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# Surgical Management of Female Breast Cancer Patients After Neo-adjuvant Chemotherapy for Infiltrating Duct Carcinoma

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## Abstract

**Background:** Neoadjuvant chemotherapy (NAC) is defined as standard of care for the management of advanced breast cancer and is being used for females with earlier-stage disease, however, this therapy has been confined for those with inoperable breast cancer.

**Aim and objectives:** To assess surgical management of woman breast cancer studied cases after neoadjuvant chemotherapy for infiltrating ductal carcinoma.

**Subjects and techniques:** This research will be carried on 60 female studied cases ranging from 20 to 60 years old, who will be recruited from the surgical oncology department in AL-Hussein and Sayed Galal hospitals and Damanhour Oncology Center, Al-Azhar University hospitals and all patients have invasive ductal carcinoma of the breast.

**Result:** Patients showed remarkable respond to NAC by clinical examination and ultrasonographic investigation in 80% of patients become T2 instead of T3 before NAC. As regards to axillary response to NAC; 5667% of patients become N0.

**Conclusion:** advanced breast cancer represented majority of breast cancer studied cases, who were mostly middle-aged women. Even though the complete clinical response was less in research, neoadjuvant chemotherapy was useful in downstaging tumour in majority of cases. If chemotherapy is regarded before mastectomy, rate of margin positivity in mastectomy specimens can be decreased. Knowing your receptor status can help you predict how you will respond to chemotherapy.

**Keywords:** Breast, Cancer, Carcinoma, Neo-adjuvant chemotherapy, Surgical

## 1. Introduction

**B**reast cancer is invasive cancer in females worldwide. It accounted for 25.2 percent of all cancers diagnosed in females in 2012.<sup>1</sup>

The common type of breast cancer is invasive ductal carcinoma, recognised as infiltrating ductal carcinoma; it accounts for 50 percent to 70 percent of all invasive breast cancers.<sup>2</sup>

Standard therapy for advanced breast cancer is neoadjuvant chemotherapy, which is being used for females with earlier-stage disease.<sup>3</sup> Purpose of neoadjuvant chemotherapy is to shrink irresectable

locally advanced breast cancer (LABC) into operable disease, increasing the possibility of conservative breast surgery.

Neoadjuvant treatment in breast cancer was developed to enable surgery in patients with advanced breast cancer.

It was proved that, in some cases, more conservative approach after NAT may be possible. Furthermore, as described, NAT is excellent scenario for new therapies by Escrivá-de-Romaní et al.<sup>4</sup> this month's problem of Breast Care Based on molecular subtype of breast cancer, NAT may include cytotoxic chemotherapy, hormone therapy, or targeted molecular agents.

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For studied cases with advanced breast cancer, neoadjuvant chemotherapy is 1st line of therapy. Goals include transforming irresectable advanced breast cancer into operable disease.<sup>5</sup> Moreover, it allows for in-vivo monitoring of tumour's chemosensitivity, as well as downstaging of disease in axilla, which eliminates the necessity for axillary therapy in some studied cases. The purpose of the research is to see how neoadjuvant chemotherapy affects different pathological kinds of advanced breast cancer cases. Impacts of neoadjuvant chemotherapy on surgical decision-making before and after neoadjuvant chemotherapy will be compared.<sup>6</sup>

Goal of the work was to evaluate surgical management of woman breast cancer studied cases after neoadjuvant chemotherapy for infiltrating duct carcinoma.

## 2. Studied cases and techniques

This retrospective research contained 60 studied cases who were diagnosed as invasive ductal and invasive lobular carcinoma and had received neoadjuvant systemic therapy, at the Department Of Clinical Oncology and Nuclear Medicine in Damnanhour oncology center.

**Inclusion criteria:** It was decided that only included in this study if she had all of the following criteria: Patient with proven histopathology of locally advanced invasive lobular or invasive ductal carcinoma of the breast, the patient had completed her neoadjuvant chemotherapy with Anthracyclin-based regimen, with or without hormonal therapy according to receptors status, age of patients (20–60) year old and Informed consent taken from the patient that she was contained in the research.

**Exclusion criteria:** studied cases were excluded if they had any of the following criteria: studied cases with early-stage of breast cancer, metastatic breast cancer, medically unfit for surgery and studied cases with histopathology other than breast cancer.

### 2.1. Techniques

Every studied case was exposed to following:

**Comprehensive medical history taking and careful clinical Examination:** For assessment of patient's physical status (PS) and ability to perform surgery.

**Laboratory investigations:** For assessment of liver and kidney functions for preparation for surgery.

**Radiological investigations:** To exclude metastasis by chest X-ray, pelvi-abdominal Ultrasound, and bone scan. Bilateral sonomammography and/or MRI breast when needed for evaluation of breast lesion response to neoadjuvant treatment.

**Surgical treatment:** All patients had been subjected to surgical therapy in form of modified radical mastectomy or conservative breast surgery.

**Modified Radical Mastectomy:** For modified radical mastectomy without immediate reconstruction a transverse elliptical incision, including the tumour mass and nipple areola complex with lateral extension near axilla. Incision planning based on tumour site and must be adjusted accordingly. Incision must not be extended across anterior axillary line to avoid scar contractures that might reduce range of shoulder movement.

Superior to the clavicle, inferior to the superior aspect of the rectus sheath, medially to the sternal border, and laterally to the latissimus dorsi muscle edge, skin flaps are elevated (Fig. 1).

Breast tissue is separated from pectoral muscle using cautery to prevent muscle bleeding. Pectoralis fascia and breast tissue are routinely excluded together.

Mobilization of the breast away from the chest wall can be aided by placing Allis clamps along the superior border of the breast, such as muscle's investing "fascia". With gentle traction, tissue is pulled up or inferiorly Fig. 2.

### 2.2. Conservative breast surgery

**Position:** studied case is lying supine, arms extended on padded arm boards at ninety degrees abduction from the chest wall. Arm positioning with more than 90 degrees of abduction raises the risk of brachial plexus stretching and must be prevented. Ipsilateral arm can be included in the prepared field, allowing it to move throughout the process.

**Incision:** For BCS a transverse elliptical incision including the tumour mass. But, incision planning

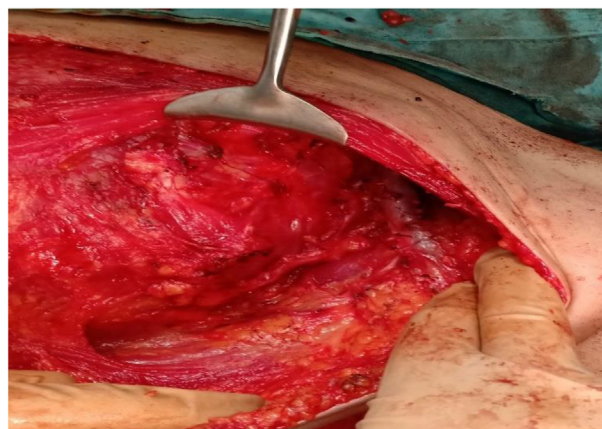


Fig. 1. Mastectomy and axillary dissection.



Fig. 2. Mastectomy closure and drain placement.

depends on the tumour site and must be adjusted accordingly (Figs. 3–5).

**Postoperative clinical follow-up:** Postoperative clinical follow-up was performed at 3 intervals and included breast and axillary palpation. Standard protocol was followed for tumour marker, mammograms, and ultrasonography. When necessary, an MRI is performed.

### 2.3. Statistical analysis

Collected data was revised, coded, tabulated and introduced to PC using Statistical package for Social Science. IBM SPSS Statistics for Windows, Version 20.0. Data was presented and suitable analysis was



Fig. 4. Tumor excision including skin in BCT.

performed based on type of data achieved for every parameter.

### 3. Results

This research conducted on 60 patients, which have been diagnosed as LABC of invasive ductal carcinoma (IDC) type.

All 60 patients received neoadjuvant systemic therapy, at the Department Of Clinical Oncology and Nuclear Medicine; all patients underwent surgery in Damanhour oncology center [Table 1](#).

Based on studied case's age and chronic diseases at time of presentation, the estimated median age



Fig. 3. Incision for BCS.



Fig. 5. Axillary dissection in BCT.

was  $51.52 \pm 6.22$ , BMI reached  $25.75 \pm 2.70$ . HTN, DM and IHD was observed in 36, 26 and 14 patients, respectively [Table 2](#).

All pre-therapeutic core needle biopsies that were confirmed to show invasive breast carcinoma were automatically subjected for automated immunostaining evaluation for estrogen receptor, progesterone receptor and HER-2/neu. 80, 76.67 and 23.33 percent of studied cases were positive for ER, PR and Her2neu [Table 3](#).

Patients showed remarkable respond to NAC by clinical examination and ultrasonographic investigation in 80% of patients become T2 instead of T3 before NAC. As regards to axillary response to NAC; 56.67% of patients become N0 [Table 4](#).

Downstaging achieved in 80% of patients and conservative surgery achieved in 41 cases (68.33%),

Table 1. Show demographic data of all 60 patients (Age, BMI and chronic diseases).

	No. = 60
Age (year)	
Mean $\pm$ SD	51.52 $\pm$ 6.22
Range	37–61
BMI	
Mean $\pm$ SD	25.75 $\pm$ 2.70
Range	24.17–32.93
HTN	
No	24 (40%)
Yes	36 (60%)
DM	
No	34 (56.67%)
Yes	26 (43.33%)
IHD	
No	46 (76.67%)
Yes	14 (23.33%)

BMI, Body Mass Index; DM, Diabetes mellitus; HTN, Hypertension; IHD, Ischemic heart diseases.

Table 2. Status of hormonal receptors and Her-2/neu expression.

	N = 60 No. (%)
ER	
Negative	12 (20%)
Positive	48 (80%)
PR	
Negative	14 (23.33%)
Positive	46 (76.67%)
Her2neu	
Negative	46 (76.67%)
Positive	14 (23.33%)

ER, estrogen receptor; PR, progesterone receptor.

Table 3. Results of clinical response to NAC.

Tumor Stage After NAC	N = 60 No. (%)
T	
T3	12 (20%)
T2	48 (80%)
N	
N0	34 (56.67%)
N1	26 (43.33%)
M	
M0	60 (100%)

NAC, Neoadjuvant chemotherapy.

Table 4. Show downstaging and type of surgery performed.

	N = 60 No. (%)
Down Staging	
No	12 (20%)
Yes	48 (80%)
Type Of Surgery	
MRM	19 (31.67%)
BCS	41 (68.33%)
Local Recurrence	
No recurrence	60 (100%)

BCS, Breast-Conserving Surgery; MRM, Modified radical mastectomy.

the BCS was the main surgical procedure 41 patients (68.33%) and MRM done for 31.67% of patients. No recurrence was observed in any case.

#### 4. Discussion

No guidelines exist to advise physicians on the best approach to cytotoxic chemotherapy prescription in lobular histology. Surgery is still important single intervention in the treatment of breast cancer. Use of NACT in era of multidisciplinary management can have significant effect on the selection of the right operation for the right studied case.<sup>7</sup>

Goal of this research was to evaluate the surgical management of woman breast cancer studied cases who had received neoadjuvant chemotherapy for invasive ductal carcinoma type.

Based on studied case's age and chronic diseases at the time of presentation, the estimated median age was  $51.52 \pm 6.22$ , BMI reached  $25.75 \pm 2.70.30$  (60%) patients had HTN, 22 (44%) had DM and 12 (24%) had IHD.

O'Connor et al.,<sup>8</sup> systematic review was carried out in accordance with PRISMA guidelines. There were researches that reported results between invasive ductal carcinoma IDCs after NACT. Using Mantel-Haenszel technique, dichotomous variables were pooled as odds ratios with 95 percent confidence intervals. *P* values < 0.05 were considered significant. The average years old at time of diagnosis was 51.1.

Alawad et al.,<sup>9</sup> performed research study contained 98 studied cases who viewed with advanced breast cancer and were handled with neoadjuvant chemotherapy between April 2009 and May 2011. Studied case's median years old at the period of diagnosis was 46 (range: 25–71). About 43.9 percent ( $n = 43$ ) of studied cases were from rural areas, whereas 56.1 percent ( $n = 55$ ) were from urban areas.

Ahmed et al.,<sup>10</sup> showed that based on studied case's age and chronic diseases at time of presentation, (the estimated median age was  $50.52 \pm 6.22$  years for IDC. There is no variation among studied groups.

Iqbal et al.,<sup>11</sup> showed that total of 54 studied cases were contained in research after excluding 2 studied cases who received aromatase inhibitors. The median years old of studied cases at period of diagnosis was 46.8 (range: 29–77). Thirty-eight studied cases (70.3%) were older than 40. Thirty-two (59.2%) studied cases were premenopausal at period of diagnosis.

All pre-therapeutic core needle biopsies that were confirmed to show invasive breast carcinoma were

automatically subjected for automated immunostaining evaluation for estrogen receptor, progesterone receptor and HER-2/neu. 40 (80%), 38 (76%) and 12 (24%) studied cases were positive for ER, PR and Her2neu.

Iqbal et al.,<sup>11</sup> showed that thirty-three (61.1%) studied cases were ER/PR positive and 21 (38.9 percent) were ER/PR negative. Expression of c-erb-B2 was identified in 21 (38.9%) of the studied cases. Thirty studied cases had grade-II tumours, while the remaining 24 (44.4%) were grade-III.

Sude et al.,<sup>12</sup> showed that receptor research provided insight into tumour behaviour, with 63 percent of cases having PR negative status, ER and HER-2/neu having nearly equal distribution.

Twenty-one cases (66 percent) of 32 studied cases with nodal disease responded to chemotherapy, which is lower than response rate in primary tumours. Studied cases with LABC who do not have lymph node involvement have better prognosis than those who do.<sup>13</sup>

All patients conducted to our study selected in T3 stage (LABC) tumour size more than 5 cm and all patients have positive axillary LN (N1) by clinical examination and ultrasonographic investigation. No skin manifestation or metastatic lesion.

Alawad et al.,<sup>9</sup> showed that before neoadjuvant chemotherapy, average tumour diameter was 9.6 cm (range 4–18 cm). The axillary nodal status was N0 in three studied cases (3.1 percent), N1 in 22 studied cases (22.4 percent), N2 in 66 studied cases (67.3 percent), and N3 in seven studied cases (7.1 percent). Thirteen (13.3 percent) studied cases had Stage IIIa disease, 77 (78.6 percent) had Stage IIIb disease, and eight (8.2 percent) had Stage IIIc disease.

Iqbal et al.,<sup>11</sup> showed that the tumour size (T) at presentation was T2 = 18 (33.3%), T3 = 27 (50%), T4 = 9 (16.6%), respectively. The nodal status being N0 = 16 (29.6%), N1 = 28 (51.8%) and N2 = 10 (18.5%) respectively. Accordingly 22 (40.7%) studied cases had stage II-B disease, 23 (42.6%) had stage III-A disease and 9 (16.6%) had stage III-B disease respectively.

Patients showed remarkable respond to NAC by clinical examination and ultrasonographic investigation in 40 (80%) patients become T2 instead of T3 before NAC. As regards to axillary response to NAC; 28 (56%) patients of become N0.

Alawad et al.,<sup>9</sup> showed that Following NAC, 33 (33.7 percent) studied cases underwent breast conservative surgery, whereas 49 (66.3 percent) underwent total mastectomy. Axillary lymph node dissection was done on all studied cases. Other sixteen studied cases continued their chemotherapy cycles. 7 studied cases (7.1 percent) had complete

pathological response (PCR), 17 (17.3 percent) had a partial response, and 58 had pathological stable disease. There was no variation in response rates based on disease stage ( $P = 0.036$ ).

Downstaging achieved in (80%) of patients and conservative surgery achieved in 34 cases (68%), the BCS was the main surgical procedure (34 patients 68%) and MRM done for 16 (32%) patients. No recurrence was observed in any case.

Iqbal et al.,<sup>11</sup> showed that while 24 patients (44.4%) had Complete Response, 14 (25.9%) of studied cases had partial response to neoadjuvant chemotherapy, whereas 16 (29.6%) studied cases had poor response to chemotherapy. Two patients developed febrile neutropenia. Complete PCR was achieved in 18 (33.33%) patients.

Several other studies such as Mohamed et al.,<sup>13</sup> in studied cases with advanced breast cancer, overall objective response of primary tumour ranged from 71 to 87 percent.

Another research by Tamer et al.,<sup>14</sup> Overall response rates to neoadjuvant chemotherapy were 54.5 percent (CR 3 percent and PR 51.5 percent). According to Kim et al.,<sup>15</sup> the overall response rate to neoadjuvant chemotherapy is 60 percent (4 percent CR and 56 percent PR).

Sude et al.,<sup>12</sup> showed that in their research of 70 studied cases, 18 (26 percent) underwent upfront surgery, while the rest 52 (74 percent) obtained neoadjuvant chemotherapy followed by surgery. All studied cases received neoadjuvant anthracycline chemotherapy: FEC100, the median number of cycles was 3 (extremes 2–6), and the median time between the last cycle of chemotherapy and surgery was 36 days.

Complete response was seen in 9 percent of cases, which is lower than showed by Taucher et al.,<sup>16</sup> (12%) and Hortobagyi et al.,<sup>15</sup> (17%). Unfortunately, there was no complete PCR, which could be attributed to late stage of the presentation. Based on National Surgical Adjuvant Breast and Bowel Project trial, adding taxanes and extending cycles could have resulted in greater response rates.

#### 4.1. Limitations

Our research has some limitations. Despite the benefit of prospective design, a smaller sample size in research may have impacted the precision of outcomes. Immunotherapy and radiotherapy might not be included in our research because of logistical issues and lack of availability at our institute, which may have impacted our findings. Detailed assessment of response difference between breast cancer molecular subtypes was not possible.

#### 4.2. Conclusion

Advanced breast cancer represented majority of breast cancer studied cases, who were middle-aged women. Even though the complete clinical response was lower in our research, neoadjuvant chemotherapy was impactful in downstaging tumour in majority of cases. If chemotherapy is regarded before mastectomy, rate of margin positivity in mastectomy specimens may be decreased. Knowing your receptor status can help you predict how you will respond to chemotherapy [Table 3](#).

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The authors have no financial interest to declare in relation to the content of this article.

#### Authorship

All authors have a substantial contribution to the article.

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#### Conflicts of interest

The authors declared that there were NO conflicts of Interest.

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