International Journal of Multidisciplinary Research and Development
Online ISSN: 2349-4182, Print ISSN: 2349-5979, Impact Factor: RJIF 5.72
www.allsubjectjournal.com
Volume 4; Issue 7; July 2017; Page No. 493-496

Comparative study between conservative breast surgery and modified radical mastectomy in T3 & T4 breast cancer after neo adjuvant chemotherapy

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Abstract
Objective: To study the comparison between breast conservative surgery (CBS) and modified radical mastectomy (MRM) as regard recurrence, metastasis and death in T3 & T4 breast cancer after neo-adjuvant chemotherapy.
Patients and methods: This prospective study was done on 60 patients diagnosed to have locally advanced breast cancer (LABC) received neo-adjuvant chemotherapy randomized into two groups, 30 of them managed by CBS and 30 managed by MRM, and followed up for one years. The preoperative assessment and investigation were done for all patients that underwent the operation.
Results: there is significant difference as regard the age between the two groups. 76.7% of patients were diagnosed by tru-cut needle biopsy and 23.3% of patients were diagnosed by incisional biopsy. 1.7% of patients have well differentiated tumours G1, 71.7% of patients have moderately differentiated tumours G2 and 26.7% of patients have poorly differentiated tumours G3. 76.7% of patients were diagnosed by incisional biopsy. 66.7% of patients have T3 lesion and 33.3% of patients have T4 lesion. 71.7% of patients had IDC, 13.3% of patients had IL and 15% of patients had other. 15% of patients had N0, 35% of patients had N1, 38.3% of patients had N2 and 11.7% of patients have N3. ER was +ve in 70% of CBS patients and 73.3% in MRM patients. PR was +ve in 63.3% of CBS patients, and 66.7% of MRM patients, and HER2 was +ve in 40.9%, and PR was +ve in 31.4% of breast cancer patients.
After one year follow up 10% of patients of CBS had recurrence and in 3.3% of patients of MRM had recurrence. Metastasis was found in 6.7% in CBS patients and 6.7% in MRM patients. Death occurs in 3.3% in CBS patients and 6.7% in MRM patients.
Conclusions: No difference in survival, recurrence and death between CBS and MRM in patients with LABC after neo adjuvant chemotherapy, postoperative chemotherapy and radiotherapy (RTH). So for young patient who is aiming for breast conservative and have LABC we recommend neo adjuvant chemotherapy followed by CBS and post-operative chemotherapy.

Keywords: breast surgery, breast cancer, T3 & T4

Introduction

Breast cancer is characterized by the uncontrolled growth of abnormal cells in the milk producing glands of the breast or in the passages (ducts) that deliver milk to the nipples [1].

Breast cancer treatment options vary depending on the stage of the cancer – its size, position, whether it has spread to other parts of the body and the physical health of the patient. Current treatments for breast cancer include surgery, RTH, chemotherapy, hormonal and targeted therapies. These therapies may be used alone or in combination depending on the stage of the disease [2].

Breast conserving therapy including postoperative irradiation of the remaining breast tissue is generally accepted as the best treatment for the majority of patients with early-stage breast cancer [3].

In recent years, an increasing number of patients with LABC are being treated with neo adjuvant chemotherapy, followed by BCS with axillary dissection and radiation as a part of the multimodality management [4].

The adoption of oncoplastic surgical techniques allows larger tumours to be excised safely without com-promising cosmetic outcomes. Currently, the only absolute contraindications to breast conservation relate to tumours with chest wall involvement, significant skin involvement, and patients with either extensive malignant microcalcifi-cations or inflammatory carcinoma.

Chemotherapy may be given prior to surgery (neo-adjuvant) with the aim of reducing tumour size and the need for extensive surgery, or after surgery (adjuvant) to reduce the chances of the cancer coming back. When the cancer has spread to other parts of the body (metastatic), chemotherapy may be used to reduce symptoms, improve quality of life and extend survival [5].

Neoadjuvant systemic therapy, also referred to as preoperative systemic therapy, describes the sequencing of systemic treatment in advance of local-regional therapy. Although early randomized studies did not show a survival benefit with neoadjuvant chemotherapy as compared to adjuvant chemotherapy several advantages were realized. Notably, these include down-staging of disease in the breast and axilla and the prognostic implications of tumor response [6].

According to the site of the tumor and its biological and pathological characteristics, the multidisciplinary team decides whether or not neoadjuvant chemotherapy is required to reduce the tumor volume before BCS. Marking the tumor before neoadjuvant chemotherapy is recommended, because any cancer downstaging after treatment may alter the initial anatomical landmarks. When microcalcifications are found

over a wide area, the multidisciplinary team will decide along with the patient whether BCS is the best option [7].

Invasive breast carcinoma exhibit a wide range of morphological phenotypes and specific histological types have particular prognostic or clinical characteristics. Infiltrating ductal carcinoma (IDC) is the most common type of invasive breast cancer and accounts for 50 to 70% of invasive cancer [8].

Infiltrating lobular carcinoma (ILC) is the second most common type of invasive breast cancer, accounting for about 5 to 10% of invasive lesions. Medullary carcinoma tends to be a fast growing type but usually does not spread to lymph node; it has been to have a better prognosis than the common IDC [9].

Chemotherapy drugs can be given intravenously (directly into the blood), or orally in a tablet. Chemotherapy is typically associated with adverse side effects such as fatigue, nausea and diarrhea; this is because of its toxic nature and non-specific mode of action, which means that all cells are attacked (even healthy cells) [10].

The management of LABC should be multidisciplinary in nature. Multimodal therapy is generally needed and the timing and nature of treatment will depend whether the disease is confined to operable areas, whether there is involvement of the internal mammary or supraclavicular lymph nodes and above all the general fitness of the patient [11].

Materials and Methods

This prospective study was done on 60 patients diagnosed to have LABC received neo-adjuvant chemotherapy randomized into two groups 30 of them managed by CBS and 30 managed by MRM managed at AL-Husain University Hospital in cairo and al-Azhar university hospital in Assiut during the period from January 2015 to January 2017 and followed up for one year.

Inclusion criteria: Include female patients with LABC (T3 & T4), pathologically proved with age below 60 years old.

Exclusion criteria: Include metastatic cases, morbid obesity, contra-indication to RTH to chest, previous radiotherapy to the chest or axillae, early breast cancer (T1 & T2 lesions), and patients did not give response to neo-adjuvant chemotherapy.

Patients were randomly classified into two groups after receiving neo-adjuvant chemotherapy; 30 patients had CBS and 30 patients had MRM. Preoperative assessments of patients were done; which included detailed history taking, general examination, and local examination. Routine preoperative laboratory investigation was done for all patients, and imaging studies included mammography, breast ultrasound (U/S), chest x-ray (CXR), & pelvi-abdominal U/S.

All patients received chemotherapy in the form of FEC. All patients managed by CBS received post-operative RTH. Patients managed by MRM received post-operative RTH according to histopathological examination. All patients were followed up by detailed history, general and local examination, routine laboratory investigation, imaging studies (mammography and breast U/S, CXR, pelvi-abdominal U/S), bone scan if patient was complaining of bone pain, and histopathology from suspicious lesions by tru-cut needle biopsy.

The results were analyzed statistically

Results

Age of the studied groups were 1.7% of patients <20, 63.3% of patients were 20-40 and 35.0% of patients were>40 years old. Site of the lesion: 41.7% of the patients have their primary site in the right breast and 58.3% of the patients have their primary site in the left breast. 76.7% of patients were diagnosed by tru-cut needle biopsy and 23.3% of patients were diagnosed by incisional biopsy.

Grades of tumour were 1.7% of patients have well differentiated tumours grading of G1, 71.7% of patients have moderately differentiated tumours G2 and 26.7% of patients have poorly differentiated tumours G3 (table 1). T stage of the primary lesion was 66.7% of patients have T staging of T3 lesion and 33.3% of patients have T4 lesion (table 2).

Pathological types were 71.7% of patients had IDC, 13.3% of patients had IL and 15% of patients had other (table 3). N-stage was 15% of patients had N stage of N0, 35% of patients had N1, 38.3% of patients had N2 and 11.7% of patients have N3 (table 4). Margin of the specimen was 10% of patients had positive margins of the specimen and 90% of patients had negative margins (table 5). Post operative RTH was in all cases of CBS and in 73.3% in MRM patients. Receptor status was ER +ve in 70% of CBS patients and 63.3% of CBS patients 66.7% of MRM patients. HER2 was +ve in 16.7% of CBS patients and 20% of MRM patients (table 6). Recurrence of the tumour after one year of follow up was 10% in patients who had CBS and 3.3% of patients who had MRM. Metastasis after one year of follow up was 6.7% in CBS patients and 6.7% MRM patients. Death after one year of follow up was 3.3% in CBS patients and 6.7% in MRM patients (table 7).

Table 1: Grades of the tumour

Grade	CBS	MRM	Total
G1	1 (3.3%)	0 (0%)	1 (1.7%)
G2	20 (66.7%)	23 (76.7%)	43 (71.7%)
G3	9 (30%)	7 (23.3%)	16 (26.7%)
Total	30 (100%)	30 (100%)	60 (100%)

Table 2: T stage of the primary lesion:

T stage	CBS	MRM	Total
T3	21(70%)	19 (63.3%)	40 (66.7%)
T4	9 (30%)	11(36.7%)	20 (33.3%)
Total	30 (100%)	30 (100%)	60 (100%)

Table 3: Pathological types.

Pathological types	CBS	MRM	Total
IDC	23(76.7%)	20(66.7%)	37 (71.7%)
IL	3(10.0%)	5(16.7%)	8 (13.3%)
Other	4(13.3%)	5(16.7%)	9 (15%)
Total	30(100%)	30(100%)	60 (100%)

Table 4: N-stage

N-stage	CBS	MRM	Total
N0	5 (16.7%)	4 (13.3%)	9 (15.0%)
N1	9 (30%)	12 (40%)	21 (35.0%)
N2	15 (50%)	8 (26.7%)	23 (38.3%)
N3	1(3.3%)	6 (20%)	7 (11.7%)
Total	30 (100%)	30 (100%)	60 (100%)

Table 5: Margin of the specimen

Margin	CBS	MRM	Total
Positive	4 (13.3%)	2 (6.7%)	6 (10%)
Negative	26 (86.7%)	28 (93.3%)	54 (90.0%)
Total	30 (100%)	30 (100%)	60 (100%)

Table 6: Receptor status

Receptor	CBS		MRM	
	Positive	**Negative**	**Positive**	**Negative**
ER	21 (70%)	9 (30%)	22 (73.3%)	8 (26.7%)
PR	19 (63.3%)	11 (36.7%)	20 (66.7%)	10 (33.3%)
HER2	5 (16.7%)	25 (83.3%)	6 (20%)	24 (80%)

Table 7: Recurrence, metastasis & death

Data	Recurrence	Metastasis	Death
CBS	3 (10%)	2 (6.7%)	1 (3.3%)
MRM	1 (3.3%)	2 (6.7)	2 (6.7%)

Discussion

The management of LABC should be multidisciplinary in nature, and based on the extent of the disease, as assessed with computed tomography (CT) scanning of chest, abdomen and pelvis, and if required isotope scanning, magnetic resonance imaging (MRI) or positron emission tomography (PET) to detect or confirm metastatic disease. The general principles of the oncological management of LABC are similar to those for less advanced disease and draw on appropriate use of surgery, including plastic and reconstructive techniques, chemotherapy, endocrine treatments and therapy with biological agents targeting specific cellular proteins [11].

The management of breast malignancy and the role of neoadjuvant systemic therapy has continued to evolve over the past 50 years. Survival equivalence with adjuvant systemic therapy is well accepted and demonstrated in several clinical trials [12].

The ability of the neoadjuvant approach to evaluate the in vivo chemosensitivity of the primary tumor has emerged as an important and powerful prognostic tool in understanding individual patient outcome [13].

In this study, we compare CBS to MRM after neo-adjuvant chemotherapy in T3&T4 breast cancer as regard recurrence, metastasis and death. 60 patients diagnosed to have T3&T4 breast cancer after neo-adjuvant chemotherapy randomized into two groups 30 of them managed by CBS and 30 managed by MRM and followed up for one year to detect recurrence, metastasis and death.

In our study 41.7% of the patients have their primary in the right breast and 58.3% of the patients have their primary in the left breast. 1.7% of patients were <20 years, 63.3% of patients were 20-40 and 35% of patients were > 40 years old. This doesn't agree with (Rick Alteri *et al.* 2014) states that the median age is 61 years old; there is significant difference as regard the age because we excluded patients over 60 years old.

In our study 76.7% of patients were diagnosed by tru-cut needle biopsy and 23.3% of patients were diagnosed by incisional biopsy. 1.7% of patients have well differentiated tumours G1, 71.7% of patients have moderately differentiated tumours G2 and 26.7% of patients have poorly differentiated tumours G3. This doesn't agree with (Elbolkainy *et al.*, 2014) who states that G1 18%, G2 37% and G3 45% this significant difference because of small number of cases in our study. 66.7% of patients have T3 lesion and 33.3% of patients have T4 lesion. This doesn't agree with (Elbolkainy et. al, 2014) who states that T1 1.2%, T2 30%, T3 26.4% and T4 42.4% this significant difference because of small number of cases and we excluded early breast cancer in our study.

In our study 71.7% of patients had IDC, 13.3% of patients had IL and 15% of patients had other. This agrees with (Lidija *et al.*, 2005) who states that 75% IDC, 5% ILC and 20% others. 15% of patients had N0, 35% of patients had N1, 38.3% of patients had N2 and 11.7% of patients have N3. This doesn't agree with (Elbolkainy *et al.*, 2014) who states that 25% have N0, this significant difference because we exclude early breast cancer. 10% of patients had positive margin and 90% of patients had negative margin. Post-operative RTH was given to all cases of CBS, and to 73.3% of MRM patient.

In our study ER was +ve in 70% of CBS patients and 73.3% in MRM patients. PR was +ve in 63.3% of CBS patients, and 66.7% of MRM patients, and HER2 was +ve in 40.9%, and PR was +ve in 31.4% of breast cancer patients.

In our study after one year follow up 10% of patients who had CBS had recurrence and in 3.3% of patients who had MRM had recurrence. This doesn't agree with (Lidija *et al.* 2005) who states that after 10 years of follow up 23% recurrence happened in both CBS and MRM. There is significant difference because of the short period of follow up in our study. After one year of follow up, metastasis was found in 6.7% in CBS patients and 6.7% in MRM patients. This doesn't agree with (Lidija *et al.* 2005) who states that after 10 years of follow up metastasis were found in 16.7% in CBS and 13.3% MRM. There is significant difference because of the short period of follow up in our study.

In our study after one year of follow up death occurs in 3.3% in CBS patients and 6.7% in MRM patients. This doesn't agree with (Lidija *et al.* 2005) who states that after 10 years of follow up death occurred in 26.66% in CBS and 30% in MRM. There is significant difference because of the short period of follow up in our study.

Conclusion

In our study, we find no difference in survival, recurrence and death between CBS and MRM in patients with LABC after neo adjuvant chemotherapy, post-operative chemotherapy and RTH. So, for young patient who is aiming for breast conservation and have LABC we recommend neo adjuvant chemotherapy followed by CBS and post-operative chemo-radiotherapy.

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