Journal of American Science

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MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

New Trends in Management of Locally Advanced Breast Cancer

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Abstract: Background: The term locally advanced breast cancer (LABC) encompasses a heterogeneous group of breast neoplasms. In the last revision of the American Joint Committee on Cancer (AJCC) staging system, all of stage III disease is considered locally advanced, including cases with involvement of supraclavicular lymph nodes and which often are initially inoperable (T4N2-3). Aim of the work: We aimed to study the new trends in management of locally advanced breast cancer. Patients and Methods: This is a prospective study included 50 female patients of locally advanced breast cancer. Some of them exposed to surgery and other exposed to neo adjuvant treatment then surgery. All patients subjected to full history, clinical examination, investigation (imaging evaluation, tumor markers and routine preoperative laboratory investigation) and treatment (modified radical mastectomy or conservative mastectomies). Results: Our results showed that, patients who received NAC, have down staging from stage II to stage I occurred in 10 (35.7%) patients, Conservative Mastectomy done in 19 (67.9%) patients and Modified Radical Mastectomy done in 9 (32.1%). Also, postoperative complications were higher in surgery group than NAC then surgery with statistically significant difference between groups (p =0.008). Recurrence was higher in surgery group (22.7%) than NAC then surgery group (10.7%) with high statistically significant difference between groups (p <0.001). Conclusion: We can conclude that, in cases selected by clinical and radiologic findings with a satisfactory response to NAC, breast conservative surgery is feasible and safe for the treatment of locally advanced tumors, provided that the tumor is completely resected, surgical margins are clear, and patients are subjected to complementary multimodal treatment.

[Mohamed Abd El Hamed Yakoup, Mahamed Abo Elfetoh Masoad , Ashraf Ebrahiem El Sharkawey, Mohamed Shehata Zarad. **New Trends in Management of Locally Advanced Breast Cancer**. *J Am Sci 2021;17(11):1-10]. ISSN 15451003 (print); ISSN 23757264 (online). http://www.jofamericanscience.org*. 1.
doi: 10.7537/marsjas171121.09.

Keywords: Breast Cancer; Trend; Management

1. Introduction

Breast cancer is the most common invasive cancer in women, and the second main cause of cancer death in women, after lung cancer ***(Adams et al., 2017).***

Breast cancer starts when cells in the breast begin to grow out of control. These cells usually form a tumor that can often be seen on an x-ray or felt as a lump. The tumor is malignant (cancer) if the cells can grow into (invade) surrounding tissues or spread (metastasize) to distant areas of the body. Breast cancer occurs almost entirely in women, but men can get breast cancer ***(Adams et al., 2017).***

Breast cancers can start from different parts of the breast. Most breast cancers begin in the ducts that carry milk to the nipple (ductal cancers). Some start in the glands that make breast milk (lobular cancers). There are also other types of breast cancer that are less common ***(Carmichael et al., 2016).***

Breast cancer can spread when the cancer cells get into the blood or lymph system and are carried to other parts of the body. The lymph system is a network of lymph (or lymphatic) vessels found throughout the body that connects lymph nodes (small bean-shaped collections of immune system cells). The clear fluid inside the lymph vessels, called lymph, contains tissue byproducts and waste material, as well as immune system cells. The lymph vessels carry lymph fluid away from the breast. In the case of breast cancer, cancer cells can enter those lymph vessels and start to grow in lymph nodes. Most of the lymph vessels of the breast drain into: lymph nodes under the arm (axillary nodes), lymph nodes around the collar bone (supraclavicular [above the collar bone] and infraclavicular [below the collar bone] lymph nodes), lymph nodes inside the chest near the breast bone (internal mammary lymph nodes) ***(Carmichael et al., 2016).***

Locally advanced breast cancer is a term that refers to most advanced-stage nonmetastatic breast tumors and includes a wide variety of clinical scenarios. These tumors remain a difficult clinical problem as most patients with locally advanced disease will experience disease relapse and eventual death. Investigators have often differed in their precise

definition of locally advanced breast cancer. We define any tumor that is greater than 5 cm or that involves the skin or chest wall as locally advanced. Locally advanced disease also includes patients with fixed axillary lymph nodes or ipsilateral supraclavicular, infraclavicular, or internal mammary nodal involvement. Thus, all of stage III disease is considered locally advanced, as is a subset of stage IIB (T3N0) ***(Singletary et al., 2010).***

Inflammatory breast cancer is a distinct clinical subtype of locally advanced breast cancer, with a particularly aggressive behavior and poor prognosis. Clinically, inflammatory breast cancer typically presents with the rapid onset of breast erythema, warmth, and edema, often without a discrete underlying mass. The swelling of the breast can be quite pronounced, producing significant tenderness. The characteristic pathology is invasion of the dermal lymphatic by tumor emboli, which results in blockage of the breast lymphatics and can lead to breast edema. Neglected locally advanced breast cancer can develop secondary inflammatory characteristics, but should be distinguished from primary inflammatory carcinoma as these secondary inflammatory breast cancers may follow a more indolent course and can be treated as other locally advanced breast tumor ***(Hortobágyi et al., 2010).***

If breast cancer is suspected, a biopsy is necessary to confirm the diagnosis. Estrogen-receptor (ER) and progesterone-receptor (PR) status, HER-2/neu status, p53 status, nuclear grade, and Ki67 can all be determined from either fine-needle aspiration or core biopsy. For women with stage III disease, the recommended evaluation includes: history and physical examination; laboratory evaluation with CBC, platelets, and liver enzymes; diagnostic bilateral mammogram and ultrasound as necessary; chest x-ray; pathology review, determination of ER, PR, and HER-2 status; optional breast magnetic resonance imaging (MRI), if borderline candidate for breast conservation; bone scan; and abdominal computerized tomography (CT) scan, ultrasound, or MRI. These tests will establish the extent of disease for further treatment planning ***(Carter et al., 2006).***

The prognostic factors for locally advanced tumors are similar to the prognostic factors for earlier stage breast cancer, with lymph node status and tumor size having the strongest effects on survival. Most patients with locally advanced disease have axillary lymph nodes involved with their tumors, but a subset of patients has large primary tumors without lymph node involvement. The prognosis for patients without lymph node metastases is better than for those patients with lymph node involvement. For patients with lymph node metastases, a greater number of lymph nodes involved and higher nodal stage predict poorer survival. The size of the primary tumor also is associated with survival; patients with larger cancers have poorer survival rates ***(Carter et al., 2006).***

Patients who were treated with primary radiotherapy also had a high risk for disease recurrence and death, as well as the complications of chest wall fibrosis, brachial plexopathy, lymphedema, skin ulceration, and skin necrosis ***(Spanos et al., 2005).***

Neoadjuvant chemotherapy was pioneered in the setting of locally advanced breast cancer. The administration of systemic chemotherapy prior to definitive local therapy is advantageous for women with locally advanced disease, since induction chemotherapy can render inoperable tumors (stage T4, N2, or N3) resectable and can increase rates of breast-conserving therapy ***(Swain et al., 2010).***

The surgical options for patients with locally advanced breast cancer include radical mastectomy, modified radical mastectomy, and breast-conserving surgery. Studies have demonstrated that radical or modified radical mastectomy as a single treatment modality leads to local relapse rates ranging from 20% to 50%, with a 5-year overall survival of only 30% to 40% and a 10-year overall survival of approximately 20% to 30% ***(Heys et al., 2011).***

Locoregional control has traditionally been achieved using mastectomy and postoperative radiotherapy. Historically, breast conservation has not been a treatment option for women with stage III disease. Recently, however, the use of induction chemotherapy has allowed increasing numbers of patients to undergo breast-conserving surgery ***(Beahrs et al., 2010).***

Breast conserving surgery numerous investigators: The absolute and relative contraindications to breast-conserving surgery are first- or second-trimester pregnancy, more than one malignancy in separate quadrants of the breast or diffuse malignant or indeterminate microcalcifications.

History of prior therapeutic radiation to the involved breast large tumor in a breast in which adequate resection would cause significant cosmetic deformity; and Subareolar location, which may result in suboptimal cosmesis due to the removal of the nipple-areolar complex ***(Winchester et al., 2007).***

Clinically suspicious mobile axillary lymph nodes or microscopically involved axillary nodes are not considered contraindications to breast-conserving surgery. Beside the usual radiotherapeutic contraindications, additional surgical concerns must be considered when a patient is evaluated for breast-conserving surgery ***(Winchester et al., 2007).***

Axillary Dissection: The prognosis of patients with locally advanced breast cancer is related to nodal status, size of the primary lesion, and estrogen/progesterone receptor status. Axillary node

status, the single most important prognostic indicator, still requires axillary dissection with histologic examination for definitive diagnosis. With breast-conserving surgery, axillary dissection is generally done through a separate axillary incision for better cosmesis ***(Schnitt et al., 2006).***

The extent of the axillary dissection depends on the extent of disease. A level I and II dissection is appropriate for most invasive tumors, with a minimum of six lymph nodes required to adequately sample the axilla. Levels I, II, and III lymph nodes that contain obvious disease are removed. The long thoracic, thoracodorsal, and medial pectoral nerves are preserved routinely ***(Bedwinek, 2008).***

Retrospective data demonstrate improved disease-free and overall survival for patients with stage IIIA or IIIB disease who received chemotherapy, surgery, and radiation therapy, as compared with those treated with surgery and radiation therapy alone. Although standard practice for managing patients with locally advanced breast cancer has been the use of local therapy combined with systemic treatment in the form of chemotherapy plus hormonal therapy, numerous trials have attempted to determine appropriate sequencing of these modalities and optimal specific therapies to employ in combined-modality regimens ***(Klassen et al., 2010).***

Hormonal manipulation has a response rate of approximately 30% to 40%. Chemotherapy can be administered as induction (preoperative or neoadjuvant) therapy, concurrent with radiotherapy, or as adjuvant therapy. The overall response rate to systemic chemotherapy is approximately 50% to 90%, with an overall survival of about 50% to 80% at 3 years and 30% to 50% at 5 years; median survival is approximately 3 to 4 years ***(Klassen et al., 2010).***

The administration of preoperative chemotherapy after a diagnosis of breast cancer has several theoretical advantages and disadvantages. The long-term effects of this approach on locoregional control and overall survival have yet to be defined. Preoperative chemotherapy has been used extensively in operable and inoperable locally advanced breast cancer with the goals of reducing tumor and facilitating local treatment via breast-conserving surgery or mastectomy and radiation therapy ***(Seidman et al., 2011).***

Aim of the Work

The aim of this work is to study the new trends in management of locally advanced breast cancer. Which Some Patient Start Neo adjuvant Chemotherpy Other Start Surgery. Follow up which is better results and prognosis.

2. Patients and Methods

This prospective study will include 50 female patients of breast cancer. A written informed consent was taken from all participants after proper explanation of study .Some of them exposed to surgery and other exposed to neo adjuvant treatment then surgery. Locally advanced breast cancer is further divided into “operable” or “inoperable” based on the probability of achieving negative margins on histopathologic examination after an initial surgical approach that would provide long-term reduction in locoregional recurrence.

Criteria of locally advanced breast cancer.

The definition includes breast cancer that fulfils any of the following criteria in the absence of distant metastasis:

- Tumors more than 5 cm in size with regional lymphadenopathy (N1–3)
- Tumours of any size with direct extension to the chest wall or skin, or both (including ulcer or satellite nodules), regardless of regional lymphadenopathy
- Presence of regional lymphadenopathy (clinically fixed or matted axillary lymph nodes, or any of infraclavicular, supraclavicular, or internal mammary lymphadenopathy) regardless of tumor stage

1. Excluded patient

I- Tumor:

Bilateral & multi-focal disease, central lesions (surgery will cause bad cosmetic appearance), paget's disease of the nipple, tumor < 4 cm or small breast, distant metastasis, fixed to muscle, high grade (grade III).

II- Patient:

Pregnancy, patient preference, contraindication to irradiation e.g. SLE, previous irradiation.

III- Breast relatively small in size.

2. Non locally advanced breast cancer.
3. Inflamatory Carcinomatosis.
4. Patient with supra clavicular involvement.
5. Skin lesions: skin nodules, sister joseph nodules, cancer en cuirasse, skin ulceration, Brawnv edema, Extensive breast edema

All patients of this study exposed to: clinical evaluation, laboratory diagnosis, imaging evaluation, tissue diagnosis.

1- Clinical Evaluation: History, personal History, complaint, present History, past History, family history, menstrual history, physical examination, general examination, local examination,

6. **Laboratory Diagnosis:** tumor markers: CA15-3 and CEA, for preoperative preparation, CBC, RBS, LFTs, KFTs.
7. **Imaging Evaluation:** mammography, ultrasound, X-ray Chest, bone Scan, pet scan if needed, Ct scan if needed.

3. Tissue Diagnosis: fine needle aspiration (FNA), core biopsy, frozen section, exional biopsy, incional biopsy, treatment

a. ***Modified radical mastectomy:*** Other patients will go

b. ***Conservative mastectomies:*** Lumpectomy, quadrantectomy, partial mastectomy or segmental mastectomy.

3. Results

This prospective study included 50 female patients of breast cancer. Some of them exposed to surgery alone (22 case) and other exposed to neoadjuvant chemotherapy (NAC) then surgery (28 cases).

Table 1: Demographic data of studied patients

	Surgery alone (n=22)	NAC and Surgery (n=28)	*Mann Whitney test*	*P* value
Age (year)				
- **Mean +SD**	58.50+11.75	48.64+11.89	1.252	0.246
- **Range**	39-78	22-66		
BMI (m2/kg)				
- **Mean +SD**	24.6+7.28	24.6+7.28	0.832	0.515
- **Range**	22-25.5	22-25.5		
Tumor size (cm)				
- **Mean +SD**	3.45+0.73	3.21+1.03	1.492	0.721
- **Range**	2-5	2-5		

This table showed that no statisticaly significant difference between surgery alone and NAC then surgery as regard to age, BMI and tumor size.

Table 2: Distribution of patients regarding side of tumor

	Surgery alone (n=22)	NAC and Surgery (n=28)	*X2* test	*P* value
	No (%)	No (%)		
Right	9 (40.9%)	15 (53.6%)		
Left	13 (59.1%)	13 (46.4%)	0.365	0.273

X^2: chi-square test

Regarding side of tumor, the most of surgery group (15 patients) have the tumor in right side while in NAC and surgery group was equal in both side (13 patients) with no statistically significant difference between both groups.

Table 3: Distribution of patients regarding site of tumor

	Surgery alone (n=22)	NAC and Surgery (n=28)	*X2* test	*P* value
	No (%)	No (%)		
Upper outer quadrant	7 (31.8%)	8 (28.6%)	1.511	0.825
Upper inner quadrant	5 (22.7%)	9 (32.1%)		
Lower outer quadrant	6 (27.3%)	6 (21.4%)		
Lower inner quadrant	2 (9.1%)	4 (14.3%)		
Lower lateral quadrant	2 (9.1%)	1 (3.6%)		

X^2: chi-square test

This table showed that no statistically significant difference between surgery alone and NAC then surgery as regard to site of tumor.

Table 4: Distribution of patients regarding histopathology

	Surgery alone (n=22)	NAC and Surgery (n=28)	Total	*X2* test	*P* value
	No (%)	No (%)	No (%)		
Invasive duct carcinoma (IDC)	19 (86.4%)	23 (82.1%)	42(84%)		
Invasive lobular carcinoma (ILC)	3 (13.6%)	5 (17.9%)	8(16%)	21.625	**<0.001****

X^2: chi-square test; ***high significant*

The majority of patients in surgery group (86.4%) and NAC then surgery group (82.1%) were Invasive duct carcinoma with statistically significant difference between groups ($p < 0.001$).

Table 5: Tumor stage of both groups at time of presentation

		Surgery alone (n=22)	NAC and Surgery (n=28)	*X2* test	*P* value
		No (%)	No (%)		
T	T1	10 (45.5%)	8 (28.6%)	1.247	0.418
	T2	12 (54.6%)	20 (71.4%)		
N	N0	15 (68.2%)	18 (64.3%)	0.813	0.214
	N1	7 (31.8%)	10 (35.7%)		
M	M0	22 (100.0%)	28 (100.0%)	0.216	0.735

X^2: chi-square test

This table showed that no statistically significant difference between surgery alone and NAC then surgery as regard to T N M classification.

Table 6: Down staging and type of surgery performed in patients who received NAC

NAC and Surgery (n=28)		
		No (%)
Down Staging		10 (35.7%)
Type of Surgery	Modified Radical Mastectomy	9 (32.1%)
	Conservative Mastectomy	19 (67.9%)

In patients who received NAC, down staging from stage II to stage I occurred in 10 (35.7%) patients, Conservative Mastectomy done in 19 (67.9%) patients and Modified Radical Mastectomy done in 9 (32.1%).

Table 7: Distribution of patients regarding type of operation

Surgery alone (n=22)		NAC and Surgery (n=28)	*X2* test	*P* value
Right conservative mastectomy	No (%)	No (%)		
	3(13.6%)	10 (35.7%)		
Left conservative mastectomy	2 (9.1%)	9 (32.1%)		
Right Modified Radical Mastectomy	6 (27.3%)	5 (17.9%)	11.020	**0.012***
Left Modified Radical Mastectomy	11(50.0%)	4 (14.3%)		

X^2: chi-square test; significant p value*

Regarding type of operation, majority of patients in surgery group have Modified Radical Mastectomy either right (27.3%) or left (50.0%) while patients in NAC then surgery group have conservative mastectomy either right (35.7%) or left (32.1%) with statistically significant difference between groups (p =0.012).

Table 8: Distribution of patients regarding Postoperative complication

	Surgery alone (n=22)	NAC and Surgery (n=28)	*X2* test	*P* value
	No (%)	No (%)		
Seroma	18 (81.8%)	18 (64.3%)	10.227	**0.008****
Infection	4 (18.2%)	1 (3.6%)		
No	0 (0%)	9 (32.1%)		

*X^2: chi-square test; **high significant*

Postoperative complications were higher in surgery group than NAC then surgery with statistically significant difference between groups (p =0.008).

Table 9: Distribution of patients regarding recurrence

	Surgery alone (n=22)	NAC and Surgery (n=28)	*X2* test	*P* value
	No (%)	No (%)		
Recurrence	5 (22.7%)	3 (10.7%)	15.862	**<0.001****

*X2: chi-square test; **high significant*

This table showed that recurrence was higher in surgery group (22.7%) than NAC then surgery group (10.7%) with high statistically significant difference between groups ($p < 0.001$).

4. Discussion

Breast cancer, a clinically common female malignant tumor with an increasing incidence in recent years, has now ranked the first among all female malignant tumors ***(Torre et al., 2015).***

Currently, it is widely believed that breast cancer is a systemic disease that is highly prone to metastasis. Locally advanced breast cancer (LABC) mainly refers to breast cancer with diameter of primary tumor lesions less than 4 cm (T3), skin and chest wall adhesion (T4) or regional lymph node fusion (N2) ***(Vieira et al., 2015).***

Studies have shown that the proportion of LABC is relatively high in new-onset breast cancer, and even reached more than 25% in developing countries. Although LABC has no distant metastatic lesion, its primary tumor lesion is large usually; so it is mainly treated with modified radical mastectomy. However, postoperative tumors tend to remain on the chest wall and skin edge, which leads to a high recurrence rate ***(Caudle et al., 2014).***

In recent years, the treatment of LABC has made great progress with the development of neoadjuvant chemotherapy, Neoadjuvant chemotherapy can degrade the clinical stages for patients, improve the surgical resection rate, facilitate the clarification of the sensitivity of chemotherapy drugs to treat tumors, and control the potential micrometastasis to prevent distant metastasis ***(Arowolo et al., 2013).***

Neoadjuvant chemotherapy (NAC) is increasingly used to treat patients with locally advanced breast cancer (LABC). Such regimens can increase rates of breast-conserving therapy (BCT) compared with post-operative chemotherapy and may minimize the need for aggressive nodal surgery with axillary lymph node dissection ***(Desantis et al., 2016).***

Other purported advantages include in vivo tumor response assessment and prognostication based on degree of response. Patients with HER2-receptor positive or triple-negative disease may also benefit from early treatment of distant micrometastases due to increased metastatic potential of these disease types ***(Deng et al., 2016).***

Despite these potential advantages, NAC has not demonstrated improved survival over adjuvant chemotherapy in randomized trials. From clinical, biological and pathologic perspectives, locally advanced breast cancer (LABC) represents a relatively heterogeneous group of tumors ***(Carrara et al., 2017).***

Although neoadjuvant chemotherapy (NC) does not increase the survival rates, it is used to improve tumor resection, increase the rates of breast conservative surgery (BCS), and identify patients with better prognoses, that is, patients who exhibit a pathologic complete response (pCR) ***(Straver et al., 2017).***

The aim of our study was to study the new trends in management of locally advanced breast cancer.

Our prospective study included 50 female patients of breast cancer. Some of them exposed to surgery alone (22 case) and other exposed to neoadjuvant chemotherapy (NAC) then surgery (28 case). As regarding Demographic data of studied patients, no statistically significant difference between surgery alone and NAC then surgery as regard to age, BMI and tumor size.

The age range in our study was 39-78 in Surgery alone group and 22-66 in NAC and Surgery. This is near what was reported by ***Harford (2011); Carrara et al. (2017), Corbex and Harford (2013).***

This incidence is near to the report of Elattar (2005), published by the National Cancer Institute of Egypt, which estimated that the mean age was 49 years, and the study done by Thompson and associates (2007) who mentioned that the mean age of patients was 49.7 years old (range 26-69 years).

A higher frequency of early onset female BC has been observed in low/middle income countries (LMIC) than in high income countries (HIC), with an observed median age for female BC diagnoses in HIC about a decade higher than in LMIC, such as some Arab or Asian countries. This observation has indicated the need to lower the age of entry into mass BC screening programs in LMIC ***(Chouchane et al., 2013).***

It is therefore important to identify factors associated with risk and outcome. Whilst breast cancer occurs equally in the right and left breasts, tumours most commonly affect the upper outer quadrant (UOQ) of the breast. However, there is only limited information as to whether the incidence has changed over time ***(Aljarrah et al., 2014).***

Numerous clinical studies, dating back decades, have shown that the upper outer quadrant (UOQ) of the breast is the most frequent site of carcinoma, but an adequate explanation for this asymmetric occurrence of breast cancer within the breast has never been established. This basic observation has become textbook fact and remains true for countries as different as India, the West Indies, and Italy and irrespective of race within any one country ***(Darbre et al., 2015).***

Furthermore, the UOQ is not only the most common site for cancer but also, in many benign breast conditions, fibroadenomas, breast cysts, and phyllodes tumours. The UOQ is also the most frequent site of male breast cancer. However, it is interesting to note that the reported incidence of

breast cancer in the UOQ of the breast appears to rise disproportionately with year of publication. In 1926, 30.9% of breast cancer was reported to be in the UOQ but reports between the years 1947–1967 suggested that the proportion of breast cancer in the UOQ was 43–48%. A study in 1994 reported 60.7% of breast cancers in the UOQ. Most of these studies are old. In a recent study in the UK, the distribution was as following, 52.5% of the cases were in the UOQ of the breast ***(Aljarrah et al., 2014).***

Previously reported studies using surveillance, epidemiology, and end-results data showed that tumors with inner quadrant locations had a negative effect on breast cancer-specific and OS rates. In addition, according to several studies with respect to tumor location as a prognostic factor, inner quadrant tumors showed higher distant metastases and lower OS rates than those shown by outer quadrant tumors ***(Wong et al., 2015).***

In our study, regarding side of tumor, the most of surgery group (15 patients) have the tumor in right side while in NAC and surgery group was equal in both side (13 patients) with no statistically significant difference between both groups. Also no statistically significant difference between surgery alone and NAC then surgery as regard to site of tumor, while most of the tumors were located in Upper outer quadrant (15), followed by Upper inner quadrant (14). This matches with ***Skandalakis et al., (2006) and Hunt et al., (2010)*** who reported that the upper outer quadrant contains the main bulk of breast tissue and thus it is the most usual site for both breast cancer and most benign breast pathologies.

In our study, as regarding histopathological type, The majority of patients in surgery group (86.4%) and NAC then surgery group (82.1%) were Invasive duct carcinoma with statistically significant difference between groups ($p < 0.001$).

Invasive ductal carcinoma (IDC), sometimes called infiltrating ductal carcinoma, is the most common type of breast cancer. About 80% of all breast cancers are invasive ductal carcinomas. This coincides with ***Weidong et al., (2011)*** who found that IDC or IDC with associated DCIS, and breast cancer with invasive micropapillary carcinoma (IMPC) component are the most frequent tumor types.

NAC allows assessment of the individual's biological response to chemotherapy. Overall clinical tumor shrinkage has been reported in 70–80% of NAC breast cancer patients, tumor shrinkage occurred in 79% and the overall pCR rate was 28% with a range from 6% in ER/PR positive/Her2 negative breast cancers to 47% in TNBCs ***(Minckwitz et al., 2012).***

NAC reduces the amount of breast tissue removed in breast-conserving procedures and this correlates with better cosmetic outcomes. This is particularly important in patients who are marginal for BCS prior to NAC. While pCR is desirable, our owned at a demonstrates that it is not necessary in order to avoid mastectomy. As noted, NAC-induced tumor shrinkage was achieved in 79% of our patients. In 16 of 51 patients, NAC was used with the specific aim of enabling BCS. Eleven subsequently had successful BCS (69%) but only four of these women had a pC ***(Brennan et al., 2013).***

In our study, NAC facilitates the use of BCS in achieving local control in the studied cases. In patients who received NAC, down staging from stage II to stage I occurred in 10 (35.7%) patients, Conservative Mastectomy done in 19 (67.9%) patients and Modified Radical Mastectomy done in 9 (32.1%).

These was consistent with ***Carrara et al. (2017),*** who reported Of the 449 patients who received neoadjuvant chemotherapy, 98 underwent breast-conserving surgery. The average diameter of the tumors was 5.3 cm, and 87.2% reached a size of up to 3 cm. Moreover, 86.7% were classified as clinical stage III, 74.5% had T3-T4 tumors, 80.5% had N1-N2 axilla, and 89.8% had invasive ductal carcinoma. A pathologic complete response was observed in 27.6% of the tumors, and 100.0% of samples had free margins. The 5-year actuarial overall survival rate was 81.2%, and the mean follow-up was 72.8 months. They concluded that, NAC followed by Breast-conserving surgery is a safe and effective therapy for selected locally advanced breast tumors.

Preoperative neoadjuvant chemotherapy in combination with BCS scheme can reduce the difficulty of operation, improve the curative effect of patients, significantly improve the prognosis of patients and prolong the survival time, which is worth clinical application ***(Zhao et al., 2015).***

For patients with LABC, the primary tumor lesions are usually large, and the effect of surgical treatment is not ideal. Some patients are easily influenced by the skin invasion, tumor chest wall fixation, axillary lymph node fusion and other factors, resulting in the inability to surgery and severely affecting the prognosis ***(Ozmen et al., 2015).***

The treatment of LABC has made great progress with the development and promotion of neo adjuvant chemotherapy, and neo adjuvant chemotherapy mainly aims to minimize the volume of tumors and reduce the preoperative clinical stages of breast cancer by administering chemotherapy to patients before surgery so that favorable conditions for surgery can be created and the surgical results can be improved ***(Nabholtz et al., 2016).***

NAC in the study of ***(Klein et al., 2019)*** resulted in improved survival but were not associated with decreased LRC. Patients who achieve a pathologic complete response (pCR) to

NAC have improved survival compared to patients who do not achieve pCR.

Our results also came in agreement with ***(Wang et al., 2017),*** who reported that, This study, with main focus on inoperable LABC, investigated the values of NAC in converting inoperable LABC into operable status and assessed the prognosis. Sixty-one patients with inoperable LABC were initially treated with neoadjuvant chemotherapy; their local conditions were improved to operable status. Radical surgery was exerted on 49 patients. Original chemotherapy was performed after surgery, followed by local radiotherapy. And endocrine therapy was optional according to the hormone receptor status.

In our study, Regarding type of operation, majority of patients in surgery group have Modified Radical Mastectomy either right (27.3%) or left (50.0%) while patients in NAC then surgery group have conservative mastectomy either right (35.7%) or left (32.1%) with statistically significant difference between groups (p =0.012).

This proves the importance of NAC as an important line of treatment in LABC. Increasing the chance of operability and the use of BCS. ***Jeon et al. (2017)*** reported that the application of neo adjuvant chemotherapy in the treatment of LABC could degrade the clinical stages to benefit surgery and clearly understand the sensitivity of breast cancer to chemotherapy drugs.

As regarding Distribution of patients regarding Postoperative complication, Postoperative complications were higher in surgery group than NAC then surgery with statistically significant difference between groups (p =0.008). This is concordant with ***Klein et al. (2019)*** who reported less complications in patients underwent NAC followed by surgery.

Also ***Carrara et al. (2017),*** reported that Breast-conserving surgery is a safe and effective therapy for selected locally advanced breast tumors with less reported post-operative complications.

SEER data evaluated for tumors more than 5 cm indicated that breast cancer specific survival did not differ between patients who received BCS and patients who underwent a mastectomy, but the women in this study were older, the IBTR and molecular subtype were not evaluated, and few patients received NC ***(Bleicher et al., 2016).***

The rate of conservative surgery after NC varies from 37% to 82%; however, only 1.7% to 28% of patients exhibit LABC. The LABC candidates who were initially selected were patients without skin or chest wall involvement and who were free of multicentric disease or extensive microcalcifications. They harbored tumors smaller than 5 cm, exhibited favorable tumor localization, had no contraindications for radiotherapy, and had negative margins. Primary inflammatory carcinoma is a contraindication for BCS ***(Houssami et al., 2016).***

Conclusion

We can conclude that, in cases selected by clinical and radiologic findings with a satisfactory response to NAC, breast conservative surgery is feasible and safe for the treatment of locally advanced tumors, provided that the tumor is completely resected, surgical margins are clear, and patients are subjected to complementary multimodal treatment.

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11/2/2021