Egypt according to the National Cancer Registry Program (2008-2011), breast cancer is the most common cancer in women.[2]

Many clinical studies including retrospective studies and randomized trials have revealed that breast conservative surgery and adjuvant radiotherapy is equivalent to modified radical mastectomy regarding overall survival for patients with early breast cancer but have a higher rate of local recurrence.[3-5] In Egypt modified radical mastectomy, rather than conservative surgery, is the most commonly performed surgical operation for early stages of breast cancer.[6]

Several studies have shown that radiotherapy can reduce the rate of loco-regional recurrence and prolong survival in breast cancer patients.[7,8] Addition of postmastectomy radiation therapy in patients with high-risk disease has reduced the frequency of local and regional recurrence and improves overall survival [9,10] Among patients with four or more positive notes, postmastectomy radiotherapy (PMRT) reduced locoregional recurrence and breast cancer mortality.[8]

The role of PMRT in patients with early-stage T1–2 disease with limited nodal metastasis (one to three positive nodes) is still controversial.[11,12] Some studies have shown that post-mastectomy radiotherapy is beneficial for patients with 1–3 positive nodes.[8, 9, 13-15] However, McBride et al. reported that patients

with 1–3 positive nodes without risk features had a low rate of locoregional recurrence, even without radiotherapy.[16]

Aim

The main objective of our study to compare between patients received PMRT and patients didn't receive PMRT regarding locoregional recurrence (LRR) rate and our secondary objective to define a subgroup of patients at high risk for locoregional recurrence (LRR) who might benefit from postmastectomy radiotherapy

Patients and Methods:

Sample size

According to He et al., locoregional recurrence rate was 10.6% in patients didn't receive postmastectomy radiotherapy versus 1.26% in patients received postmastectomy radiotherapy. [17] Taking power of 0.8 and alpha error of 0.05, a minimum sample size of 124 patients was calculated for each group. [18]

Patients

We performed this retrospective analysis based on archived data of clinical oncology and nuclear medicine department, Faculty of Medicine Zagazig university, Egypt for patients with breast cancer treated at our institute between 2009 and 2014. Patients fitting all the following criteria were included: female, histologically confirmed invasive adenocarcinoma operated by modified radical mastectomy including level I and II axillary dissection, early Breast Cancer (T1 or T2 tumors) and one to three positive axillary lymph nodes (N1). Male patients, locally Advanced (T3 or T4 tumors), Node negative disease, more than three positive axillary lymph nodes (N2 or N3), metastatic breast cancer, operated by breast conservative surgery or received neoadjuvant chemotherapy were excluded from our analysis. We included 124 patients didn't receive postmastectomy radiotherapy (No PMRT, group I) and 124 patients received postmastectomy radiotherapy (PMRT, group II).The study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. As the study was retrospective, this committee waived the need for patient consent.

Operational design

We collected the following data: age, tumor laterality, site of tumor, pathological type, tumor grade, T, absolute number of axillary lymph nodes (ALN) removed, number of lymph nodes involved (1, 2, or 3), estrogen receptor (ER) status, progesterone receptor (PR) status, HER2 status, molecular subtype (non-triple negative or triple negative), type of adjuvant systemic therapy delivered (chemotherapy with or without trastuzumab and/or hormonal treatment), chemotherapy regimen, type of hormonal treatment (tamoxifen and/or aromatase inhibitors) and details of radiotherapy in group II. Locoregional recurrence, defined as a first recurrence in ipsilateral chest wall, axilla, supraclavicular fossa, and/or internal mammary nodes with or without simultaneous distant recurrence. Local Recurrence Free Survival (LRFS) was calculated as the time from date of surgery to date of local recurrence or the most recent follow-up contact that patient was known as local recurrence free. Regional Recurrence Free Survival (RRFS) was calculated as the time from date of surgery to date of regional recurrence or the most recent follow-up contact that patient was known as regional recurrence free. Locoregional Recurrence Free Survival (LRRFS) was calculated as the time from date of surgery to date of local or/and regional recurrence or the most recent follow-up contact that patient was known as locoregional recurrence free. Overall Survival (OS) was calculated as the time from diagnosis to death or the most recent follow-up contact (censored).

Statistical Analysis

All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows [19] and MedCalc 18 for windows.[20] Continuous Quantitative variables were expressed as the mean (range), and categorical qualitative variables were expressed as absolute frequencies (number) & relative frequencies (percentage). Categorical data were compared using Chi-square test or Fisher's exact test when appropriate. Stratification of survival was done according PMRT. These time-to-event distributions were estimated using the method of Kaplan-Meier plot and compared using two-sided exact log-rank test. Cox proportional-hazards regression analysis was used to perform univariate and multivariate models to find independent predictors for locoregional recurrence (LRR). All tests were two sided. P-value< 0.05 was considered statistically significant.

Results:

Demographic and Clinicopathological Characteristics

Mean age at diagnosis in group I was 50 years (range, 27–77 years) versus 51 years (range, 27–75 years) in group II. One eighty-seven patients (70.2%) of group I was older than 45 years versus 67.7% in group II. Seventy patients (56.5%) in group I were postmenopausal versus 57.3% in group II. The most common side in both groups was left breast cancer (57.3% versus 62.9% in group I and II respectively). The most common site of tumor in both groups was upper outer quadrant (65.3% versus 64.5% in group I and II respectively). The most common pathological type was invasive ductal carcinoma not otherwise specified (81.5% versus 89.5% in group I and II respectively). The most frequent pathological grade was grade II (63.7% versus 57.3% in group I and II respectively). The mean number of dissected axillary lymph nodes among group I was 17 (range, 11–30) versus 16 (range, 10–33) in group II. (Table 1)

Adjuvant Systemic Treatment

Both groups were comparable regarding adjuvant systemic treatment. One patients (0.8%) in group I received adjuvant hormonal treatment. Eighty-one patients (65.3%) in group I received adjuvant

chemotherapy and hormonal treatment versus 69.4% in group II. The most common utilized regimen was CAF where 52.4% of group I had received CAF versus 51.6% of group II. Twenty-eight patients (22.6%) in group I had received adjuvant trastuzumab versus 21% in group II. The most common utilized hormonal treatment in group I was tamoxifen (37.9%) versus the most common utilized hormonal treatment in group II was aromatase inhibitors (37.9%). Among PMRT (group II), 66.9% received radiotherapy to chest wall and regional lymphatics and 48.4% received 50Gy, 2Gy per fraction in 25 fractions over 5 weeks. (Table 1)

Outcome

The median follow-up duration was 60 months (Range, 11-72 months). Patients received adjuvant postmastectomy radiotherapy had lower rates of local recurrence, regional recurrence, and locoregional recurrence than patients didn't receive radiotherapy (2.4% versus 35.5%, 1.6% versus 16.9%, 3.2% versus 35.5% respectively). Five years local recurrence free survival was significantly higher in patients received postmastectomy radiotherapy than patient didn't receive radiotherapy. Five years regional recurrence free survival was significantly higher in patients received postmastectomy radiotherapy than patient didn't receive radiotherapy. Five years locoregional recurrence free survival was significantly higher in patients received postmastectomy radiotherapy than patient didn't receive radiotherapy. (Table 2, Figures 1-3)

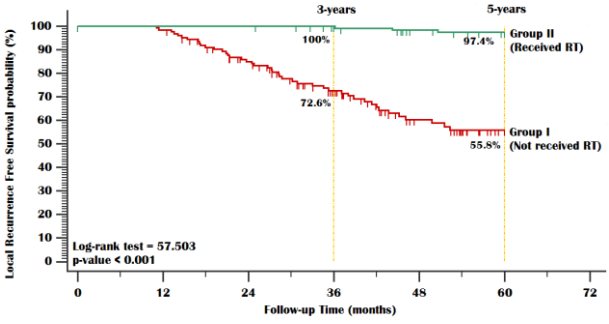

Figure (1): Kaplan Meier plot shows comparison between group I (No PMRT) and group II (PMRT) regarding Local Recurrence Free Survival

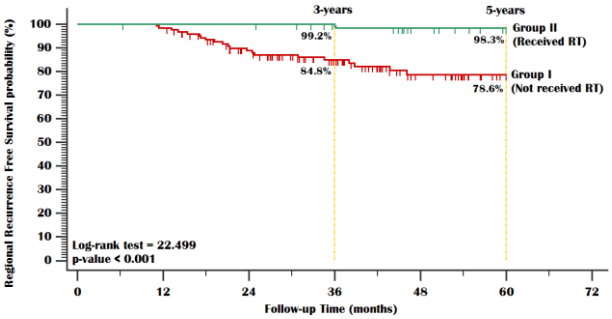

Figure (2): Kaplan Meier plot shows comparison between group I (No PMRT) and group II (PMRT) regarding Regional Recurrence Free Survival

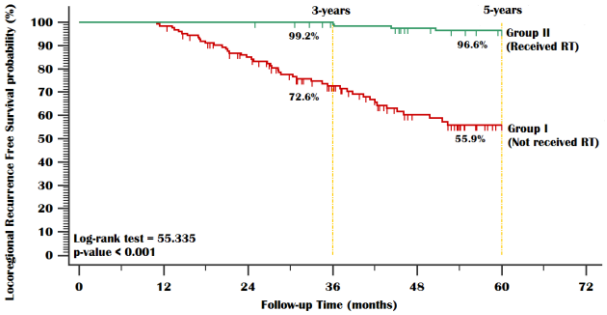

Figure (3): Kaplan Meier plot shows comparison between group I (No PMRT) and group II (PMRT) regarding Locoregional Recurrence Free Survival

Characteristics of patients according to locoregional recurrence (LRR)

We evaluated the LRR in different subgroups of T1–2 N1 breast cancer patients according to demographic, clinicopathologic characteristics and treatment. LRR occurred more frequently in triple negative patients (9 of 22, 40.9%) than in non-triple negative patients (39 of 226, 17.3%) (P-value = 0.019) and patients didn't receive radiotherapy (44 of 124, 35.5%) than patients received radiotherapy (4 of 124, 3.2%) (P-value< 0.001). (Table 3)

Cox regression analysis for independent predictors for locoregional recurrence free survival (LRRFS) among all studied patients

On univariate analysis, we found that triple negative (HR=3.889), didn't received chemotherapy (HR=16.931), didn't received hormonal treatment (HR=2.004) and didn't receive radiotherapy (HR=17.626) were the independent predictors for worse

locoregional disease free survival. On multivariate Cox regression analysis, we found that age less than 45 years (HR=1.923), triple negative (HR=16.542), didn't receive chemotherapy (HR=17.791), and didn't receive radiotherapy (HR=28.169) were the adjusted independent predictors for worse locoregional disease free survival.(Table 4)

Clinicopathological characteristics of locoregional recurrence (LRR) according to postmastectomy radiotherapy (PMRT)

We analyzed LRR in T1–2 N1 breast cancer patient subgroups with or without PMRT. In group I, LRR was significantly higher in patients younger than 45 than patients older than 45 years (48.6% versus 29.9% respectively, P-value = 0.046) also LRR was significantly higher in triple negative patients than non-triple negative patients (61.5% versus 32.4% respectively, P-value = 0.038). Radiotherapy reduced LRR in all subgroups except special pathological type, T1/One+ve LNs, T1/Two+ve LNs, T1/Three+ve LNs subgroups. Absolute decrease in LRR in patients with IDC-ILC pathology was significantly higher than in patients with special type pathology (32.8% versus 12.5% respectively, P-value <0.001). Absolute decrease in LRR in patients with three +ve lymph nodes was significantly higher than in patients two +ve lymph nodes and one +ve lymph nodes (45% versus 26.2% versus 33.3% respectively, P-value <0.001).(Table 5)

Cox regression analysis for independent predictors for locoregional recurrence free survival (LRRFS) among group I (No PMRT)

On univariate analysis, we found that triple negative (HR=10.176), didn't receive chemotherapy (HR=8.061) and didn't receive hormonal treatment (HR=2.557) were the independent predictors for worse locoregional disease free survival. On multivariate Cox regression analysis, we found that age less than 45 years (HR=1.903), triple negative (HR=14.784) and didn't receive chemotherapy (HR=17.278) were the adjusted independent predictors for worse locoregional disease free survival. (Table 6)

Discussion:

Before 2015, modified radical mastectomy was the routine surgical procedure in our hospital for all breast cancer patients whatever the initial stage as multidisciplinary team was not yet established at that time. The uncertainty and controversy concerning postmastectomy radiotherapy for patients with T1–2 and one to three positive axillary lymph nodes are mainly due to the discrepancy of the locoregional recurrence rates reported in different trials and treatment eras.[14,21-25] Our results showed that during decade in which low rate of utilization of taxanes containing regimens and aromatase inhibitors as adjuvant systemic treatment, the cumulative incidence of 5-year LRR was 35.5% for these patients who didn't received radiotherapy. The 5-year LRR rate in our study (35.5 %) was higher than rate reported in many studies. Tendulkar et al. (2012) conducted a retrospective review of all 369 breast cancer patients with 1-3 positive lymph nodes who underwent mastectomy without neoadjuvant systemic therapy between 2000 and 2007 at Cleveland Clinic and reported that the 5-year locoregional failure rate was 8.9% among patients didn't receive radiotherapy.[26] Lu et al. (2013) retrospectively analyzed clinicopathologic features and survival in 368 breast cancer patients who had T1 or T2 primary tumours and 1–3 histologically involved axillary lymph nodes and who were treated with modified radical mastectomy without adjuvant radiotherapy and found that 5-year locoregional failure rates was 7.2%.[27] Moo et al. (2013) identified 1,331 patients who underwent mastectomy and had 1 to 3 positive nodes and reported that the 5-year locoregional failure rates was 4.3% among patients didn't receive radiotherapy.[28] Wu et al. (2014) performed an analysis of clinical pathological data from 221 female Chinese breast cancer patients aged 35 years or younger treated between 1998 and 2007 and found that 5-year locoregional failure rate was 19.1%among patients who did receive PMRT.[29] McBride et al. (2014) retrospectively analyzed the locoregional recurrence rates in 505 patients with T1-2 breast cancer with 1 to 3 positive lymph nodes treated with mastectomy and adjuvant chemotherapy with or without PMRT during an early era (1978-1997) and found that the 5-year locoregional failure rate was 9.5% among patients didn't receive radiotherapy.[16] Jwa et al. (2015) enrolled 83 patients with pT1-2N1breast cancer who underwent total mastectomy without adjuvant radiotherapy from 2002 to 2011 and found the 5-year locoregional failure rate was 3%.[30] Shen et al. (2015) retrospectively studied breast cancer patients with T1–T2 tumors and 1–3 positive ALNs and found the 5-year locoregional failure rate was 17.6% among patients didn't receive radiotherapy.[31] Park et al. (2016)retrospectively analyzed one thousand three hundred eighty-two pT1-2N1M0 breast cancer patients treated with mastectomy without PMRT between 2005 and 2010 and found the 5-year locoregional failure rate was 6.1%.[32] Wadasadawala et al. (2017) looked at 242 patients with early breast cancer with 1–3 positive axillary nodes treated by modified radical mastectomy without radiotherapy and found that the 5-year locoregional failure rate was 6.6%.[33] Bazan et al. (2018) reviewed patients with pT1-2N1 breast cancer treated with mastectomy without PMRT from 2000 to 2013 and found that the 5-year locoregional failure rate was 4.1%.[34] Asaga et al. (2019) included428 patients with T1-2 tumor and 1-3 positive axillary nodes (pT1-2 N1) treated using total mastectomy without radiotherapy in their study and found that the 5-year locoregional failure rate was 4.7%.[35]

Table (1): Demographic, clinicopathological characteristics and treatment in the studied patients.

Parameters		Group I (No PMRT) (N=124)		Group II (PMRT) (N=124)		P-value[a]
		No.	%	No.	%	
Age group	≤45 years	37	29.8%	40	32.3%	0.681
	>45 years	87	70.2%	84	67.7%	
Laterality	Right breast	53	42.7%	46	37.1%	0.364
	Left breast	71	57.3%	78	62.9%	
Pathological type	IDC-ILC	116	93.5%	122	98.4%	0.053
	Special	8	6.5%	2	1.6%	
Grade	Grade I	17	13.7%	19	15.3%	0.718
	Grade II-III	107	86.3%	105	84.7%	
T stage	T1	31	25%	29	23.4%	0.767
	T2	93	75%	95	76.6%	
Positive LNs	One	42	33.9%	36	29%	0.132
	Two	56	45.2%	48	38.7%	
	Three	26	21%	40	32.3%	
T/ Positive LNs	T1/One	13	10.5%	10	8.1%	0.352
	T1/Two	14	11.3%	9	7.3%	
	T1/Three	4	3.2%	10	8.1%	
	T2/One	29	23.4%	26	21%	
	T2/Two	42	33.9%	39	31.5%	
	T2/Three	22	17.7%	30	24.2%	
HR	Negative	31	25%	23	18.5%	0.218
	Positive	93	75%	101	81.5%	
HER2	Negative	90	72.6%	94	75.8%	0.562
	Positive	34	27.4%	30	24.2%	
Molecular Subtype	Non-TN	111	89.5%	115	92.7%	0.372
	TN	13	10.5%	9	7.3%	
Adjuvant Treatment	Chemotherapy	123	99.2%	124	100%	1.000
	Trastuzumab	28	22.6%	26	21%	0.758
	Hormonal	93	75%	101	81.5%	0.218
Chemotherapy regimen	No	1	0.8%	0	0%	0.098
	CMF	7	5.6%	7	5.6%	
	CAF	65	52.4%	64	51.6%	
	FEC	7	5.6%	19	15.3%	
	AC-Taxol	44	35.5%	34	27.4%	
Hormonal treatment	No	31	25%	23	18.5%	0.061
	Tam	47	37.9%	34	27.4%	
	AI	34	27.4%	47	37.9%	
	Tam then AI	12	9.7%	20	16.1%	

Categorical variables were expressed as number (percentage); HR: Hormone Receptors; TN: Triple Negative; AI: Aromatase Inhibitors; Tam: Tamoxifen; a: Chi-square test; $p<0.05$ is significant.

Table (2): Outcome among the studied patients.

Outcome		Group I(No PMRT) (N=124)		Group II(PMRT) (N=124)		P-value
		No.	%	No.	%	
Local Recurrence	Absent	80	64.5%	121	97.6%	**<0.001**[a]
	Present	44	35.5%	3	2.4%	
Local Recurrence Free Survival (LRFS)	Mean (95% CI)	47.15 months (44.04 – 50.26)		59.57 months (59.07 – 60.07)		**<0.001**[b]
	3-year LRFS	72.6%		100%		
	5-year LRFS	55.8%		97.4%		
Regional Recurrence	Absent	103	83.1%	122	98.4%	**<0.001**[a]
	Present	21	16.9%	2	1.6%	
Regional Recurrence Free Survival (RRFS)	Mean (95% CI)	52.88 months (50.11 – 55.65)		59.59 months (59.03 – 60.15)		**<0.001**[b]
	3-year RRFS	84.8%		99.2%		
	5-year RRFS	78.6%		98.3%		
LR Recurrence	Absent	80	64.5%	120	96.8%	**<0.001**[a]
	Present	44	35.5%	4	3.2%	
Locoregional Recurrence Free Survival (LRRFS)	Mean (95% CI)	47.16 months (44.06 – 50.27)		59.38 months (58.75 – 60.01)		**<0.001**[b]
	3-year LRRFS	72.6%		99.2%		
	5-year LRRFS	55.9%		96.6%		
Mortality	Alive	124	100%	124	100%	1.000[a]
	Died	0	0%	0	0%	
Overall Survival (OS)	3-year OS	100%		100%		1.000[b]
	5-year OS	100%		100%		

Categorical variables were expressed as number (percentage); a: Chi-square test; b: Log-rank test; CI: Confidence Interval; P-value< 0.05 is significant (bold).

Table (3): Characteristics of patients according to locoregional recurrence (LRR) among all studied patients (N=248)

Parameters			Locoregional recurrence (LRR)				
			Absent (N=200)		Present (N=48)		P-value[a]
		N	No.	%	No.	%	
Age group	≤45 years	77	57	74%	20	26%	0.077
	>45 years	171	143	83.6%	28	16.4%	
Laterality	Right breast	99	79	79.8%	20	20.2%	0.783
	Left breast	149	121	81.2%	28	18.8%	
Pathological type	IDC NOS	212	176	83%	36	17%	0.052
	ILC	23	15	65.2%	8	34.8%	
	Special type	3	3	100%	0	0%	
	Mixed	10	6	60%	4	40%	
Grade	Grade I	36	31	86.1%	5	13.9%	0.660
	Grade II	150	120	80%	30	20%	
	Grade III	62	49	79%	13	21%	
T stage	T1	60	50	83.3%	10	16.7%	0.545
	T2	188	150	79.8%	38	20.2%	
Positive LN	One	78	64	82.1%	14	17.9%	0.720
	Two	104	85	81.7%	19	18.3%	
	Three	66	51	77.3%	15	22.7%	
T/Positive LNs	T1/One	23	20	87%	3	13%	0.821
	T1/Two	23	18	78.3%	5	21.7%	
	T1/Three	14	12	85.7%	2	14.3%	
	T2/One	55	44	80%	11	20%	
	T2/Two	81	67	82.7%	14	17.3%	
	T2/Three	52	39	75%	13	25%	
HR	Negative	54	40	74.1%	14	25.9%	0.167
	Positive	194	160	82.5%	34	17.5%	
HER2	Negative	184	147	79.9%	37	20.1%	0.610
	Positive	64	53	82.8%	11	17.2%	
Molecular Subtype	Non-TN	226	187	82.7%	39	17.3%	**0.019**
	TN	22	13	59.1%	9	40.9%	
Adjuvant chemotherapy	No	1	0	0%	1	100%	0.293
	CMF	14	11	78.6%	3	21.4%	
	CAF	129	107	82.9%	22	17.1%	
	FEC	26	21	80.8%	5	19.2%	
	AC-Taxol	78	61	78.2%	17	21.8%	
Adjuvant trastuzumab	No	194	156	80.4%	38	19.6%	0.860
	Yes	54	44	81.5%	10	18.5%	
Adjuvant hormonal	No	54	40	74.1%	14	25.9%	0.140
	Tam	81	62	76.5%	19	23.5%	
	AI	81	69	85.2%	12	14.8%	
	Tam then AI	32	29	90.6%	3	9.4%	
Postmastectomy radiotherapy	No	124	80	64.5%	44	35.5%	**<0.001**
	Yes	124	120	96.8%	4	3.2%	

Categorical variables were expressed as number (percentage); HR: Hormone Receptors; TN: Triple Negative; AI: Aromatase Inhibitors; Tam: Tamoxifen; a: Chi-square test; P-value< 0.05 is significant (bold).

Table (4): Cox regression analysis for independent predictors for locoregional recurrence free survival (LRRFS) among all studied patients (N=248)

Variables	Univariate model			Multivariate model		
	HR	(95%CI)	P-value	HR	(95%CI)	P-value
Age group						
≤45 years	1.607	(0.905 – 2.852)	0.105	1.923	(1.063 – 3.479)	**0.031**
>45 years	1.000			1.000		
Pathology						
IDC-ILC	0.376	(0.135 – 1.050)	0.062	0.502	(0.173 – 1.453)	0.204
Special type	1.000			1.000		
Grade						
Grade I	1.000			1.000		
Grade II-III	1.586	(0.628 – 4.005)	0.329	1.517	(0.583 – 3.944)	0.393
T/ Positive LNs						
T1/One	1.000			1.000		
>T1/One	1.580	(0.491 – 5.084)	0.443	1.551	(0.467 – 5.147)	0.474
Subtype						
Non-TN	1.000			1.000		
TN	3.889	(1.880 – 8.045)	**<0.001**	16.542	(3.747 – 73.034)	**<0.001**
Chemotherapy						
No	16.931	(2.226 – 128.761)	**0.006**	17.791	(2.197 – 144.063)	**0.007**
Yes	1.000			1.000		
Trastuzumab						
No	0.952	(0.474 – 1.912)	0.890	0.585	(0.233 – 1.464)	0.252
Yes	1.000			1.000		
Hormonal treatment						
No	2.004	(1.074 – 3.740)	**0.029**	0.678	(0.204 – 2.256)	0.527
Yes	1.000			1.000		
Postmastectomy radiotherapy						
No	17.626	(6.305 – 49.270)	**<0.001**	28.169	(9.473 – 83.762)	**<0.001**
Yes	1.000			1.000		

HR: Hazards ratio; 95%CI: 95% confidence interval; P-value< 0.05 is significant (bold).

Table (5): Clinicopathological characteristics of locoregional recurrence (LRR) according to postmastectomy radiotherapy

	Group I (No PMRT) (N=124)					Group II (PMRT) (N=124)					P-value[a]
	N	No LRR		LRR		N	No LRR		LRR		
		No.	%	No.	%		No.	%	No.	%	
Age (years)											
≤45 years	37	19	51.4%	18	48.6%	40	38	95%	2	5%	**<0.001**
>45 years	87	61	70.1%	26	29.9%	84	82	97.6%	2	2.4%	**<0.001**
P-value[a]			**0.046**					0.440			
Pathology											
IDC-ILC	116	75	64.7%	41	35.3%	122	119	97.5%	3	2.5%	**<0.001**
Special type	8	5	62.5%	3	37.5%		2	50%	1	50%	1.000
P-value[a]			0.902					**<0.001**			
Grade											
Grade I	17	12	70.6%	5	29.4%	19	19	100%	0	0%	**0.016**
Grade II-III	107	68	63.6%	39	36.4%	105	101	96.2%	4	3.8%	**<0.001**
P-value[a]			0.573					0.387			
T											
T1	31	21	67.7%	10	32.3%	29	29	100%	0	0%	**0.001**
T2	93	59	63.4%	34	36.6%	95	91	95.8%	4	4.2%	**<0.001**
P-value[a]			0.666					0.572			
+ve LNs											
One	42	28	66.7%	14	33.3%	36	36	100%	0	0%	**<0.001**
Two	56	39	69.6%	17	30.4%	48	46	95.8%	2	4.2%	**0.001**
Three	26	13	50%	13	50%	40	38	95%	2	5%	**<0.001**
P-value[a]			0.210					**<0.001**			
T/+ve LNs											
T1/One	13	10	76.9%	3	23.1%	10	10	100%	0	0%	0.229
T1/Two	14	9	64.3%	5	35.7%	9	9	100%	0	0%	0.116
T1/Three	4	2	50%	2	50%	10	10	100%	0	0%	0.066
T2/One	29	18	62.1%	11	37.9%	26	26	100%	0	0%	**<0.001**
T2/Two	42	30	71.4%	12	28.6%	39	37	94.9%	2	5.1%	**0.005**
T2/Three	22	11	50%	11	50%	30	28	93.3%	2	6.7%	**<0.001**
P-value[a]			0.518					0.635			
HR											
Negative	31	18	58.1%	13	41.9%	23	22	95.7%	1	4.3%	**0.002**
Positive	93	62	66.7%	31	33.3%	101	98	97%	3	3%	**<0.001**
P-value[a]			0.386					0.565			
HER2											
Negative	90	56	62.2%	34	37.8%	94	91	96.8%	3	3.2%	**<0.001**
Positive	34	24	70.6%	10	29.4%	30	29	96.7%	1	3.3%	**0.006**
P-value[a]			0.387					1.000			
Subtype											
Non-TN	111	75	67.6%	36	32.4%	115	112	97.4%	3	2.6%	**<0.001**
TN	13	5	38.5%	8	61.5%	9	8	88.9%	1	11.1%	**0.031**
P-value[a]			**0.038**					0.263			

Categorical variables were expressed as number(percentage); a: Chi-square test; P-value< 0.05 is significant (bold).

Table (6): Cox regression analysis for independent predictors for locoregional recurrence free survival (LRRFS) among group I (No PMRT) (N=124)

Variables	Univariate model		Multivariate model	
	HR (95%CI)	P-value	HR (95%CI)	P-value
Age group				
≤45 years	1.683 (0.922 – 3.070)	0.090	1.903 (1.022 – 3.546)	**0.043**
>45 years	1.000		1.000	
Pathology				
IDC-ILC	0.905 (0.280 – 2.926)	0.867	0.688 (0.205 – 2.309)	0.545
Special type	1.000		1.000	
Grade				
Grade I	1.000		1.000	
Grade II-III	1.402 (0.552 – 3.558)	0.477	1.358 (0.518 – 3.564)	0.534
T/ Positive LNs				
T1/One	1.000		1.000	
>T1/One	1.763 (0.546 – 5.695)	0.343	1.465 (0.440 – 4.878)	0.534
Subtype				
Non-TN	1.000		1.000	
TN	10.176 (4.284 – 24.172)	**<0.001**	14.784 (3.131 – 69.813)	**0.001**
Chemotherapy				
No	8.061 (1.060 – 61.315)	**0.044**	17.278 (2.107 – 141.683)	**0.008**
Yes	1.000		1.000	
Trastuzumab				
No	0.941 (0.451 – 1.966)	0.872	0.671 (0.247 – 1.819)	0.433
Yes	1.000		1.000	
Hormonal treatment				
No	2.557 (1.317 – 4.964)	**0.006**	0.828 (0.237 – 2.898)	0.768
Yes	1.000		1.000	

HR: Hazards ratio; 95%CI: 95% confidence interval; P-value< 0.05 is significant (bold).

In current study, the 5-year locoregional recurrence rate in group who received radiotherapy was 3.2% in agrees with many studies. Tendulkar et al. (2012) reported that the 5-year locoregional failure rate was 0%.[26] Moo et al. (2013) found that the 5-year locoregional failure rate was 3.2%.[28] He et al. (2015) retrospectively reviewed the file records of 79 patients with T1-2 breast cancer and 1-3 positive axillary lymph nodes receiving PMRT and reported that the 5-year locoregional recurrence rate was 1.3%.[36] Yin et al. (2017) performed retrospective analysis of 1674 breast cancer patients with T1-2 and 1-3 positive axillary lymph nodes and found the 5-year locoregional failure rate was 1.5%. The 5-year LRR rate in group who received radiotherapy in our study (3.2 %) was lower than rate reported in many studies.[37] Wu et al. (2014) found that 5-year locoregional failure rate was 9.1% among patients who received PMRT.[29]

Most studies have concluded that locoregional treatment with postmastectomy radiotherapy improved survival by reducing locoregional failure rate.[26,38,39] In current study, we found a statistically significant improvement in the influence of postmastectomy radiotherapy on locoregional recurrence free survival rate in T1–T2 tumors with 1–3 positive axillary lymph nodes patients, while it did not show significance in affecting overall survival.

Among entire cohort of our study, we found locoregional recurrence was associated with triple negative molecular subtype and absence of PMRT. Our results are consistent with previous studies with similar designs. Shen et al.(2015) conducted retrospective study studied breast cancer patients with T1–T2 tumors and 1–3 positive ALNs according to molecular subtype: Luminal A, Luminal B, human epidermal growth factor receptor-2 (Her-2) positive, and Triple negative, founded that triple negative patients who received postmastectomy radiotherapy had a significant reduction in locoregional recurrence rate.[40] A more recent study conducted by Li et al. (2020) reveled that triple negative patients had a higher risk for locoregional failure and founded that postmastectomy radiotherapy can decrease risk of locoregional recurrence in such stratum of patients.[41]

Limitations

Our retrospective study had several limitations, including a short follow-up time and the intrinsic defects of nonrandomized retrospective studies. Many factors, such as lymphovascular invasion and size of lymph node metastasis, were not available and may have influenced overall results. Despite our efforts to adjust for this bias via multivariate analysis, it is likely that other unknown biases influenced our results. Limited use of regional nodal irradiation was also a limitation of this study.

Conclusion:

Postmastectomy radiotherapy decreases locoregional recurrence rate (LRR) in early breast cancer with T1-2 and positive 1-3 axillary lymph nodes especially in patients had triple negative molecular subtype.

Declarations of interest: none

Conflicts of Interest

All authors declare that they have no conflict of interest.

Ethical Approval

All procedures involving human participants performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

As the study was retrospective, research ethical committee of Faculty of Medicine, Zagazig University waived the need for patient consent.

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