



Retrospective study of the effect of neo-adjuvant chemotherapy as primary treatment of advanced Breast cancer and its effect on surgical modalities.

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Abstract:

Aim of the work: neoadjuvant chemotherapy in downstaging of each the primary tumor and axillary disease, reach pathological complete response to neo-adjuvant remedy have had a marked effect on loco-regional remedy concerns, boom opportunities facilitating surgical intervention compare its impact on surgical management of breast cancers either mastectomy or BCS.

Patients and Method: This retrospective study is carried out on one hundred female patients with documented breast cancer, examined in the medical oncology department & nuclear medicine remedy Sohag University Hospital and sohag cancers institute, at the period from (2013 - 2018).

Results: Number of patients identified before receiving neo-adjuvant chemotherapy as T2 become 15 instances (15%), 32 cases (32%) become T3, 24 cases (24%) was T4a, 24 instances (24%) T4b, 3 instances (three%) changed into T4c and 2 cases (2%) became T4d. The number of instances identified before receiving neo-adjuvant chemotherapy as N0 was 4 cases (4%), N1 turned into 37 instances (37%), N2 became fifty-two instances (fifty-two %) and N3 turned into (7%).

Number of cases that identified postoperative T0 was 10 cases (10%), T1 turned into 10 instances (10%), T2 was 47 instances (forty seven%), T3 was 21 cases (21%), T4a turned into 5 cases (5%) and T4b turned into 7 instances (7%).

Some instances that turned into postoperative N0 turned into 11 cases (eleven%), N1 turned into 57 cases (fifty-seven %), N2 was 29 cases (29%) and N3 turned into 3 cases (3%).

Conclusion: Neo-adjuvant chemotherapy plays a vital role in downstaging of breast and axillary disease, facilitates surgical resection, takes part in pathological entire response and testing response to chemotherapy.

Keywords: neoadjuvant, chemotherapy, breast cancer, advanced

Introduction:

Breast cancer is the most common site-specific cancer in women and is the most leading cause of cancer death for women aged 20 to 59 years. It accounts for 26% of all newly diagnosed cancers in females

and is responsible for 15% of cancer-related deaths in American women (1). In Egypt, breast cancer is the most common cancer among women, representing 18.9% of total cancer cases (35.1% in women)

with an age-adjusted rate of 49.6 per 100 000 population(2).

Aim of the work: to decide the effect neo-adjuvant chemotherapy (NAC) in downstaging of both the primary tumor and axillary disease, the increasing rates of pathological complete response (pCR) to neoadjuvant therapy have had a marked effect on locoregional-treatment considerations, as it can increase opportunities facilitating surgical intervention evaluate its impact on surgical management of breast cancer either mastectomy or BCS.

Patients and Methods:

This retrospective study is conducted on a number of cases of 100 female patients with documented breast cancer Place of study in the department of medical oncology & nuclear medicine Sohag university hospitals and sohag cancer institute Study period during a period from (2013 - 2018).

Eligibility criteria

Inclusion criteria:

- Female patients at any age.
- Stages (IIB, IIIA, B, C) breast cancer
- Any histological type of breast cancer.
- All grades of breast cancer.

Exclusion criteria:

- Noninvasive breast cancer.
- Stage (I) breast cancer.
- Metastatic breast cancer (MBC)
- Recurrent breast cancer.

Statistical analysis:

Data Analysis

The data acquired from the patients were analyzed by STATA version 12.1. Quantitative data were represented as mean, standard deviation, median, and range. Qualitative data were presented as numbers and percentages. The data were considered significant with $P < 0.05$.

Results:

- After revision of files of the breast cancer patient in sohag university hospital and sohag cancer institute, 100 female patients with locally advanced breast cancer during the period from 2013 to 2018.

- Age of patients more than 40 years was 76 cases (76%) with a median age of 49.5 years .number of patients diagnosed before starting neoadjuvant chemotherapy was 59 cases (59%) with breast ultrasound, 23 cases (23%) with sonomammography, and 18 cases (18%) with breast MRI.

-Number of cases diagnosed pathologically before neoadjuvant chemotherapy as IDC was 98 cases (98%), 1 case mixed IDC and ILC (1%), and 1 case (1%) diagnosed as adenocarcinoma.

-Number of cases diagnosed before starting neoadjuvant chemotherapy as grade 2 was 58 cases (58%) and 42 cases (42%) diagnosed as grade 3.

-Number of patients diagnosed before receiving neoadjuvant chemotherapy as T2 was 15 cases (15%), 32 cases (32%) was T3, 24 cases (24%) was T4a, 24 cases (24%) T4b, 3 cases (3%) was T4c and 2 cases (2%) was T4d.

-Number of cases diagnosed before receiving neoadjuvant chemotherapy was N0 was 4 cases (4%), N1 37 cases (37%), N2 was 52 cases (52%) and N3 was (7%).

-Number of patients who received anthracyclines based chemotherapy as neoadjuvant was 87 cases (87%), 13 cases (13%) were received anthracyclines and taxanes.

-After chemotherapy our cases re-evaluated with 62 (62%) with breast ultrasound, 20 cases with sonomammography and 18 cases (18%) with MRI.

-Number of cases that underwent MRM was 67 cases (67%) and BCS were 33 cases (33%).

-Number of patients pathologically diagnosed postoperatively as IDC was 96 cases (96%), 1 case (1%) mixed lobular and ductal type, 1 case was adenocarcinoma (1%) and 2 cases (2%) no tumor residual after neoadjuvant treatment.

-Number of cases T0 was 10 cases (10%), T1 was 10 cases (10%), T2 was 47 cases (47%), T3 was 21 cases (21%), T4a was 5 cases (5%) and T4b was 7 cases (7%).

-Number of cases that were postoperative N0 was 11 cases (11%), N1 was 57 cases (57%), N2 was 29 cases (29%) and N3 was 3 cases (3%).

-IDC presented in 98% of cases pre-operative CTH but presented in 96% of cases postoperative.

Adenocarcinoma presented in 1% of cases pre-operative CTH and postoperative. mixed lobular and ductal carcinoma presented in 1% of cases in neo-adjuvant and postoperative.

-14% of cases were T2 before neoadjuvant but 47% of cases were T2 post-operative. 31% of cases were T3 before neo-adjuvant but 21% of cases were T3 post-operative.

-25% of cases were T4a before neo-adjuvant but 5% of cases were T4a postoperative. 24% cases were T4b before neo-adjuvant but 7% cases were T4b postoperative. 3% cases were T4c before neo-adjuvant but 0% cases were T4c postoperative. 2% of cases were T4d before neo-adjuvant but 0% of cases were T4d postoperative. Also, 10% of cases were T0 postoperative and 10% were T1.

-N0 was presented in 4% of cases before neo-adjuvant and 11% of cases postoperative. N1 was presented in 37% of cases before neo-adjuvant and 57% of cases postoperative. N2 in 52% of cases before neo-adjuvant and 29% of cases postoperative. N3 in 7% of cases before neo-adjuvant and 3% of cases postoperative.

Discussion:

-Breast cancer is the most common malignancy in women around the world. It includes 1.7 million new cases per year and 25% of all types of cancers and is the second common cancer(3).

-Invasive breast cancer five main types, IDC is the common type of breast carcinoma accounting for 65% to 80% of all breast cancer(4)

-ILC is the second most frequently encountered subtype of invasive carcinoma. Approximately 10% of cancer are classified as ILC(5).-In our study of 100 cases of female patients with advanced breast cancer with 79% above the age of 40 years, IDC presented in 98% of cases and 1% is mixed lobular and ductal carcinoma.

-Tumour grade is a good indicator in early and advanced-stage breast cancer and about 96% of cases are grade 2 and grade 3(6).

In this study, 42% of cases were grade 3 and 58% were grade 2 that reflects the role of grade in disease aggressiveness. the highest breast cancer incidence rates among women aged 40 years and older; however, incidence rates are converging among white and African American women, particularly among women aged 50 years to 59 years(7).

-Breast Ultrasound was initially used to differentiate solid masses from cystic masses, but it has become an important adjunct to mammography and is an excellent method for guiding some interventional procedures. Ultrasound is not a breast screening tool(8).

-Breast Magnetic resonance imaging (MRI). is being used with increasing frequency for the screening and diagnosis of breast cancer. While mammography remains the gold standard, MRI is emerging as an important modality for evaluating breast diseases (9). In our current study

breast ultrasound has a major role to diagnose our cases (59% as a primary tool) and (62% in re-evaluation after neoadjuvant). 58% in whose core biopsy had confirmed the presence of breast carcinoma underwent breast MRI prior to beginning chemotherapy and before surgical excision. Patients were assigned to groups with nonresponse (NR), partial response (PR), and complete response (CR)(10).

- According to our study breast MRI diagnose advanced disease in 18% of our cases.

NACT was originally designed to be used in patients with locally advanced disease in order to convert inoperable tumors into operable tumors, increasing the rate of conservation therapy, downstaging of the tumor of the patients who were originally candidates for conservation therapy required a mastectomy because of disease progression while receiving NACT (11).

-In this current study 53% of T4 patients before receiving NACT opposite to 12% post neoadjuvant, 31% of cases were T3 pre neoadjuvant management opposing 21% post NACT.

-Neoadjuvant treatment with docetaxel for patients initially receiving anthracycline-based neoadjuvant treatment. Responders to the initial regimen were randomly assigned to remain on the anthracycline-based regimen or switch to docetaxel. Nonresponders to the initial regimen all switched to docetaxel and lowest in nonresponders docetaxel.

-The pathologic complete response (pCR) rate was highest in responders who switched(12).

-In this study 87% of cases the response to an anthracycline-based regimen and 13% of cases response to a second-line, taxanes based regimen, 20% of patients achieve PCR after an appropriate neoadjuvant chemotherapy regimen, including

a taxane and an anthracycline, and an anti-HER2 drug for HER2-positive disease(13).

-Pathological complete response (pCR) of the axilla is achieved in 41–75% of patients with HER2-positive or triple-negative cancer receiving NACT.

-Especially among patients with an ultrasound-positive or cytological-positive axilla who had a clinical response with downstaging to negative axilla(14).

-In this study, about 96% of nodal positive before NACT converted to 89% after it and 4% cases were N0 before NACT opposite to 11% after receiving chemotherapy.

70% of cancer patients across the US, use of neoadjuvant chemotherapy for younger and generally healthy women and lowest at the community, this finding was seen in women with locally advanced breast cancers as well as those with potentially borderline lumpectomy-eligible cancers. The use of neoadjuvant chemotherapy generally increased with stage, while the use of neoadjuvant endocrine therapy alone was rare. Hormone receptor-negative and HER2-positive subtypes were associated with greater use of neoadjuvant chemotherapy(15).

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<u>Age</u>	<u>Median age 49.5</u>	<u>%</u>
<u>Less than or equal 40</u>	<u>24</u>	<u>24.00</u>
<u>More than 40</u>	<u>76</u>	<u>76.00</u>

<u>Preoperative</u>	<u>No</u>	<u>%</u>
<u>PreCTH Imaging</u>		
- <u>Ultrasound</u>	<u>59</u>	<u>59.00</u>
- <u>MRI</u>	<u>18</u>	<u>18.00</u>
- <u>SonoMammography</u>	<u>23</u>	<u>23.00</u>
<u>Preop pathology</u>		
- <u>IDC</u>	<u>98</u>	<u>98.00</u>
- <u>Mixed</u>	<u>1</u>	<u>1.00</u>
- <u>Adenocarcinoma</u>	<u>1</u>	<u>1.00</u>
<u>Preoperative grading</u>		
- <u>G2</u>	<u>58</u>	<u>58.00</u>
- <u>G3</u>	<u>42</u>	<u>42.00</u>
<u>Preoperative chemotherapy</u>		
- <u>Anthracyclin</u>	<u>87</u>	<u>87.00</u>
- <u>Taxanes</u>	<u>0</u>	<u>0.00</u>
- <u>Combination</u>	<u>13</u>	<u>13.00</u>
<u>Preoperative T</u>		
- <u>T2</u>	<u>15</u>	<u>15.00</u>
- <u>T3</u>	<u>32</u>	<u>32.00</u>
- <u>T4a</u>	<u>24</u>	<u>24.00</u>
- <u>T4b</u>	<u>24</u>	<u>24.00</u>
- <u>T4c</u>	<u>3</u>	<u>3.00</u>
- <u>T4d</u>	<u>2</u>	<u>2.00</u>
<u>Preoperative node</u>		
- <u>No</u>	<u>4</u>	<u>4.00</u>
- <u>N1</u>	<u>37</u>	<u>37.00</u>
- <u>N2</u>	<u>52</u>	<u>52.00</u>
- <u>N3</u>	<u>7</u>	<u>7.00</u>
<u>Surgical management</u>		
- <u>MRM</u>	<u>67</u>	<u>67.00</u>
- <u>BCS</u>	<u>33</u>	<u>33.00</u>

<u>postoperative</u>	<u>No</u>	<u>%</u>
<u>Post CTH image</u>		
- <u>Ultrasound</u>	<u>62</u>	<u>62.00</u>
- <u>MRI</u>	<u>18</u>	<u>18.00</u>
- <u>Sonomamography</u>	<u>20</u>	<u>20.00</u>
<u>Postoperative pathology</u>		
- <u>IDC</u>	<u>96</u>	<u>96.00</u>
- <u>Mixed</u>	<u>1</u>	<u>1.00</u>
- <u>Adenocarcinoma</u>	<u>1</u>	<u>1.00</u>
- <u>Negative</u>	<u>2</u>	<u>2.00</u>
<u>Postoperative T</u>		
- <u>T0</u>	<u>10</u>	<u>10.00</u>
- <u>T1</u>	<u>10</u>	<u>10.00</u>
- <u>T2</u>	<u>47</u>	<u>47.00</u>
- <u>T3</u>	<u>21</u>	<u>21.00</u>
- <u>T4a</u>	<u>5</u>	<u>5.00</u>
- <u>T4b</u>	<u>7</u>	<u>7.00</u>
<u>Postoperative node</u>		
- <u>N0</u>	<u>11</u>	<u>11.00</u>
- <u>N1</u>	<u>57</u>	<u>57.00</u>
- <u>N2</u>	<u>29</u>	<u>29.00</u>
- <u>N3</u>	<u>3</u>	<u>3.00</u>

<u>Postoperative chemotherapy</u>	<u>No</u>	<u>%</u>
<u>Anthracyclin</u>	<u>9</u>	<u>9.00</u>
<u>Taxanes</u>	<u>80</u>	<u>80.00</u>
<u>Combination</u>	<u>7</u>	<u>7.00</u>
<u>Refused</u>	<u>1</u>	<u>1.00</u>
<u>Negative</u>	<u>3</u>	<u>3.00</u>

			postoperative pathology				Total	P value
			IDC	mixed	adenocarcinoma	negative		
preoperative pathology	IDC	Count	96	0	0	2	98	.000
		% within preoperative pathology	98.0%	.0%	.0%	2.0%	100.0%	
	Mixed	Count	0	1	0	0	1	
		% within preoperative pathology	.0%	100.0%	.0%	.0%	100.0%	
	adenocarcinoma	Count	0	0	1	0	1	
		% within preoperative pathology	.0%	.0%	100.0%	.0%	100.0%	
Total	Count	96	1	1	2	100		
	% within preoperative pathology	96.0%	1.0%	1.0%	2.0%	100.0%		

		postoperative T						Total	P value
		T2	T3	T4a	T4b	T0	T1		
preoperative T	T2	Count	4	4	0	0	3	3	.235
		%	28.6%	28.6%	.0%	.0%	21.4%	21.4%	
	T3	Count	17	5	0	2	3	4	
		%	54.8%	16.1%	.0%	6.5%	9.7%	12.9%	
	T4a	Count	8	8	4	0	3	2	
		% within preoperative T	32.0%	32.0%	16.0%	.0%	12.0%	8.0%	
	T4b	Count	13	3	1	5	1	1	
	% within preoperative T	54.2%	12.5%	4.2%	20.8%	4.2%	4.2%		
T4c	Count	3	0	0	0	0	0		
	% within preoperative T	100.0%	.0%	.0%	.0%	.0%	.0%		
T4d	Count	1	1	0	0	0	0		
	% within preoperative T	50.0%	50.0%	.0%	.0%	.0%	.0%		
Tx	Count	1	0	0	0	0	0		
	% within preoperative T	100.0%	.0%	.0%	.0%	.0%	.0%		
Total	Count	47	21	5	7	10	10		
	% within preoperative T	47.0%	21.0%	5.0%	7.0%	10.0%	10.0%		

		postoperative node				Total	P value
		no	n1	n2	n3		
preoperative node	N0	Count	1	0	3	0	.051
		% within preoperative node	25.0%	.0%	75.0%	.0%	
	N1	Count	6	23	6	2	
		% within preoperative node	16.2%	62.2%	16.2%	5.4%	
N2	Count	4	30	18	0	52	
	% within preoperative node	7.7%	57.7%	34.6%	.0%		
N3	Count	0	4	2	1	7	
	% within preoperative node	.0%	57.1%	28.6%	14.3%		
Total	Count	11	57	29	3	100	
	% within preoperative node	11.0%	57.0%	29.0%	3.0%		