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Research Article

Sequelae of Adjuvant Irradiation of Breast Cancer on the Shoulder Region (Influence of Different Doses and Techniques)

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Abstract

Introduction: Globally, breast cancer (BC) is the most frequently diagnosed cancer; about 2.2 million new cases are expected to be diagnosed with BC in 2020. Furthermore, with over 680,000 deaths, it is the primary cause of cancer-related mortality among women. Multim odalities have been described in treatment of breast cancer; surgery, chemotherapy, hormonal therapy, targeted therapy and radiotherapy. In addition, adverse effects from breast cancer treatment could include fibrosis, shoulder and arm pain, limited movement, and breast cancer-related lymphedema (BCRL). Breast cancer patients' arm pain has been linked mostly to radiation therapy (RT). **Subjects and Methods:** The female patients over the age of eighteen who had primary breast cancer and metastasized to the axillary lymph nodes underwent adjuvant regional nodal irradiation (RNI) in this retrospective longitudinal research. Minia University Hospital (MUH) provided the data, which were gathered between 2017 and 2022. The American Joint Committee on Cancer (AJCC 2018) TNM staging approach was utilized to stage the patients, and immunohistochemistry was employed for molecular categorization. **Results:** Relation between shoulder affection and weight, age, median dose of radiation to the shoulders and number of lymph nodes dissected. **Conclusion**: There was a correlation between the mean radiation dose and the volume of the shoulder receiving doses of 10 Gy, 20 Gy, and 30 Gy, as well as shoulder affection following radiotherapy, in addition to the patient's age, weight, and surgical dissection of the axillary lymph nodes.

Key words: breast, radiotherapy, shoulder

Introduction

Globally, breast cancer (BC) is the most frequently diagnosed cancer; about 2.2 million new cases are expected to be diagnosed with BC in 2020. Furthermore, with over 680,000 deaths, it is the primary cause of cancer-related mortality among women. [1].

There are several ways to treat breast cancer, including radiation, chemotherapy, and surgery. It is established that postmastectomy radiation therapy raises the disease-free survival rate [3] and provides strong evidence for a significant reduction in the locoregional recurrence rate after radiation therapy to the chest wall and regional nodal areas [4].

Radiation therapy frequently has some form of physical, psychological, or psychosocial adverse effects. women with breast cancer report that discomfort, skin responses, and exhaustion are among the most frequent adverse effects of radiation treatment [5].

In addition, adverse effects from breast cancer treatment could include fibrosis, shoulder and arm pain, limited movement, and breast cancer-related lymphedema (BCRL). Breast cancer patients' arm pain has been linked mostly to radiation therapy (RT) [2] RT has also been regularly documented as a risk factor for BCRL, in conjunction to mastectomy and axillary dissection[6]. Adjuvant RT may increase the risk of post-operative BCRL and limited arm/shoulder mobility [(7)]. Depending on the overall treatment plan used and the assessment method, the reported prevalence of limited arm/shoulder mobility varies significantly amongst breast cancer patients undergoing radiation therapy (RT) [(8)]. Moreover, patients undergoing radiotherapy after mastectomy have been found to be at risk for shoulder morbidity if they had subcutaneous fibrosis. [(9)]

It is anticipated that arm/shoulder morbidity among breast cancer patients will decline with the recent introduction and advancement of innovative surgical and radiotherapeutical methods, such as sentinel lymph node biopsy or CT-based RT planning, albeit morbidity will not entirely disappear.

Therefore, it is still essential to investigate the link between RT and arm/shoulder morbidity in order to reduce these harmful consequences. [(10)]

Shoulder joint discomfort can appear months after treatment and is regarded as a late consequence of surgery and radiation for breast cancer. [(11)]

Aim of the work

The purpose of this study is to determine the radiation dose that the shoulders received from breast irradiation using the 3D conformal radiation therapy (3DCRT) technique. Additionally, different doses will be correlated with patient reports of long-term (≥6 months) shoulder affection using the q-DASH, and imaging will be used to identify the shoulders as an organ at risk (OAR) during treatment planning.

Patient and Methods

The female patients over the age of eighteen who had primary breast cancer and metastasized to the axillary lymph nodes underwent adjuvant regional nodal irradiation (RNI) in this retrospective longitudinal research. Minia University Hospital (MUH) provided the data, which were gathered between 2017 and 2022. The American Joint Committee on Cancer (AJCC 2018) TNM staging approach was utilized to stage the patients, and immunohistochemistry was employed for molecular categorization.

- Inclusion Criteria:

1. Female patients who underwent adjuvant regional nodal irradiation and had initial breast cancer with axillary lymph node metastases
2. Older than eighteen
3. No history of radiation to the chest wall or ipsilateral breast

- Exclusion Criteria:

1. Male gender
2. Patients without metastasis in axillary Lymph nodes (N0/ Node negative breast cancer) who did not receive regional nodal irradiation
3. Previous radiotherapy to ipsilateral breast or chest wall (breast reirradiation)
4. Known cases of rheumatological disorders; scleroderma, rheumatoid arthritis, osteoarthritis
5.simultaneous distant metastatic spread

Methods:

First, from 2017 to 2022, we identified patients with adjuvant RNI-treated lymph node-positive breast cancer. The shoulder is retroactively contoured as an organ at risk (OAR) from 2 cm above the ipsilateral supraclavicular (SCLN) planning target volume (PTV) to the inferior SCLN PTV slice. The volume of the OAR receiving 10–40 Gy (V10–V40) is calculated, along with the mean and maximum doses of radiation that reach the shoulder. Following the completion of RNI, a minimum of six months (≥six months) is required to assess long-term shoulder affection using the q-DASH questionnaire and radiologically with an MRI shoulder.

Utilizing 3DCRT for Radiation Simulation and Treatment Planning:

Using a breast board (or prone in other situations) and a free-breathing CT scan, participants experienced computed tomography (CT) simulation while supine. Breast boards are specialized immobilization devices intended for use in radiation therapy for patients with breast cancer. While reducing exposure to healthy tissues, these devices offer support, improve patient comfort, and guarantee precise radiation delivery to the target area. Following the transfer of CT scans to an automated treatment planning system, target volumes were contoured using the RTOG Contouring Atlas. The normal OAR contoured were the contralateral breast, the bilateral lungs, the heart, and the spinal cord. The recommended dosage for the breast/chest wall and regional nodes was 5,000 cGy in 25 fractions over 5 weeks or 4,000 cGy in 15 fractions over 3 weeks. The treatment physician may choose to administer an extra boost to the mastectomy scar or lumpectomy cavity, after which the plan was reviewed and approved.

The shoulder OAR is defined as the posteriorly contoured shoulder area for each case, encompassing the soft tissues and muscles of the neck, shoulder joint, and back. There is no widely accepted classification for the shoulder OAR because only a small number of RNI studies have classified the shoulder as an OAR. Since all of them are essential to the anatomy and physiology of the shoulder and are radiation-sensitive, the shoulder OAR structures in this study comprise the muscles, soft tissues, bone, and vasculature.

The posterior neck, shoulder, and upper arm region were contoured starting 2 cm superior to the most cranial slice of the supraclavicular (SCLN) PTV and ending at the most caudal SCLN PTV slice. All muscle, soft tissues, vascular, and bones (apart from the vertebra) were included in this process. The muscles of the shoulder OAR comprise the following: pectoralis major, biceps brachii, deltoid, subscapularis, infraspinatus, latissimus dorsi, trapezius, levator scapulae, deep cervical muscles, posterior scalene, and all posterior chest wall muscles, soft tissues, and vasculature (apart from the ribs and vertebrae), starting one slice inferior to the caudal slice of the SCLN PTV and extending to 2 cm inferior to the most caudal chest wall/PTV slice. The anterior border of the latissimus dorsi muscle (excluding the pectoralis muscles and the other intercostal muscles anterior to the latissimus) was the anterior most limit of the posterior chest wall. The latissimus dorsi, serratus anterior, subscapularis, infraspinatus, supraspinatus, trapezius, and erector spinae were among the muscles involved in the shoulder and back OAR. OAR for the shoulder and back may contain portions of specific muscles because of their size and length (e.g., latissimus dorsi, trapezius, subscapularis).

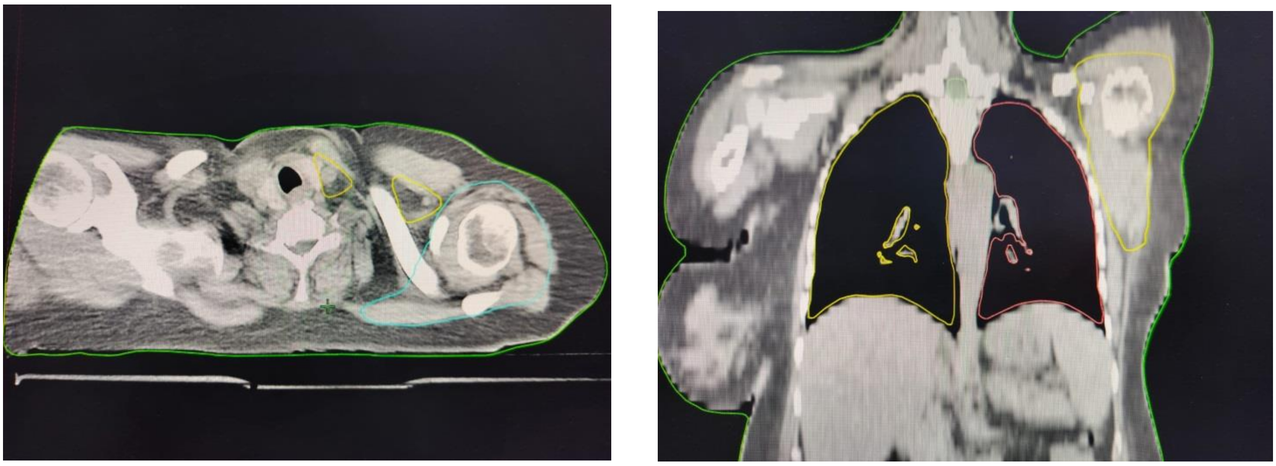

Fig (1): Contouring of shoulder OAR

Results

Table (1): Demographic data :

Demographic data	Cases (N = 103)
Age (yrs.):	
• **Mean ± SD**	**49.1 ± 11.2**
• **Range**	**29 – 71**
Age groups (%):	
• **≤ 35 y**	**14 (13.6%)**
• **> 35 y**	**89 (86.4%)**
Menopause:	
• **Pre-menopausal**	**47(45.6%)**
• **Post-menopausal**	**56(54.3%)**
Sex N (%)	
• **Male**	**0 (0%)**
• **Female**	**103 (100%)**
Weight:	
• **Mean ± SD**	**82.6 ± 17.1**
• **Range**	**44 – 129**
Marital status N (%):	
• **Single**	**9(8.73%)**
• **Married**	**74(71.8%)**
• **Widow**	**15(14.5%)**
• **Divorced**	**5(4.85%)**
Lactation:	
• Yes	**6 (5.82%)**
• No	**97 (94.1%)**

Table (1) revealed that; number of cases in the study is 103 cases, the ages varied from 29 to 71 years (mean 49.1 years),89 cases were > 35 years (mean 86.4%) and only 14 cases were ≤ 35 years(mean13.6%). 47 cases were premenopausal (mean 45.6%) and 56 cases were postmenopausal (mean 54.3%) 100% of the studied cases were females, weight of the cases ranged from 44 to 129 kgs (mean 82.6 ± 17.1kgs), 74 cases were married, 15 cases were widows,9 cases were singles and 5 cases were divorced, 6 cases were lactating (mean 5.82%), 97 cases were not lactating mean (94.1%).

Table (2): Data of breast cancer :

Data of breast cancer	**Cases (N = 103)**
Laterality	
- **Right**	53(51.4%)
- **Left**	50(48.5%)
Type of surgery	
- MRM	65(63.1%)
- BCS	37(35.9%)
- Simple mastectomy	1(0.97%)
Number of dissected lymph nodes:	
• Mean ± SD	9.96 ± 2.48
• Range	3 – 15
Pathological type of the cancer:	
• IDC	84(81.5%)
• ILC	11(10.6%)
• IDC WITH DCIS	3(2.91%)
• Florid DC	1(0.97%)
• Invasive mixed L&DC	2(1.94%)
• IDC with DCIS&LCIS	2(1.94%)
IHC:	
• Luminal A	33(32.0%)
• Luminal B	30(29.1%)
• HER 2 enriched.	11(10.6%)
• Triple negative	29(28.1%)

Table (2) revealed that 53 cases were right sided breast cancer (mean 51.4%) and 50 cases were left sided breast cancer (mean 48.5%). 63 cases underwent MRM. 37 cases underwent BCS and one case underwent simple mastectomy. Number of lymph nodes dissected in surgeries varied from 3 to 15 lymph nodes (mean 9.96 ± 2.48). Histopathological examination revealed different pathological types; 84 cases were Invasive ductal carcinoma (IDC) (mean 81.5%), 11 cases were Invasive lobular carcinoma (ILC) (mean10.6%) , 3 cases were IDC with ductal carcinoma insitu (DCIS)(mean2.91%), 1 case was florid ductal carcinoma (mean 0.97%), 2 cases were mixed ILC and IDC (mean1.94%) and 2 cases were IDC with DCIS&LCIS (mean1.94%), 33 cases were luminal A(mean 32.0%) , 30 cases were luminal B(mean 29.1%) ,29 cases were triple negative (mean 28.1%) and 11 cases were HER2 enriched (mean 10.6%).

Table (3): Staging of the breast lesions:

Staging of breast cancer	Cases (N = 103)
T Staging according to tumer size:	
• **T1**	10(9.70%)
• **T2**	58(56.3%)
• **T3**	31(30.0%)
• **T4**	4(3.88%)
N Staging according of number of lymph nodes positive for malignancy:	
• **N1(1-3 LNs)**	50(48.5%)
• **N2(4-9 LNs)**	27(26.2%)
• **N3(more than 10 LNs)**	24(23.3%)
• **N x(nodal status not known)**	2(1.94%)

Table (3) revealed that 10 cases were T1 (tumor size is less than or equal to 2 centimeters), 58 cases were T2 (tumor size is more than 2cm but less than or equal to 5 cm), 31 cases were T3 (tumor size is more than 5 cm) and only 4 cases were T4 (attached to skin or chest wall). 50 cases were N1, 27 cases were N2, 24 cases were N3 and 2 cases were Nx as nodal status of them not known.

Table (4): Dose of radiation reaching shoulder joint:

Radiation dose reaching the shoulder joint	Cases (N = 103)	
	Mean ± SD	**Range**
Mean dose of radiation reaching shoulder joint (Grey)	9.29 ± 1.44	5.4 - 13.1
Maximum dose of radiation reaching shoulder joint (Grey)	41.3 ± 3.34	34.5 - 53.1
V10(volume of shoulder received 10 gy)%	26.15 ± 5.4	12.7 - 42.5
V20(volume of shoulder received 20 gy)%	16.3 ± 5.04	5.3 - 29.8
V30(volume of shoulder received 30 gy)%	8.8 ± 3.5	2.5 - 26.6
V40(volume of shoulder received 40 gy)%	4.97 ± 1.68	1.6 - 13.8

Table (4): revealed that Mean Dose of radiation reaching the shoulder region ranged from 5.4Gy to 13.1 Gy (mean 9.29 ± 1.44 Gy), Maximum Dose reaching the shoulder region ranged from 34.5 Gy to 53.1 Gy (mean 41.3 ± 3.34 Gy). V10 varied from 12.7% to 42.5%, V20 varied from 5.3% to 29.8% , V30 varied from 2.5 % to 26.6% , V40 varied from 1.6% to 13.8% .

Table (5): Correlation between QuickDash total score and other variables:

Variables	QUICK DASH questionnaire	
	r value	p value
Age	.458*	<0.001*
Weight	.388*	<0.001*
Time from surgery to RT	-.118	.237
Dose of RT to shoulder joint - mean dose	.306*	0.002*
Dose of RT to shoulder joint - max dose	.052	.599
Number of dissected LNs	.708*	<0.001*

N.B: Grades of correlation: $r \leq 0.19$ means no or very weak correlation, r = 0.2 - 0.4 means weak correlation, r = 0.4 - 0.6 means moderate correlation, r = 0.6 - 0.8 means strong correlation, and $r \geq 0.8$ means very strong correlation.

Table (5) revealed that there was statistically significant Positive correlation between age and quickdash questionnaire score. There was statistically significant Positive correlation between weight and quickdash questionnaire score. There was statistically significant Positive correlation between mean dose of radiotherapy to shoulder and quickdash questionnaire score. There were statistically significant Positive correlation between number of dissected LNs and quickDash questionnaire score. There were non statistically significant correlation between QuickDash questionnaire score and maximum dose of radiation to shoulder or time from surgery to radiation.

Table (6): Correlation between QiuckDash score and V10,20,30,4:

Volume (%)	QUICK DASH questionnaire	
	r value	p value
volume of joint with dose 10 Gy (%)	.235	**.017***
volume of joint with dose 20 Gy (%)	.223	**.024***
volume of joint with dose 30 Gy (%)	.211	**.032***
volume of joint with dose 40 Gy (%)	0.003	.979

N.B: Grades of correlation: r ≤0.19 means no or very weak correlation, r = 0.2 - 0.4 means weak correlation, r = 0.4 - 0.6 means moderate correlation, r = 0.6 - 0.8 means strong correlation, and r ≥ 0.8 means very strong correlation.

Table (6) revealed that there were statistically significant Positive correlation between QuickDash questionnaire score and V10,20,30 but there were non statistically significance between QuickDash score and V40.

Table (7): Multivariate linear regression analysis for predictors of Quick DASH score:

Independent Variable	Unstandardized Coefficients		Standardized Coefficients	t	P value
	B	Standard error	Beta		
Number of dissected LNs	3.446	.421	.575	8.178	**<0.001***
Dose of RT to shoulder joint - mean dose	2.412	.661	.235	3.649	**<0.001***
Weight	.195	.055	.225	3.536	**0.001***
Age	.254	.093	.191	2.721	**0.008***
Time from surgery to RT	-.715	.351	-.125	-2.039	**0.04***
Dose of RT to shoulder joint - max dose	-.453	.290	-.102	-1.558	0.122
Type of surgery	1.451	1.860	.049	.780	0.437
Type of chemotherapy	-.005	1.837	.000	-.003	0.998

NB: R^2 = 0.662

Table (7) revealed that according to multivariate linear regression, the number of dissected LNs is a predictor of QuickDash score; the more the number of dissected LNs, the higher the quickDash score (beta=0.575, P<0.001). Mean dose of radiotherapy to shoulder region is a predictor of quickDash score; the higher the mean dose to shoulder, the higher the quickDash score (beta=0.235, P<0.001). Weight is a predictor of quickDash score; the higher the weight, the higher the quickdash score (beta=0.225, P=0.001). Age is a predictor of QuickDash score; the older the age, the higher the score (beta=0.191, P=0.008) . Time from sugery to radiotherapy is a negative predictor of QuicDash score; the shorter the duration, the higher the score (beta=-0.125, P=0.04).

The set of predictors represents (66.2%) of the total variance of QuickDash questionnaire score among studied cases.

Table (8): Correlation between MRI findings and other variables:

	Affected MRI cases. (N=21)	Free MRI cases (N=82)	p value
Age:			
• Mean + SD	60.1 ± 11.2	48.35 ± 11.1	**0.02***
• Range	33 - 70	29 - 71	
Weight:			
• Mean + SD	88.33 ± 20.6	81.21 ± 15.9	0.09
• Range	60 - 129	44 - 123	
Time from surgery to RT:			
• Mean + SD	4.78 ± 2.73	4.55 ± 2.58	0.722
• Range	1 - 9	0.75 - 10	
Number of dissected LNs:			
• Mean + SD	12.19 ± 1.86	9.39 ± 2.3	**<0.001***
• Range	8 - 15	3 - 14	
Type of surgery (%):			
• MRM	13(61.9%)	52(63.4%)	0.862
• BCS	8(38.1%)	29(35.4%)	
• Mastectomy	0 (0%)	1(1.2%)	
Type of chemotherapy (%):			
• No chemo	1(4.8%)	3(3.6%)	0.360
• Adjuvant	16(76.2%)	50(61%)	
• Neoadjuvant	4(19%)	29(35.4%)	
QUICK DASH questionnaire score (%):			
• Mean + SD	59.7 ± 10.08	38.7 ± 12.7	**<0.001***
• Range	43.2 - 81.8	11.4 - 77.3	
QUICK DASH score levels (%):			
➢ Below 25	0 (0%)	10(12.2%)	
➢ 25 – 49	2(9.5%)	57(69.5%)	**<0.001***
➢ 50 – 75	17(81%)	14(17.1%)	
➢ Above 75	2(9.5%)	1(1.2%)	

NB : Analyzed by independent sample t test and Chi square test.
*: Significant difference at P value < 0.05, (a) means value of t test

Table (8) revealed that there were statistically positive correlation between age and MRI finding (P=0.02) , there were statistically significant positive correlation between the number of dissected LNs and MRI findings (P<0.001) and there were statistically positive correlation between quickDash questionnaire score and finding of MRI on shoulder region (P<0.001) but there were non statistically significant correlation between MRI findings and (weight, type of surgery, type of chemotherapy received and duration between surgery and radiotherapy).

Table (9): Correlation between MRI findings and Radiotherapy:

Radiation	Affected MRI cases. (N=21)		Free MRI cases (N=82)		p value
	Mean ± SD	Range	Mean± SD	Range	
Dose of RT to shoulder joint - mean dose:	10.8 ± 1.06	9 - 13.1	8.9 ± 1.27	5.4 - 12.7	<0.001*
Dose of RT to shoulder joint - max dose:	42.2 ± 3.8	37.3-51.7	41.1 ± 3.18	34.5 - 53.1	0.145
volume of joint with dose 10 Gy (%):	27.6 ± 5.2	21 - 40.9	23.8 ± 3.9	12.2 - 38.7	<0.001*
volume of joint with dose 20 Gy (%):	19.7 ± 4.15	12.9-29.1	16.7 ± 3.9	6.76 - 34.2	0.002*
volume of joint with dose 30 Gy (%):	11.6 ± 3.12	6.36 - 17	8.62 ± 3.2	1.72 - 19.36	<0.001*
volume of joint with dose 40 Gy (%):	1.03 ± 1.04	0 - 3.1	0.83 ± 0.91	0 - 3.91	0.366

Table (9) revealed that there was statistically positive correlation between mean dose of radiotherapy reaching shoulder region and MRI shoulder findings(P<0.001). there was statistically significant positive correlation between MRI findings and V10,20,30 (P<0.001, P=0.002, P<0.001) respectively, but there was non-statistically significant correlation between MRI findings and maximum dose reaching shoulder & non-statistically significant correlation between MRI findings and V40.

Discussion

Globally, breast cancer (BC) is the most frequently diagnosed cancer; about 2.2 million new cases are expected to be diagnosed with BC in 2020. Furthermore, with over 680,000 deaths, it is the primary cause of cancer-related mortality among women. Since breast cancer is thought to be a diverse disorder, it is important to evaluate as many clinical and pathological variables as possible in order to provide the most accurate prognosis [(1)].

Adjuvant regional nodal irradiation (RNI) was administered to female patients over the age of 18 who had primary breast cancer and metastasized to axillary lymph nodes. The study was cross-sectional in nature. Minia University Hospital (MUH) provided data on patients who were diagnosed and treated between 2017 and 2022.

The following variables were examined: tumor size; histopathological classification; molecular subtypes; age; weight; family history; history of hormonal treatment; laterality of the cancer; type of surgery; number of dissected lymph nodes; radiation therapy (including technique, dose, and fractionation); duration from surgery to radiotherapy; radiation dose to the shoulder region; and reflection on shoulder region health assessed by QuickDash questionnaire score and MRI over shoulder region.

The majority of patients in this study (86.4%) were over 35 years old, and those under 35 years old (13.6%) were; these numbers were marginally higher than those reported by Brinton et al., Approximately 5–7% of breast cancer patients are under 40 years old. [(12)]. Furthermore, compared to Sharma and Singh's findings, which indicated that the bulk of cases included postmenopausal and elderly women, 5.6% of breast cancer patients are younger than 35.

According to this study, 54 patients (52.4%) had previously used hormonal contraception, and 49 patients (47.5%) had never used any form of birth control. These findings were consistent with those from Tsui AO, et al., It has been demonstrated that both previous and current users of hormonal contraceptives are more likely to develop breast cancer. Modern contraceptives, which include exogenous hormones, are used differently throughout sub-Saharan Africa. Women from better socioeconomic class are more likely to use contraceptives, with Middle and Western Africa having the lowest use and Southern Africa having the greatest. [(13)]

16 patients (15.6%) in our study had a positive family history, while 87 patients (84.4%) had no family history. Which is comparable to the 15% of study participants who had a first-degree family history described by Bodicoat et al., [14].

With respect to pathological findings, our data revealed that 90 patients (87.3%) had IDC, 11 patients (10.6%) had ILC, and 2 patients (1.9%) had other pathology. [15] They stated that the most common histologic type of malignancy was invasive ductal carcinoma. Invasive lobular cancer was the second most prevalent form. Moreover, matched with Asiri S, et al., who verified that invasive ductal carcinoma ranks among the most common malignancies overall and in women under 40 [16].

50 patients had (N1) in this study, and 48.5% of the positive lymph nodes were in the (1-3) range. N2 status (positive LNs 4-9) comprised 27 patients (26.2%), while N3 status (positive LNs >10) comprised 24 patients (23.3%). The majority of patients (58 patients, or 56.3%) had tumors that were between 20 and 50 mm (T2; 31 patients, or 30% of the total), followed by T3 patients, or 31 patients with a mean tumor size of 30.0%; 10 patients, or 9.7%, had T1 patients with tumors under 20 mm, and only 4 patients had T4 patients (tumors attached to the skin or chest wall; 38.8%). These results differed slightly from those reported by Noha Yehia et al., 2019 [17] who found that 71.2% of cases had tumors smaller than 5 cm and roughly 28.8% of cases had tumors larger than 5 cm. and discovered that 41% of cases were N2 and N3, and 20.1% of cases were N1.

According to our analysis, there were 33 cases (32%) of luminal A subtypes, 30 cases (29.1%) of luminal B, 11 cases (10.6%) of HER2 enriched cases, and 29 cases (28.1%) of triple negative cases. These molecular categorization incidences were consistent with the investigations listed below.

A diverse group of breast tumors with the characteristics of being ER-negative, PR-negative, and HER2-negative is known as Triple-Negative Breast Cancer (TNBC). They account for around 20% of all cases of breast cancer. TNBC is more prevalent in African-American women and women under 40 [18].

The Turkish study Özmen V, et al., 2019 [19] found that 57.7% of the tumors were luminal A, 20.6% were luminal B, 9.6% were HER-2 type (ER and PR negative, HER-2 positive), and 12.1% were triple negative (basal like). This information was based on the molecular sub-type analysis of the tumors.

About 70% of all instances of breast cancer in Western nations are luminal breast cancers, which are ER-positive tumors [20]. Ten to fifteen percent of breast cancers belong to the HER2-enriched category. It is distinguished by the strong expression of HER2 and the lack of PR and ER. P.-K. [21].

While 37 instances (35.9%) and 65 cases (63.1%) received BCS in our study, Noha Yehia Ibrahim et al., 2019 [17] report that the majority of patients (62.6%) underwent Modified Radical Mastectomy (MRM), while only 15.1% underwent Breast Conservative Surgery (BCS).

Due to clinically or pathologically proven lymph node metastasis, adjuvant regional nodal irradiation was administered to all cases in our study. We concur with Whelan et al., 2002[22] that adjuvant RT with RNI is still the recommended course of treatment for patients presenting with clinical N2/N3 disease.

According to Shah C et al., 2014 [23], the radiation technique used in our study was 3D conformal radiotherapy, which is a suitable way to prevent organs from being at risk. RT evolved to incorporate three-dimensional (3D) treatment planning with the use of a computed tomography scanner, leading to significantly more accurate treatment delivery. These developments made it possible to calculate doses to the breast more precisely and to develop methods for lowering doses to nontarget organs that are at danger (such as the heart and lungs).

In our study, 11 patients (10.7%) received normal fractionation radiotherapy 45-50 grey in 25 fractions with (1.8-2 grey per fraction) over 5-7 weeks that's meet the criteria, and 92 patients (89.3%) received hypofractionated regemin 40 Grey in 15 fractions with higher dose per fraction (2.5-3 Grey per fraction) over three weeks. Haviland JS, Owen JR, Dewar JA, et al., 2013; Analysis for START-pilot, START-A, and START-B showed that, regardless of different patient and tumor characteristics, the treatment effect (Hypofractionated RT vs. 50 Gy/25 fx) was similar in both ipsilateral breast tumor recurrence and moderate/marked normal tissue effects. In addition, following both the 50 Gy/25 fx arm and hypofractionated RT, late adverse events such as lung fibrosis, rib fractures, and cardiac toxicity were uncommon in the START-A and START-B trials.

In this study, we evaluate the mean and maximum radiation doses that reach the shoulder region (shoulder OAR), which includes the shoulder joint, muscles, soft tissue, bone, and shoulder and back vasculature. However, Johansen et al., 2014 [10] defined the shoulder OAR by contouring the acromion, the coracoid process, and the outer border of the humerus, with a 5 mm margin. Additionally other study by Lipps et al., 2019 [24] contoured the shoulder and chest wall's nine unique muscles as distinct structures. The absence of a standardized definition for shoulder OAR has caused a delay in comprehending and mitigating shoulder morbidity associated with RNI because there is no reliable way to evaluate shoulder function.

Conclusion

Our findings demonstrated the complex nature of shoulder morbidity following breast cancer treatment. There was a correlation between the mean radiation dose and the volume of the shoulder receiving doses of 10 Gy, 20 Gy, and 30 Gy, as well as shoulder affection following radiotherapy, in addition to the patient's age, weight, and surgical dissection of the axillary lymph nodes.

Recommendations

Regarding our outcomes:

-Delineating the outside area of the shoulder (OAR) during treatment planning is strongly recommended in order to prevent excessive doses of radiation and to reduce the volumes of shoulder getting radiation ≥10 gray (V10)

-In order to prevent shoulder morbidity and lymphedema due to breast cancer, patients are advised to have sentinel lymph node biopsy (SLNB) and Target Axillary Dissection (TAD) rather than Axillary Lymph Node Dissection (ALND).

-Being overweight is advised to be avoided while receiving breast cancer treatment.

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