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## Research Paper

Breast conservation after neoadjuvant therapy for tumors  $\geq 5$  cm:  
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## ABSTRACT

**Introduction:** Neoadjuvant therapy (NT) can facilitate breast conservation (BC). Similar oncologic outcomes have been reported with BC and mastectomy for T1 and T2 lesions, but studies of BC results for tumors  $\geq 5$  cm are limited. Our experience with BC for tumors  $\geq 5$  cm is reported.

**Patients and methods:** A retrospective analysis of a prospectively collected database of all breast cancer patients treated with NT at our institution between 2003 and 2010 was performed to identify patients treated with BC for tumors  $\geq 5$  cm. Demographics, stage, tumor histology, pathologic response, tumor margins, failure patterns and rates, as well as survival rates were recorded.

**Results:** Thirty patients treated with BC after NT for large tumors were identified. The only selection criteria for BC were technical ability with acceptable cosmetic results and negative margins. Patients with genetic predisposition for additional breast cancer were excluded. The mean follow-up was 43 months and the mean age at diagnosis was 51. The mean tumor size at diagnosis was 6.4 cm and the mean pathological size was 2.1 cm. Four of thirty (13.3%) had either systemic progression or regional recurrence. Three patients had systemic progression, 2 had regional recurrence and none had local recurrence. At a mean follow-up of 43 months, the success rate of BC on intent to treat basis was 96.7%, with an overall survival of 86.7% and disease-free survival of 83.3%.

**Conclusion:** BC after NT is a safe option for carefully selected patients with tumors  $\geq 5$  cm. In this series, the oncologic results for the duration of the study were comparable to those reported after mastectomy.

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## 1. Introduction

Multiple prospective randomized trials [1], some with a follow-up of 20 years, have established equivalent survival rates between breast conservation (BC) with negative margins and mastectomy. The EBCTCG meta-analysis [2] further demonstrated improved overall survival with the addition of radiation to surgery. Neoadjuvant therapy (NT) has become a common approach for management of locally advanced breast cancer. The theoretical advantage of this strategy is threefold: an earlier systemic therapy targeting micro metastases, the ability to assess tumor response in vivo and the possible downsizing of the tumor enabling BC.

The use of BC for larger tumors downsized by NT presents some concerns regarding the adequacy of the resection and the possibility of a piecemeal tumor response resulting in residual satellite nodules in the field of the original tumor. The data for T3 tumors are limited because such large tumor sizes at presentation are rare

nowadays. In fact NSABP B-18 had only 13% of patients with T3 tumors [3] and NSABPB-27 had 29% of such patients [4]. Furthermore those patients are usually offered a mastectomy and little consideration is given to BC. In our institution we treat a relatively large percentage of patients presenting with locally advanced tumors. We sought to investigate the feasibility of BC in this very specific group of patients. The aim of this study was to report the survival rates and failure patterns for tumors  $\geq 5$  cm treated by BC after NT at our institution.

## 2. Patients and methods

After appropriate institutional IRB approval, a retrospective analysis of a prospectively collected database of all breast cancer patients treated with NT at our institution between 2003 and 2010 was performed to identify patients treated with BC for tumors  $\geq 5$  cm, not including T4 disease. All patients received NT, which consisted of either hormonal or chemotherapy treatments. At our institution patients with advanced locoregional and no systemic disease are usually offered NT; these include patients with tumors  $\geq 5$  cm. The decision for BC was made by the surgeon and the patient's preference,

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as well as surgical feasibility based on breast size, tumor location and residual tumor volume according to previously published principles [5]. A second attempt for breast conservation was done if positive margins were obtained, If not feasible completion mastectomy was performed. Advanced oncoplastic techniques and contralateral breast reduction were done when deemed necessary for cosmetic reasons. We refer to BC combined with bilateral breast reductions as an “oncoreductive procedure.” Tumor size was assessed at presentation by mammography and ultrasound, and response to NT was characterized according to the RECIST criteria by measuring pathological size [6]. Tumor stage, histology grade, and receptor status were recorded and were available in the vast majority of the cases. Local, regional and systemic failure patterns were recorded during the follow-up interval. Qualitative and quantitative variables were analyzed by chi square and Student t test, respectively;  $P < 0.05$  was considered significant. The work has been reported in line with the STROBE criteria [7].

### 3. Results

Two hundred ninety patients received NT, of whom 84 had tumors  $\geq 5$  cm and were not classified as T4. Fifty-four patients were not offered breast conservation because of patient preference, genetic predisposition for breast cancer, or because of surgical and oncologic inability. Thirty patients treated with breast conservation after NT make up the main study group. The average follow-up interval was 43 months and the mean age at diagnosis was 51 years. Tumor histology was ductal in 24/30 (80%) patients and lobular in 6/30 (20%). NT consisted of chemotherapy for 25/30 (83.3%) patients (23/25 ductal and 2/24 lobular) and hormonal therapy for 5/30 (16.7%) patients (1/5 ductal and 4/5 lobular). The mean tumor size at diagnosis was 6.4 cm. Estrogen receptors (ER) were positive in 17/30 (56.7%) patients and Her2 was amplified in 10/30 (33.3%) patients. Low grade was found in 6 (20%) patients, intermediate grade in 11 patients (37%) and high grade in 13 (43%) patients. Twenty four had an axillary dissection, 5 had SLNB and in 1 patient no axillary staging was done due to old age at diagnosis.

Negative margins were obtained at the first attempt in 28 patients and on the second attempts in one patient. One patient underwent a completion mastectomy for grossly positive margins. Eight patients underwent an oncoreductive procedure. The mean pathological size at the time of resection was 2.1 cm, and 6/30 (20%) patients had pCR in the breast and lymph nodes. Thirteen out of thirty (43.3%) patients had a complete clinical response, 8/30 (26.7%) had partial response and 9/30 (30%) had stable disease. Table 1 summarizes the characteristics of the study group. Patients undergoing mastectomy had statistically larger tumors at presentation and lower rates of HER2 amplified tumors.

Postoperative treatment consisted of radiation therapy to all but one patient who did not receive therapy due to old age at diagnosis. Adjuvant hormonal therapy was given to all ER positive patients, and one patient discontinued therapy. All Her-2 positive patients received trastuzumab.

Overall, at 43 months of follow-up, the success rate of BC on intent to treat basis was 96.7%. The disease-free survival was 83.3% and the overall survival was 86.7%, with four patients dying during the follow-up interval, 3 from metastatic disease and one from unrelated causes. The fourth patient was diagnosed at the age of 91 and had no evidence of disease at the time of death.

Local, regional and systemic failures, as well as breast cancer mortality and overall mortality, were compared between the BC and the mastectomy groups and are summarized in Table 2. There were no statistically significant differences in any of those parameters. In the BC group, three patients (10%) developed systemic progression, of whom one had concomitant regional recurrence. An additional patient had isolated regional recurrence for a total of 2/30 (6.7%)

**Table 1**  
Clinical characteristics.

	Breast conservation	Mastectomy	P value
Age			
Mean	51.4	52.9	Not significant (NS)
<50	17 (57)	22 (41)	
$\geq 50$	13 (43)	32 (59)	
Histology			
Ductal	24 (80)	38 (70)	NS
Lobular	6 (20)	16 (20)	
No data	0	2	
ER positive	17 (57)	33 (63)	NS
Her2 positive	10 (33)	5 (4)	
Grade			
I	6 (20)	6 (11)	NS
II	11 (37)	21 (39)	
III	13 (43)	27 (50)	
Clinical size			
Mean	6.4	7.2	0.027
NT			
Chemotherapy	25 (83)	51 (95)	NS
Hormonal	5 (17)	3 (5)	
Pathological size			
Mean	2.2	2.5	NS
Pathological nodal status <sup>a</sup>			
N0/N1	22 (76)	40 (74)	NS
N2/N3	7 (24)	14 (26)	
Response			
Complete response	13 (43)	18 (33)	NS
Partial response	8 (27)	19 (35)	
No response	9 (30)	17 (32)	

<sup>a</sup> In 1 patient no axillary staging was done due to old age at diagnosis.

**Table 2**  
Failure pattern and outcome at mean follow-up of 43 months.

	Breast conservation	Mastectomy	P value
Failure pattern	n = 30	n = 54	
Systemic	3/30 (10)	9/54 (18.5)	NS
Regional	2/30 (6.7)	2/54 (5.5)	
Local	0	0	
Breast cancer-specific death	3/30 (10)	5/54 (9.3)	NS
Death	4/30 (13.3)	9/54 (16.7)	

regional recurrence. No in breast local failure occurred. All patients with systemic progression or recurrence did not reach complete response to NT. In more details, one patient with positive margins who was treated by completion mastectomy developed regional recurrence 18 months after diagnosis and died 10 months following regional recurrence. The second patient developed bone metastasis 32 months after diagnosis and died 18 months following the systemic progression. The third patient developed bone, liver and lung metastasis 44 months after diagnosis and died 6 months following the systemic progression. The fourth patient developed regional recurrence in the axilla 44 months after diagnosis and was treated with local excision.

In comparison 9/54 patients treated with mastectomy had systemic failure (16.7%), 2 with concurrent regional failures (3.7%), and there were no local failures.

Similarly, 9/54 (16.7%) patients in the mastectomy group died from all causes, of which 5 (9.3%) were breast cancer deaths.

### 4. Discussion

NT is increasingly used for locoregional advanced disease. With the adoption of complex oncoplastic techniques, including oncoreductive procedures, patients with larger residual tumors following NT are candidates for BC. Our aim was to study a very specific group of patients presenting with very large tumors of  $\geq 5$  cm. This

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