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Research Article

The Role of Neoadjuvant Chemotherapy in the Management of Breast Cancer: A Retrospective Study of 72 Cases

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Abstract

Purpose: The aim of this study is to determine predictive factors of complete pathological response after neoadjuvant CT and analyze conservation surgery, survival and local recurrence rates.

Methods: This study examines retrospectively patients with breast cancer treated with neoadjuvant CT between 2011 and 2014. Most of the patients received the same neoadjuvant CT regimen, consisting of FEC followed by taxanes than underwent surgery. Clinical and pathological responses and were assessed and recurrence and survival rates were analyzed.

Results: Seventy two patients with locally advanced and inflammatory breast cancer met eligibility criteria, 50% of them had T2 or T3 tumors, and 38,9% had lymph node involvement. After neoadjuvant chemotherapy, the objective clinical response rate was 70.28%, of which 16.14% was complete. Fifty nine patients (81,9%) underwent mastectomy and breast-conserving surgery was performed for 13 patients (18,1%). According to Sataloff's classification, the complete pathological response rate in breast (TA) and nodes (NA) was 19,4% and 9,7% respectively. After multivariate analysis, the complete pathological response was significantly influenced by negative estrogen receptors status (OR 2,72; 95% IC; p = 0,027) and over expression of HER2 (OR = 1,66; 95% IC; p = 0,032). At a median follow up of 38, 4 months, 19 patients (26,4%) developed recurrence and 11,1% of the patients had died.. The 2-, 3-, and 4-year overall survival rates were 95,8%, 85,2% and 81,9% respectively. The 2-, and 4-year disease free survival rates were 95,5%, and 76,4% respectively. There was a tendency for OS in favor of patients who achieved a pCR (p = 0,068). BCS did not influence outcome.

Conclusion: Preoperative chemotherapy is established as the standard of care for patients with LABC. BCS after primary chemotherapy is be feasible for appropriately selected patients without compromising long term outcome.

Keywords: *Neoadjuvant Chemotherapy; Breast Cancer; Preoperative Chemotherapy*

Introduction

Breast cancer is the most common cancer among women in the world accounting 25% of newly diagnosed cancers and remains the most lethal malignancy among them. In Tunisia, nearly two thousand new cases of breast cancer are diagnosed each year [1]. The situation continues to be critical, given the increasing incidence and the occurrence of advanced stages of this cancer.

Management of invasive breast cancer is based on surgery, radiotherapy, chemotherapy, endocrine and targeted therapies. The optimal therapeutic approach depends on tumor's and patient's characteristics and should be discussed on a multidisciplinary meeting.

Historically, neoadjuvant chemotherapy (CT) has been used in the treatment of inflammatory and locally advanced breast carcinoma (LABC) to improve local control and hence achieve operability. More recently, this strategy has been extended to the management of patients with operable disease, to increase the possibility of breast conservation [2] and became a standard treatment for breast cancer.

However, this therapeutic approach raised new questions. In fact, the oncologist now has the opportunity to evaluate the efficacy of systemic therapy *in vivo*, and assess if complete pathological response (pCR) is achieved. On the other hand, safety of breast conserving surgery(BCS) in terms of local control of the disease, for selected patients with LABC who achieve pCR is still unclear. Moreover, identification of factors that can reliably predict tumor response to primary CT and thus breast conservation surgery, and defining their potential clinical implications remains a challenge.

The main purpose of the current study is to determine predictive factors of complete pathological response after neoadjuvant CT. Moreover, we analyze conservation surgery, survival and local recurrence rates in our study population.

Patients and Methods

Patient population

In the present study, we have looked retrospectively at 72 patients with breast cancer treated with neoadjuvant CT at the maternity and neonatology centre of Monastir between January 2011 and December 2014.

Patients eligible for the study included those with pathologically proven invasive breast cancer. The indication of primary CT was made on a multidisciplinary meeting. Patients who had local or locoregional recurrence, distant metastasis, or received neoadjuvant radiotherapy or neoadjuvant endocrine therapy were excluded.

Diagnosis

The baseline workup included a complete history and clinical examination, bilateral mammography, and bilateral breast ultrasound. MRI was not systematic. Tumor size used for TNM classification was measured at the clinical examination before biopsy.

Diagnosis of carcinoma ware established through ultrasound guided core biopsy.

Treatment modalities

Most of the patients received the same neoadjuvant CT regimen, consisting of three to four cycles of FEC100 (5 Fluorouracile (5FU), Epirubicin 100 mg/m^2, Cyclophosphamide), followed by three to four cycles of taxanes (docetaxel or paclitaxel). Chemotherapy was administrated intravenously at 21 day interval. None of the patients over expressing Her 2 neu received Trastuzumab in a neoadjuvant matter.

Clinical response to CT was assessed by clinical examination only.

Patients underwent appropriate surgery (conservation breast surgery or mastectomy) after 4 to 6 weeks following the completion of primary CT. The decision of surgical modality was made according to the size of their residual tumor compared to the size of the breast, tumor response and the patient's desire. Patients with positive margins were subjected to margin revision to attain a free pathological margin.

The pathologic responses in breast and nodes were graded according to the classifications of Sataloff., *et al* [3].

Follow up

After completing the primary treatment, all patients were followed up at 1 month, at 3 months and then at 6 monthly intervals. Clinical examination was performed at each consultation and mammography and ultrasound were performed annually.

Statistical analysis

Proportions and means were compared by the chi-square and the Student's t test, respectively. Cox regression was used to evaluate possible predictors of pathological response. P value of < 0.05 was considered significant. Overall survival (OS) and disease free survival (DFS) rates (from the beginning of the treatment) were estimated according to the Kaplan-Meier method. The log-rank test was used for comparison between survival rates. All statistical analysis was carried out using SPSS 20 statistical package program.

Results

Patient and tumors characteristics

Seventy two patients with locally advanced and inflammatory breast cancer met eligibility criteria. Age of patients ranged from 29 to 76 years (mean: 48,68), with 54,2% of the women in the menopausal age group. Mean time to consultation was 4,97 months. Most of the patients (75%) presented for a palpable mass.

Tumor's characteristics are outlined in table 1. The mean clinical tumor size at presentation was 5,7 cm (range, 0 - 15 cm). According to the AJCC staging system 2002, 50% of the patients had T2 or T3 tumors, and 38,9% had lymph node involvement. Histologic examination of the tumor biopsies diagnosed an infiltrating ductal carcinoma in 98,6% of the cases, and 31,9% of the patients had an SBR grade III tumor. Hormonal receptors were positive in 49 patients (68%). Her2 expression was determined for all the patients, and was over expressed in 40,3% of the tumors. Nine patients had triple negative tumors (12,5%).

Characteristics	n (%)
T2	19 (26,4)
T3	17 (23,6)
T4a	4 (5,6)
T4b	22 (30,6)
T4c	1 (1,4)
T4d	9 (12,5)
N0	44 (61,1)
N1	23 (31,9)
N2	5 (6,9)
Invasive ductal	71 (98,6)
Invasive lobular	1 (1,4)
SBR I	9 (12,5)
SBR II	40 (55,6)
SBR III	23 (31,9)
Estrogen receptors (+)	48 (66,7)
Progesterone receptors (+)	36 (50)
Her-2 overexpression	29 (40,3)
Luminal A	4 (5,6)
Luminal B	45 (62,5)
HER-2-positive	14 (19,4)
Triple negative	9 (15,5)

Table 1: *Tumor's characteristics.*

Neoadjuvant chemotherapy and clinical response

Ninety six patients (95,8%) received a FEC regimen (cyclophosphamide, epirubicin and 5-fluorouracil) followed by taxanes sequentially, with a mean number of 6,43 cures. One patient received only a FEC regimen, another received taxanes as a single agent, and a third received an AC regimen (adriamycin, cyclophosphamide). Six patients failed to complete the planned treatment due to progressive disease or severe side effects.

Clinical response was assessed at the time between the 6th and the 7th CT cure (median; 7th cure). Mean time between the beginning of chemotherapy and clinical response evaluation was 18,5 weeks (median: 20 weeks). Table 2 summarizes clinical response to primary CT. The objective response rate was 70.28%, of which 16.14% was complete (cCR).

Surgery and pathological response

Fifty nine patients (81,9%) underwent mastectomy. Breast-conserving surgery was performed for 13 patients (18,1%), and in 63,15% of T2 tumors. Three patients underwent a second operation for positive margins. Mean interval between biopsy and surgery was 6,01 months (median, 5,83; range, 3, 17 - 11, 20) and mean interval between the last neoadjuvant CT cure and surgery was 32,62 days (median, 34; range, 23 - 95). None of the histological features of the tumors analyzed was significantly associated with BCS.

Mean pathological tumor size was 17,3 mm (range; 0 - 125 mm). Among patients who underwent BCS, only one had positive margins and had to undergo re-excision surgery. The mean clear margin width was 4,41 mm (median; 4, range; 0 - 20).

The mean number of lymph nodes (LN) excised for patients who underwent LN dissection was 14,83 (range, 2 - 43). A total of 32 patients (44%) had node involvement with a mean number of positive LN of 2,5 (range, 1 - 16).

Table 2 summarizes pathological response to primary CT. According to Sataloff's classification, the complete pathological response rate in breast (TA)and nodes (NA) was 19,4% and 9,7% respectively.

Response	n (%)
Clinical response	
Complete response	26 (36,1)
Partial response	40 (55,5)
Stable	5 (7)
Progression	1 (1,4)
Pathological response	
Sataloff's classification in breast	
TA	14 (19,4)
TB	26 (36,1)
TC	27 (37,5)
TD	5 (7)
Sataloff's classification in nodes	
NA	7 (9,7)
NB	22 (30,6)
NC	25 (34,7)
ND	18 (25)

Table 2: *Clinical and pathological response to primary chemotherapy.*

After univariate analysis there was a significant correlation between complete pathologic response according to the classification of Sataloff (29) and the small initial clinical tumor size (p < 0,05), negative oestrogen receptors status (p = 0,08), and triple negative status (0,013). Over expression of HER2 was borderline significant (p = 0,052).

After multivariate analysis, the complete pathological response was significantly influenced by two predictive factors: negative oestrogen receptors status (OR 2,72;95% IC; p = 0,027)and over expression of HER2 (OR = 1,66; 95% IC; p = 0,032).

Adjuvant treatment

As adjuvant treatment, 58 (80.6%) patients received radiotherapy, five (6,94%) patients received chemotherapy (four patients received capecitabine + vinorelbine (80%) and one received taxanes), and 46 (63,9%) patients with HR-positive tumors received endocrine therapy (tamoxifen (43,1%); aromatase inhibitors (19,4%); sequential association (1,4%). A chemical castration was performed for six patients (8,3%). Among the 29 patients with over expressed Her-2 tumors, 22 (75,9%) received trastuzumab for a year.

Outcome

At a median follow up of 38,4 months (range; 8 - 48), 19 patients (26,4%) developed recurrences, including loco regional recurrence (n = 5; 6,9%) and systemic metastases (n = 14; 19,4%).The mean time to tumor recurrence (from the date of diagnosis) was 14,12 months (median, 10,5; range, 4 - 49).

At the time of the analyses, 11,1% of the patients had died, and 77,7% were surviving and in complete remission. The 2-, 3-, and 4-year overall survival rates were 95,8%, 85,2% and 81,9% respectively. The 2-, and 4-year disease free survival rates were 95,5%, and 76,4% respectively.

We have compared the OS and the DFS in patients who achieved a pCR versus those who didn't. There was a tendency for OS in favor of patients who achieved a pCR (p = 0,068). No significant difference was found for DFS (p = 0,523). There was no significant difference for OS or DFS when comparing patients who had BCS versus those who had mastectomy (p = 0,392; p = 0,187 respectively). We also compared the OS and the DFS for the different molecular subtypes. No significant difference was found.

Discussion

Neoadjuvant chemotherapy

Neoadjuvant chemotherapy has an established role in the management of locally advanced and inflammatory breast cancers [4]. Anthracycline-based and taxane-based therapies are frequently used as preoperative treatments.

Reports from various trials on Anthracycline-based neoadjuvant therapy demonstrated clinical response rates of 60% -80% in both breast and nodes [5].

A large study by the National Surgical Adjuvant Breast and Bowel Project (NSABP) on 1523 patients with operable breast cancer randomized to receive AC on a neoadjuvant or adjuvant basis showed a cCR and a pCR of 36% and 12% respectively, and a decrease of 37% in lymph node involvement in the neoadjuvant arm. Moreover, this group had an increase in BCS rate of 12% compared to the adjuvant group (68% vs 60%; p = 0,001). After a 16 year follow up, no significant difference in disease-free or overall survival between the two arms has been demonstrated. However, a trend towards a greater locoregional recurrence risk was reported (13% vs 10%; p = 0,21) [6]. In another large study conducted by the European Organisation for Research and Treatment for Cancer (EORTC), among the patients who were initially thought to require mastectomy in this group, 23% were eligible to BCS as a result of preoperative CT. This trial showed no significant differences in either overall (82% vs 84%; p = 0,38), distant disease-free survival (65% vs 70%; p = 0,27), or locoregional recurrence rates between the two treatment arms [7].

Lippman [8] reported results concerning 51 patients with LABC treated with primary CT, and found that the median time to achieve a cCR was five cycles and the median time to achieve a cPR was four cycles of chemotherapy. This statement is of importance since in LABC, neoadjuvant CT should not delay locoregional treatment if response is not achieved or in case of progression of the tumor. The aim of neoadjuvant CT should be to achieve operability and potentially treat micro metastatic disease at the earliest opportunity [9].

In our series, the mean number of neoadjuvant CT cycles was 6,43, with Anthracycline-based therapy administered to 98,6% of the patients. The clinical objective response (cOR) rate was 90,2% including a 36,1% cCR rate.

More recently, the role of taxanes as preoperative CT is investigated. The NSABP B27 trial investigated the use of docetaxel in a neoadjuvant matter. Adjunction of taxanes doubled the pCR rates, and reduced lymph node involvement rates compared to anthracycline based chemotherapy as a single agent. However, BCS rates were equivalent in the three arms; such was OS and DFS rates [10]. The advantages of taxanes based therapies was further demonstrated by The European Cooperative Trial in Operable Breast Cancer (ECTO) trial, which was a randomized phase III study designed to evaluate the effects of adding paclitaxel to an anthracycline-based regimen and to compare the same regimen given preoperatively and postoperatively. The neoadjuvant group achieved a pCR rate of 23% and a higher rate of breast-conserving surgery compared to the adjuvant group (65% vs 34%; $P < 0.001$) [11].

The German Preoperative Adriamycin Docetaxel Trial (Gepar-DUO) compared the effectiveness of sequential and combination of docetaxel regimens. The pCR and BCS rates were higher in the sequential group (14,3% vs 7%; $p < 0,001$ and 63,4% vs 58,1%; $p = 0,05$ respectively) [12]. In the current study, sequencing taxanes following the anthracycline based therapy was used for 97,2% of the patients.

Another interesting fact about preoperative therapy is the opportunity to monitor tumor response and potentially to tailor treatment based on response. However, the results of the Aberdeen trial [13,14], suggest that tumors not responding to one chemotherapy regimen are unlikely to show dramatic response to another regimen. In our series, patients with lack of response or tumor progression are often planned for mastectomy. This approach used for six patients after only one cure of neoadjuvant CT.

Neoadjuvant targeted therapies

Clinical benefits achieved using targeted agents, namely trastuzumab have been demonstrated in neoadjuvant settings by several investigators [15,16]. In the NOAH (Neoadjuvant Herceptin) trial [17], the pCR rate was significantly increased by addition of Trastuzumab (43% vs 23%; $p = 0,002$), and event-free survival was improved in patients with HER2-positive breast cancer (3-year event-free survival, 71% [95% CI 61 - 78; n = 36 events] with trastuzumab, vs 56% [46 - 65; n = 51 events] without; (hazard ratio 0·59 [95% CI 0.38 – 0.90]; $p = 0.013$). Moreover, trastuzumab was well tolerated. None of our patients received any targeted therapy with neoadjuvant chemotherapy, since trastuzumab was not available during our study period. This might partly explain the low pCR rate in our series.

A number of other HER-2–targeted agents have been evaluated such as lapatinib and pertuzumab. The Dual-HER2 blockade has been tested in the Neo-ALTTO [18] and the NeoSphere [19] trials, and they both showed significant improvement of pCR rates.

Clinical response to CT

Although clinical examination remains important, it is of limited performance for the evaluation of response to neoadjuvant CT. Rosen [20] found a correlation coefficient of 0,65 between the estimated clinical tumor size and pathological tumor size. This coefficient was 0,53 in our series (cCR: 36,1%; pCR: 19,1%). In Peitinger 's report [21], mammographic combined to ultrasonography assessment had a sensitivity of 78,6% for predicting pCR and it offered an accurate estimation of residual tumor size in 69% of the patients. MRI has a better accuracy in correctly estimating residual tumor size than clinical examination, mammography and ultrasonography (63%, 52%, 38%, and 43% respectively) [22]. Several studies have shown that the correlation coefficient between the final MRI tumor size and actual pathological size ranges between 0.75 and 0,89 [20,23,24]. FDG-PET is also shown to have a high global accuracy in assessing the response for neoadjuvant CT in breast cancer. In order to have better correlation with pathological response, studies suggest performing

FDG-PET after the second cycle of neoadjuvant CT [25]. In the present study, the assessment of clinical response to neoadjuvant CT was based on clinical examination only.

Pathological response

The complete response to neoadjuvant CT is the ultimate goal for a successful chemotherapy treatment. Different studies have reported clinical tumor response rates ranging between 49% and 90,7% according to the CT regimen, with a clinical complete remission rates between 6,6% and 63,6%, and a histological complete remission rates of 4% to 31%. Patients without any node involvement ranged between 38% and 67% of the cases [7,10,13]. In the current study, results were comparable, with an objective clinical response (cCR + cPR) rate of 91,6% including a cCR rate of 36,1%. The pCR rate in breast was 19,4%. After neoadjuvant CT, 40,3% of our patients had no evidence of node invasion (Sataloff NA+NB).

Several predictive factors of pCR have been identified. High grade tumors and elevated mitotic index make a tumor more sensitive to neoadjuvant CT [26]. Some reported that breast cancers with high Ki-67 expression, responded well to primary chemotherapy [27]. Negative oestrogen receptor (ER) tumors have also been associated with a better response to neoadjuvant CT [28]. HER2neu status is also proposed to predict and monitor response to primary CT [29]. Moreover, several studies showed that invasive lobular carcinoma ILC were less likely to achieve a pathologic complete response compared with patients with invasive ductal carcinoma (IDC) (1% - 3% vs 8% - 15%) [28,30]. Higher clinical and pathological response rates are also seen in smaller tumor sizes [6]. Rouzier., *et al*. [31] investigated whether the molecular subtype of a tumor affected chemotherapy sensitivity. They evaluated the gene expression profiles of 82 patients treated with neoadjuvant paclitaxel followed by fluorouracil, doxorubicin, and cyclophosphamide. The pathologic complete response rate was 45% for the basal-like and HER2-positive subtypes and 6% for the luminal tumors ($p < 0,001$). On multivariate analysis, only hormonal status (ER-negative) was an independent predictive factor of response to chemotherapy. In the present study, The pCR rates for triple negative, luminal A, luminal B and HER2-positive tumor subtypes were 55.5%, 0%, 15.5% and 28.5% respectively. Triple negative tumors significantly had better pCR rates ($p = 0,013$). Furthermore, ER-negative, and overexpressed Her2 status were predictive of a pCR.

Recently, gene expression profiling has identified several molecular signatures that mostly have prognostic value and some prediction significance. Liedtke., *et al*. [32] evaluated the ability of a genomic expression signature called genomic grade index (GGI) to predict response to neoadjuvant CT in a study concerning 229 tumour samples collected before the beginning of CT with docetaxel and to fluorouracil, doxorubicin and cyclophosphamide (FAC). A high GGI was associated with greater response than low-risk GGI (40% versus 12%; $P < 0.001$). This correlation was also demonstrated for the RE+ as for the RE- subtypes. A 21-gene assay (Oncotype DX) has been reported as well to predict benefit from chemotherapy for patients with RE+ breast cancer [33]. Giani., *et al*. [34] demonstrated that a higher recurrence score was significantly associated with a better response to chemotherapy.

Surgical management after neoadjuvant chemotherapy

The most clearly established advantage of neoadjuvant CT is its ability to allow more BCS. A response to chemotherapy including a partial response can result in a significant number of patients having their tumors downstaged, and hence be eligible to BCS. In fact, in the NSABP B-18 [35] trial,67% of the patients had BCS, among them, 79% achieved a clinical response (cPR: 43%, cCR: 36%). In Giani., *et al* 's [36] report, cCR and cPR rates were 49% and 29% respectively in the neoadjuvant arm. neoadjuvant CT was significantly associated with a higher breast conserving surgeries (63 vs34%; $p < 0,001$).However, cCR and cPR rates only allowed BCS for 19,1% of the patients in our series. This difference could be explained by the frequency of voluminous tumors in our study. In fact, T3 and T4 tumors represented 23,6% and 50% respectively, and the mean tumor size at presentation was 5,7 cm.

The investigators in Rouzier's [37,38] report developed a predictive score of BCS to guide the therapeutic management of breast cancer. This nomogram included tumor size, histological grade and type, multicentricity, and hormonal status. We attempted to determine predictive factors of BCS with the intention of developing a similar score. Unfortunately, the number of patients in the present study was

insufficient to demonstrate a significant correlation of the various factors with BCS. In addition, the retrospective aspect of the current study was limiting. The initial tumor size (< 5 cm) was the only predictive factor of BCS (T2 61,3% vs T3 5,8%).

Sentinel lymph node biopsy (SLNB) is now considered a standard procedure for clinically node negative disease. Some authors suggested that SLNB after neoadjuvant CT would theoretically limit the morbidity associated with axillary lymph node dissection (ALND) [39]. However, performance and feasibility of SLNB after neoadjuvant CT is still controversial, and it remains unclear whether initially invaded LN could be left undissected without increasing the risk of locoregional recurrence. In a meta-analysis on the subject, Xing., *et al*. [40] found a global sensitivity for SLNB after neoadjuvant CT of 94%. Despite the inconsistent success rate, most studies have concluded that SLNB is technically feasible after primary CT [41].

Prognosis

Evidence in most studies show that response to neoadjuvant CT is one of the most important prognostic factors. Breast and lymph node response were significantly correlated with DFS in study conducted by Bonadonna [42]. The NSABP B18 [6,35] trial demonstrated a DFS relative risk of 0,47 ($p < 0,0001$) for patients who achieved a pCR. The pCR has also emerged as an important prognostic factor for OS, with an OS relative risk of 0,32 according to the NSABP B18 [6,35] trial, and of 0,86 ($p < 0,0008$) according to the EORTC trial [7].

Based on these results, the complete response to primary CT has become the ultimate endpoint of a successful neoadjuvant chemotherapy treatment, such as in the present study.

However the prognostic value of pCR as a single prognostic factor is questionable. In fact, In the NSABP B27 trial [6,10], 2,411 patients with operable breast cancer were randomized to anthracyclines with or without taxanes. Although the pathologic complete response was doubled (26.1% v 13.7%) with the adjunction of taxanes, there was no significant improvement with regard to overall and disease free survival. This suggests that other factors play a potential role in patients' outcome. In the present study, there was a trend towards a better OS for patients who achieved a pCR ($p = 0,068$). However, there was no significant benefit in terms of DFS. This might be due to the small size of our population study.

Outside of clinical trials, the use of additional chemotherapy after a neoadjuvant treatment is discouraged, since there is no clear evidence that patients with a poor response would benefit from additional CT courses. However, a recent study, evaluated the role of adjuvant chemotherapy (capecitabine) after a standard course of treatment in patients who did not achieve a pCR to neoadjuvant CT (no pCR or ypN+), and found that patients who received capecitabine showed better DFS at 5 years (74,1 vs 67,7% (HR = 0,70; IC95%: 0,53 - 0,93). The OS rates were also higher in the capecitabine arm. (89,2 versus 83,9%) [HR = 0,60; IC95: 0,40 - 0,92] [43]. In our series, 59,7% of our patients had node involvement after neoadjuvant CT. Adjuvant chemotherapy was administered to five patients, four of whom received a navelbine-capecitabine regimen. Surgery is a key prognostic factor in the treatment of breast cancer. BCS before neoadjuvant CT have been shown to be associated with a greater likelihood of local recurrence but without compromising overall survival. In the NSABP B-18 [6,35] trial, the locoregional recurrence rates were higher in patients who were candidates for mastectomy at diagnosis and then converted to BCS compared with those who were candidates for breast conservation before the neoadjuvant CT (15.7% vs. 9.9%, respectively; $p = 0.04$). However, these results have not been confirmed by other studies [7,10]. In agreement with these studies, BCS did not increase the risk of recurrence ($p = 0,187$) in the present study. These results emphasize the fact that BCS should not be prohibited on some patients on the basis of a greater risk of recurrence. However, candidates for this surgery should be carefully selected.

Conclusion

In summary, preoperative chemotherapy is established as the standard of care for patients with LABC. Identification of predictive markers of response to therapy is of great interest. Gene profiling appears to hold a promise of identifying specific profiles that are associated with response to chemotherapy, however, none of the gene sets has enough predictive power to be implemented in a clinical setting

at present. Currently, histological type, hormone receptor negativity and HER2 amplification, and degree of proliferation (Ki67, mitotic index) are most associated with response to chemotherapy.

Despite the retrospective aspect of the present study and the limited size of our population, the present study showed that BCS is be feasible for appropriately selected patients without compromising long term outcome.

Further studies are required to enhance clinical and radiological evaluation of response to neoadjuvant CT, and investigate other predictive and prognostic factors and thus refine selection criteria for the appropriate surgical management and implement an individual tailored approach for LABC patients.

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