the risk of death due to cardiac reasons at almost 10-15 years after treatment [8].

This study aims to evaluate the cardiotoxcity of two fractionation protocols in the adjuvant setting of breast cancer.

## Patients and Methods

This is a prospective randomized trial conducted at clinical oncology department-Menoufia University the objectives of this study were to compare the cardiotoxcity of hypofractionated protocol *vs.* normal fractionation protocol in post-mastectomy breast cancer patients in adjuvant setting. Between August 2009 and June 2010, 120 patients who were indicated for adjuvant radiotherapy was randomize into two groups each group 60 patient.

**Group A:** conventional fractionation radiation (50 Gy/ 25 fractions/5 weeks, at 2 Gy/fraction).

**Group B:** Hypo-fractionated radiotherapy (HFR) (40 Gy in 15 fractions over 3 weeks, at 2.67 Gy/fraction). Patients were included if female between 18 and 75 years. T2, T3 or T4 primary lesion and N1, N2, N3, Nx, N0 nodal status. Post modified radical mastectomy status.

Metastatic work up including isotope bone scan, chest X-ray and abdominal ultrasound or CT chest and pelviabdomial if indicated. Adjuvant chemotherapy was completed before radiation. Patients were planned on 2D planning system and Treated on Linac machine 6 Mev. Two tangential portals for the chest wall were planned on simulator with central lung distance (CLD) not exceeding 2.5 cm. if indicated direct anterior filed to the supraclavicular and axillary areas was planned.

Echocardiography (ECHO), Electrocardiography (ECG) was performed at base line before chemotherapy, at start of radiotherapy, after 6 months, then annually. Written consent was taken before starting the treatment. Data was statistically described in terms of median, mean and percentages. Independent t test and chi square were used for comparing variables. SPSS program (inc. Chicago, IL, USA) version 16 for windows was used for analysis.

## Results

One hundred and twenty patients were randomized into two groups, the age ranges from (23-70) median 47.5 years group A, and (25-68) median 47 for group B. Both treatment groups were comparable as regard age, performance status, stage, menopausal status. Most of the patients were post-menopausal 70% in group A *vs.* 73.4% in group B (Table 1). At the time of the study Trastuzumab was not available for patients treated with government reimbursement so patients with +ve HER2neu didn't receive it, also most of the patients in two arms received Anthracyclin based regimen without Taxanes (Table 2). There was no significant difference between two fractionation protocols in regard to EF during follow-up; allover median decrease in EF didn't exceed 10% in both groups. However 5 patients has a decrease > 10 but <20% three patients in group A, two patients in group B. After 3 years of follow-up one patient in (group A) develop congestive heart failure patient was 70 years old with uncontrolled hypertension (Table 3). Patients with left sided breast cancer have a significant decrease in EF in correlation with right side in both groups however it didn't exceed 10% (Table 4).

| Parameters | Group A | Group B |
|---|---|---|
| **Age** (mean, median, range) | 48.8, 47.5 (23-70) | 48.5,47, (25-68) |
| **Site** | | |
| Left breast | 32/60 (53.3%) | 35 (58.3%) |
| Right breast | 28/60 (46.7%) | 25(41.7%) |
| **Stage** | | |
| II | 33 (55%) | 35 (58.3%) |
| III | 27 (45%) | 25 (41.7%) |
| **Menopausal status** | | |
| Pre-menopausal | 18 (30%) | 16 (26.6%) |
| Post-menopausal | 42 (70%) | 44 (73.4%) |
| **ER +ve** | 49 (82%) | 52 (87%) |
| HER2neu +ve | 8 (13%) | 10 (17%) |
| HER 2neu not assessed | 15 (25%) | 13 (22%) |
| HER2NEU -ve | 37 (62%) | 37 (61%) |
| **Hypertension** | | |
| Yes | 13/60 (21.7%) | 15/60 (25%) |
| No | 47/60 (88.3%) | 45/60 (75%) |

**Table 1:** Clinico-pathological criteria of both groups.

| Treatment | Group A | Group B |
|---|---|---|
| **Chemotherapy** | | |
| 6 cycles *FEC | 48 (80%) | 45 (75%) |
| 3 cycles FEC followed by 3 DOCETAXEL | 6 (10%) | 4 (7%) |
| **Hormonal treatment** | | |
| T | 15/49 (31%) | 19/52 (36%) |
| Aromatase Inhibitors (AIs) | 34/49 (69%) | 33/52 (64%) |
| ***FEC** (5 Flurouracil, epirubcin, cyclophosamide) | | |

**Table 2:** Types of adjuvant systemic treatment received in both arms.

| | Group A | Group B | P value |
|---|---|---|---|
| **Base Line Ef** | 63.3 | 64.9 | 0.6 |
| **2nd** | 61.9 | 63.2 | 0.1 |
| **3rd** | 60.9 | 62 | 0.1 |
| **4th** | 60.2 | 60.7 | 0.6 |
| **5th** | 59.4 | 59.3 | 0.9 |
| **Last evaluation EF** | 58.8 | 58.1 | 0.6 |

**Table 3:** Correlation of ejection fraction (EF) during follow up between two groups.

| | Right Side (Mean, SD) | Left Side (Mean, SD) | P value |
|---|---|---|---|
| Number of patients | 57/120 | 63/120 | - |
| Base line Ef | 64.5, (SD 4.8) | 63.8, (SD 4.6) | 0.4 |
| 2nd | 63.4, (SD 4.8) | 61.7, (S.D4.5) | 0.04 |
| 3rd | 62.6, (SD 4.8) | 60.6, (SD 4.4) | 0.02 |
| 4th | 61.9, (SD 5.2) | 59.1, (SD 4.6) | 0.003 |
| 5th | 61.1, (SD 5.6) | 57.8, (SD 4.3) | 0.01 |
| Last evaluation EF | 60.6, (SD 5.7) | 56.5, (SD 4.5) | 0.001 |

**Table 4:** Correlation between right side and left side in both groups.

## Discussion

The use of hypofarctionation in the adjuvant setting of breast cancer has gained a lot of popularity during the last two decades. A lot of trials have proven its efficacy and comparable side effects like Start A & Start B trials. It's also proved to be a cost effective protocol especially in developing countries given the lack of adequate numbers of machines.

In our department a number of clinical trials has been started to evaluate the value of hypofractionantion radiotherapy especially post modified radical mastectomy since it's the most common type of operations performed here and since most of the studies done was post breast conservative surgery (BCS). Concerning post radiotherapy side effects there has always been a deep concern about cardio toxicity especially in patients with left sided breast cancer. Due to the contour of the chest wall some Portion of the heart must be included in the

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