



## The role of oncoplastic breast conserving treatment for locally advanced breast tumors. A matching case-control study



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### HIGHLIGHTS

- A matched case-control study evaluates oncoplastic techniques for locally advanced breast cancer.
- The size of tumors were bigger than other series.
- The matched case-control study was selected base on tumor size and year of diagnosis to decrease possible bias selection.
- The security of this procedure was evaluated based a long follow up.
- Oncoplastic surgery has the same results than conventional breast conserving surgery for locally advanced breast tumors.

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### ABSTRACT

**Background:** Breast conserving surgery (BCS) after neoadjuvant chemotherapy (NC) in patients with locally advanced breast cancer (LABC) is an infrequent procedure. In these patients the association with BCS and oncoplastic surgery (OS) is reported as a possible procedure in case-series, but there are limited case-control studies.

**Methods:** A matched case-control study evaluated LABC submitted to NC and BCS. We evaluated 78 patients submitted to doxorubicin-cyclophosphamide regimen followed by paclitaxel regimen. The match case-control proportion was 2:1 and the patients were selected by tumor size, clinical T stage and year of diagnosis.

**Results:** 52 underwent classic BCS and 26 OS. The average size tumor was 5.25 cm and 88.5% of the tumors were larger than 3 cm. The clinical and pathological group characteristics were similar, except the weight of surgical specimens ( $p = 0.004$ ), and surgical margins ( $p = 0.06$ ), which were higher in OS group. The rate of complete pathologic response was 26.9%. 97.4% received postoperative radiotherapy. At 67.1 months of follow up, 10.2% had local recurrence (LR) and 12.8% locoregional recurrence (LRR) and 19.2% died because disease progression. The overall survival at 60 months was 81.7%. After surgery the disease free-survival at 60 months was 76.5%. There was no difference between groups related to pathologic response ( $p = 0.42$ ), LR ( $p = 0.71$ ), LRR ( $p = 1.00$ ), overall survival ( $p = 0.99$ ) and disease specific survival ( $p = 0.87$ ).

**Conclusion:** This study corroborates the fact that OS is a safety procedure for LABC, offering the similar oncologic results observed in patients submitted to classic BCS.

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### 1. Background

Breast-conserving surgery (BCS) [1,2] was initially indicated for tumors up to 2 or 4 cm but is now used when the tumor/breast

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volume ratio is favorable [3]. The use of radiotherapy made BCS a safe procedure [1,2]. Quality of life and cosmesis have become important points to be considered to improve results [4] and oncoplastic surgery (OS) arises in this context [4–6]. OS includes resection of more breast tissue, ease in obtaining safe margins and better cosmetic effect [3–5,7–9], but there is limited evaluation of the long-term effects, whether in terms of recurrence, cosmesis or quality of life [4–6,10–12].

When evaluating BCS in patients undergoing neoadjuvant chemotherapy (NCT) [13], we observed that it is feasible [14] and safe [15,16]. Various factors are involved in its indication, with only a subset of 37–82% [17,18] of patients undergoing this treatment; of these patients, only 1.7%–28% have locally advanced breast cancer (LABC) [18,19]. OS technique [20,21] increase the indications of BCS [11,18].

Case-control studies evaluating OS are limited and based on retrospective analyses [6,11,12,22]. They reported patients with and without NCT [6,11,22–24], but NCT was not the main endpoint. OS depends on the surgeon's training, the tumor's characteristics and the patient's wishes. Likewise, OS involves various procedures at different levels of complexity that come together under the title of OS, a fact that limits prospective studies. The literature reporting the use of OS techniques in the BCS of patients exclusively in undergoing NCT is limited [20]. But, conducting a matched case-control study that exclusively evaluates the role of OS in patients undergoing BCS and NCT is an interesting proposal, and it was this fact that motivated us to conduct this study.

## 2. Materials and methods

This retrospective sequential case-control study evaluated patients with clinical non-metastatic, non-inflammatory, untreated LABC, treated in a Tertiary Oncological Hospital, from 10/2005 to 12/2011, and who underwent NCT and BCS. During this period, 486 patients underwent NCT, 98 BCS, and 26 BCS combined with oncoplastic breast surgery. A convenience study was performed, but the cases were matched to decrease a possible bias selection. The patients undergoing OS were considered to be cases. The control group of patients undergoing classic BCS was chosen at a ratio 1: 2, where patients were selected based on tumor size, accepting a standard deviation of 5 mm, followed by T clinical staging and the year of the initiation of treatment. The final sample consisted of 52 control patients and a total of 78 patients for analysis.

In this period, the standard neoadjuvant regimen was 4 AC cycles (doxorubicin 60 mg/m<sup>2</sup> [2] + Cyclophosphamide 600 mg/m<sup>2</sup> [2]), followed by 4 T cycles (Taxol [paclitaxel] 175 mg/m<sup>2</sup>). At the end, the 4AC + 4T regimen was performed in 83.3% of cases, 4AC + 12T in 10.2% and other regimens in 6.4%, depending on disease progression or treatment toxicity.

The patients were selected from a clinical and radiological point of view before and after NCT. Intraoperative frozen-section examination was available during surgery in all cases. Standard surgical treatment was quadrantectomy combined with level III axillary node dissection with was performed in 97.4% of patients.

All patients were evaluated postoperatively by a multidisciplinary team. 97.4% of patients undergo breast adjuvant radiotherapy (5.040 cGy) associated with tumor bed boost (1.000 cGy) and 85.9% received radiation therapy of the supraclavicular fossa. Patients with estrogen receptor/progesterone receptor (ER/PR)-positive tumors received hormone therapy. Adjuvant chemotherapy was not performed on every patient; it was only used in a palliative manner where there was disease recurrence. Only two patients received adjuvant trastuzumab.

Total follow-up was considered to be the time between the first

and last visits. The disease-free interval was considered to be the time between quadrantectomy and either recurrence or last follow-up date. The response to chemotherapy, local recurrence (LR), locoregional recurrence (LRR), and survival were evaluated. Local recurrence was defined as breast recurrence, even if secondary to local infiltration. LRR was defined as local recurrence associated with regional lymph node disease.

The TNM clinical status was used (7th edition, 2010). The slides were reviewed by pathologists (CSN, MM). Where bilateral tumors were present, the one with the highest stage was considered. To evaluate pathologic response we used Chen et al. [16] and NSABP classifications. Complete pathological response was defined as an absence of invasive disease in the breast and axilla. Molecular subtype was evaluated based on an immunohistochemistry technique [25].

### 2.1. Statistical analysis

Data were collected were tabulated and analyzed using SPSS 20.0 software for Mac<sup>®</sup>. Initially, the frequencies of categorical variables and the means and standard deviations of continuous variables were analyzed. To compare group characteristics, the chi-square test was used for categorical variables, and Fisher's exact test was used when there were fewer than five patients. The Student's t or Mann-Whitney test was used to compare continuous variables. The Kaplan-Meier method was used for analysis of the risk of disease-free recurrence and overall and specific survival, and the log-rank method was used for the evaluation of differences between groups. The level of statistical significance used was  $p < 0.05$ .

## 3. Results

This matched case-control study evaluated patients with LABC who underwent NCT and BCS, where 26 underwent OS (Table 1) and 52 underwent classic quadrantectomy.

The average age of patients was 48.8 years (range 21.3–75.1 years) and the average tumor size was 5.25 cm (range 2.0–8.5 cm). 69.2% of the women had low education levels, 51.3% of the tumors were on the right side, 89.7% of the tumors were clinical stage III, 78.2% tumors were clinical stage T3 and T4, 82.1% of patients had lymph node metastasis, 91.0% of tumors were invasive ductal carcinomas, 94.7% of tumors were Nottingham histologic grade 2/3, 92.1% were nuclear grade 2/3, 61.5% were ER-positive, 52.6% were PR-positive and 23.1% were Her2-positive. Table 2 compares the groups regarding pre-treatment clinical and pathological characteristics, and it should be noted that group stratification revealed no differences between groups.

The breast oncoplastic surgical procedures used were central quadrantectomy (n = 8), dermoglandular rotation flap (n = 7), periareolar quadrantectomy (n = 5), inferior pedicle (n = 4) and superior pedicle (n = 2). All patients in the control group (n = 52) underwent classic quadrantectomy. Contralateral surgery was performed in 12.8% of cases due to benign changes or for obtaining symmetrization (10.3%) or due to the presence of a synchronous contralateral tumor (2.6%). The margins were free in all patients, with a mean of 13 mm (range 1–40 mm), and they were smaller than 2 mm in only three patients (3.9%).

Analysis of post-chemotherapy treatment characteristics revealed that the average weight of the surgical specimen was 241 g (range 41.5–980.0 g), and the mean follow-up time was 63.3 months (range 13.4–105.7 months). Table 3 compares the groups regarding post-treatment clinical and pathological characteristics. In the group stratification, it can be observed that the weight of the surgical specimens of patients undergoing OS was higher ( $p = 0.04$ ) and that the margins were higher in this group, although not

**Table 1**  
Clinical characteristics of patients undergoing oncoplastic surgery.

Patient	Initial tumor size	EC-TNM	Oncoplastic surgery	MDA [16] response	PCR	Locoregional recurrence	Follow up	Final status
1	2,0	III A	Periareolar	Without residual disease	Present	Absent	73,68	Recurrence free
2	2,0	III B	Flap rotation	Multifocal disease	Absent	Absent	46,71	Recurrence free
3	3,0	III C	Central quadrantectomy	Solid mass	Absent	Absent	20,33	ADD
4	3,5	III B	Superior pedicle quadrantectomy	Without residual disease	Present	Absent	67,93	CD
5	3,5	III B	Central quadrantectomy	Solid mass	Absent	Absent	79,77	Recurrence free
6	3,5	III B	Central quadrantectomy	Without residual disease	Present	Absent	58,78	Recurrence free
7	4,0	III B	Periareolar	Multifocal disease	Absent	Internal mammary/sternum and breast	71,61	CD
8	4,5	II A	Periareolar	Multifocal disease	Absent	Absent	61,05	Recurrence free
9	4,5	III A	Plug flap	Solid mass	Absent	Absent	57,47	Recurrence free
10	5,1	III A	Flap rotation	Solid mass	Absent	Absent	55,66	Recurrence free
11	5,2	III A	Flap rotation	Solid mass	Absent	Absent	55,92	Recurrence free
12	5,5	III A	Inferior pedicle quadrantectomy	Without residual disease	Present	Absent	68,36	Recurrence free
13	5,5	III A	Central quadrantectomy	Multifocal disease	Absent	Local and systemic	24,24	CD
14	6,0	III B	Inferior pedicle quadrantectomy	Solid mass	Absent	Absent	33,49	ADD
15	6,0	III A	Periareolar	Without residual disease	Present	Absent	54,77	Recurrence free
16	6,0	III A	Flap rotation	Solid mass	Absent	Absent	69,24	Recurrence free
17	6,0	III A	Flap rotation	Solid mass	Absent	Homolateral SCF	61,78	CD
18	6,0	III A	Central quadrantectomy	Stable disease	Absent	Absent	60,59	Recurrence free
19	6,0	III A	Periareolar	Without residual disease	Present	Absent	66,35	Recurrence free
20	6,0	III A	Superior pedicle quadrantectomy	Solid mass	Absent	Absent	46,38	Recurrence free
21	6,0	III A	Inferior pedicle quadrantectomy	Without residual disease	Present	Absent	39,41	Recurrence free
22	6,6	III A	Central quadrantectomy	Solid mass	Absent	Absent	78,06	Recurrence free
23	7,0	III A	Inferior pedicle quadrantectomy	Solid mass	Absent	Absent	92,99	Recurrence free
24	7,0	II B	Flap rotation	Solid mass	Absent	Absent	68,13	Recurrence free
25	8,0	III B	Central quadrantectomy	Solid mass	Absent	Absent	96,48	Recurrence free
26	8,5	III A	Flap rotation	Solid mass	Absent	Absent	51,18	Recurrence free

CD = Cancer death; ADD = associated diseases death; SCF = supraclavicular fossa; PCR = Pathologic complete response; MDA = M.D.Anderson.

significantly so ( $p = 0.06$ ).

The mean follow-up for live patients after surgery was 67.1 months. In the follow-up period, there were 8 local recurrences (LR, 10.2%), 3 of which were LR and systemic, 2 LR and locoregional recurrences, 2 mammary and sternal and 1 exclusively mammary. During follow-up, there were 10 LRRs (12.8%), with metastatic disease observed in 20.5%, and with the major distant metastatic sites being bone (12.8%), lung (10.3%), liver (7.7%) and brain (3.3%). At the end of the study, 19.2% had died of disease progression, 1.3% from associated diseases, and 5.1% due to indeterminate causes; 3.8% were still alive with the disease, and 70.5% were alive and free of disease. 6.1% were consider lost of follow up. The global overall survival at 60 and 96 months was 81.7% and 61.5%, respectively. After surgery the disease free-survival at 60 months was 76.5%. In evaluating the influence of OS on recurrence and survival, the chi-square test showed no differences in terms of local recurrence, LRR and survival, and this was true in the analysis of both disease free survival in relation to the risk of local recurrence, locoregional

recurrence (Fig. 1), overall survival and specific overall survival (Fig. 2).

#### 4. Discussion

A priori OS was initially used for tumors under 4 cm, provided that the surgery was associated with the oncological principles of margins free of neoplastic involvement and resulted in acceptable cosmetic results [3,5,6] and acceptable recurrence rates [4], that were lower than those obtained using traditional BCS [5]. The literature reveals a rate of margin involvement of up to 18.9%, with good cosmetic results in 84–90.3% of patients and recurrence rates of up to 7% [3–6]. When evaluating OS and BCS [8,26], type I and II procedures are generally used [26], and the technique used depends on tumor location, breast volume, presence of ptosis, the surgeon's experience, and, in patients undergoing NCT, the response to chemotherapy [20,26,27]. In terms of OS complexity [28] 10/26 procedures were level I, and 16/26 were level 2.

**Table 2**  
Comparison between groups across the preoperative variables.

Category	Variable	Control	Oncoplastic surgery	Total	p
Age	Media	48.27 ± DP 1.69	49.75 ± DP 1.80	48.76 ± DP 1.25	0.58
Initial size	Media	5.25 ± DP 1.52	5.26 ± DP 1.66	5.25 ± DP 1.56	0.97
Period	2006–2008	29 (55.8%)	12 (46.2%)	41 (52.6%)	0.48
	2009–2010	23 (44.2%)	14 (53.8%)	37 (47.4%)	
Schooling	<11 years	37 (71.2%)	17 (65.4%)	54 (69.2%)	0.61
	≥11 years	15 (28.8%)	9 (34.6%)	24 (30.8%)	
Side	Right	28 (53.8%)	12 (46.2%)	40 (51.3%)	0.53
	Left	22 (42.3%)	14 (53.8%)	36 (46.2%)	
	Bilateral	0 (3.8%)	0	2 (2.5%)	
EC/TNM	II	6 (11.5%)	2 (7.7%)	8 (10.3%)	0.71
	III	46 (88.5%)	24 (92.3%)	70 (89.7%)	
EC/TNM	Ila	2 (3.8%)	1 (3.8%)	3 (3.8%)	0.91
	Ilb	4 (7.7%)	1 (3.8%)	5 (6.4%)	
	IIla	28 (53.8%)	16 (61.5%)	44 (56.4%)	
	IIlb	14 (26.9%)	7 (26.9%)	21 (26.9%)	
	IIlc	4 (7.7%)	1 (3.8%)	5 (6.4%)	
EC-T/TNM	T2	12 (23.1%)	5 (19.2%)	7 (21.8%)	0.90
	T3	28 (53.8%)	14 (53.8%)	42 (53.8%)	
	T4	12 (23.1%)	7 (26.9%)	19 (24.4%)	
EC-N/TNM	N0	9 (17.3%)	5 (19.2%)	14 (17.9%)	0.89
	N1	30 (57.7%)	16 (61.5%)	46 (59.0%)	
	N2 + 3	13 (25.0%)	5 (19.2%)	18 (23.1%)	
Histology	Ductal Invasive	47 (90.4%)	24 (92.3%)	71 (91.0%)	1.00
	Other	5 (9.6%)	2 (7.7%)	7 (9.0%)	
Nuclear grade	G1	4 (8.0%)	2 (7.7%)	6 (7.9%)	1.00
	G2 + G3	46 (92.0%)	24 (92.3%)	70 (92.1%)	
Histology grade	G1	3 (60.0%)	1 (3.8%)	4 (5.3%)	1.00
	G2 + G3	47 (94.0%)	25 (96.2%)	72 (94.7%)	
RE	Positive	34 (65.4%)	14 (53.8%)	48 (61.5%)	0.34
	Negative	18 (34.6%)	12 (46.2%)	30 (38.5%)	
RP	Positive	29 (55.8%)	12 (46.2%)	41 (52.6%)	0.48
	Negative	23 (44.2%)	14 (53.8%)	37 (47.4%)	
Her2	Absent	43 (82.7%)	17 (65.4%)	60 (76.9%)	0.10
	Present	9 (17.3%)	9 (34.6%)	18 (23.1%)	
Molecular subtype	Luminal/Her–	31 (59.6%)	9 (34.6%)	40 (51.3%)	0.08
	Luminal/Her+	5 (9.6%)	8 (30.8%)	13 (16.7%)	
	Her +	4 (7.7%)	2 (7.7%)	6 (7.7%)	
	Triple negative	12 (23.1%)	7 (26.9%)	19 (24.4%)	
Tumor markup	Absent	42 (80.8%)	17 (65.4%)	59 (75.6%)	0.17
	Present	10 (19.2%)	9 (34.6%)	19 (24.4%)	
Previous radiologic evaluation	MMG	8 (15.4%)	2 (7.7%)	10 (12.8%)	0.35
	MMG + US	35 (67.3%)	16 (61.5%)	51 (65.4%)	
	MMG + US + RNM	9 (17.3%)	8 (30.8%)	17 (21.8%)	

MMG = mammography; US = ultrasound; RNM = magnetic resonance; EC = clinical stage.

**Table 3**  
Comparison between groups across the postoperative variables.

Category	Variable	Control	Oncoplastic surgery	Total	p
Surgical weight	g	208.62 ± DP 139.97	307.40 ± DP 221.04	241.55 ± DP 176.17	0.04
Surgical margin	mm	11.85 ± DP 8.36	16.44 ± DP 8.64	13.23 ± DP 8.64	0.06
Follow up	Months	64.88 ± DP 24.53	60.01 ± DP 18.19	67.13 ± DP 22.61	0.33
Bilateral surgery	Absent	47 (90.4%)	21 (80.8%)	68 (87.2%)	0.17
	Benign	3 (5.8%)	5 (19.2%)	8 (10.3%)	
	Tumor	2 (3.8%)	0	2 (2.6%)	
MDA [16] response	Stable	2 (3.8%)	1 (3.8%)	3 (3.8%)	1.00
	Mass	27 (51.9%)	14 (53.8%)	41 (52.6%)	
	Multifocal	8 (15.4%)	4 (15.4%)	12 (15.4%)	
	Without disease	15 (28.8%)	7 (26.9%)	22 (28.2%)	
PCR	Present	16 (30.8%)	5 (19.2%)	21 (26.9%)	0.42
	Absent	36 (69.2%)	21 (80.8%)	57 (73.1%)	
Local recurrence	Absent	46 (88.5%)	24 (92.3%)	70 (89.7%)	0.71
	Present	6 (11.5%)	2 (7.7%)	8 (10.3%)	
Locoregional recurrence	Absent	45 (86.5%)	23 (88.5%)	68 (87.2%)	1.00
	Present	7 (13.5%)	3 (11.5%)	10 (12.8%)	
Final status	CD	11 (21.2%)	4 (15.4%)	15 (19.2%)	0.55
	ADD	3 (5.8%)	2 (7.7%)	5 (6.4%)	
	Recurrence	3 (5.8%)	0	3 (3.8%)	
	Recurrence free	35 (67.3%)	20 (76.9%)	55 (70.5%)	

CD = Cancer death; ADD = associated diseases death; PCR = pathologic complete response; MDA = M.D.Anderson.

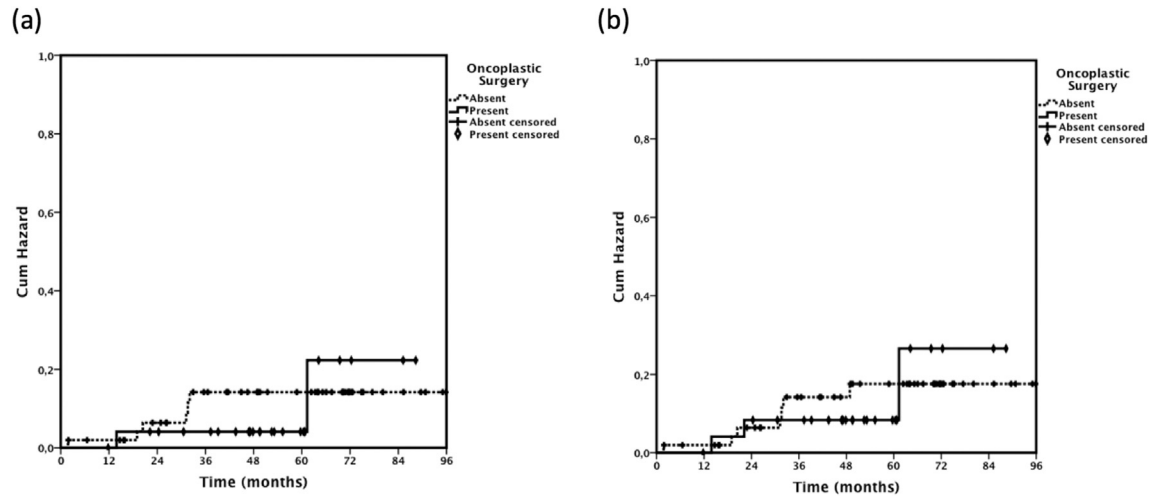


Fig. 1. Risk of recurrence according to the groups a) Local recurrence ( $p = 0.65$ ); b) Locoregional recurrence ( $p = 0.85$ ).

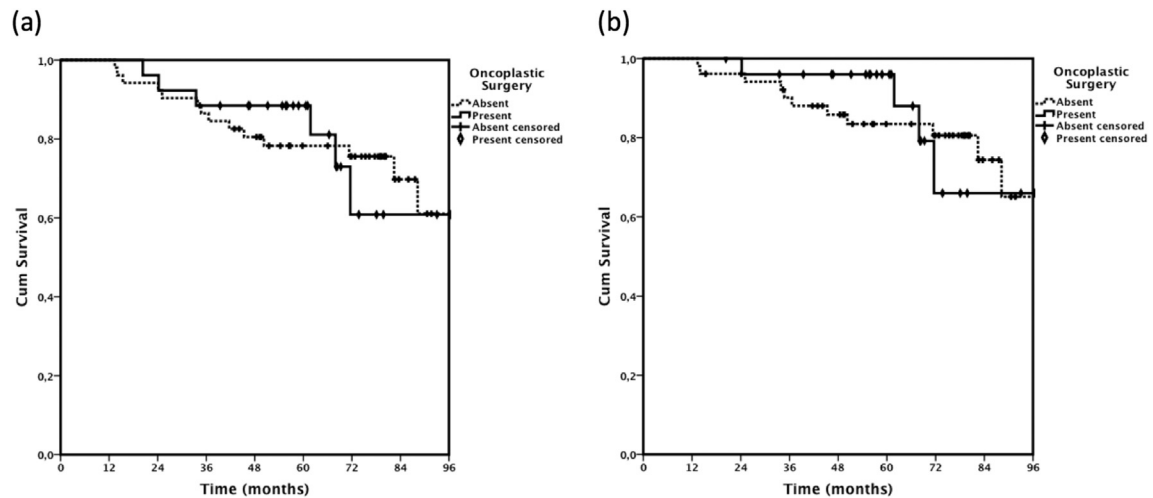


Fig. 2. Survival function between groups. a) Overall survival ( $p = 0.99$ ); b) Disease specific survival ( $p = 0.87$ ).

NCT provides the same overall survival as adjuvant chemotherapy and has the advantage of identifying patients with a better prognosis [29]. Patients submitted to NCT and BCS have lower initial T-TNM stage, higher complete pathological response rate and increased ER-negative, PR-negative and triple-negative tumor rates [30].

Comparing the groups, we observed similar clinical characteristics between the groups (Table 2). The only characteristic with a marginal difference was the molecular subtype, as the high incidence of luminal/her negative patients in the control group and proportional high incidence of triple negative and Her positive patients in the OS group. Her positive and triple negative breast cancer are associated with high local recurrence [31] and better neoadjuvant response [32]. In the NCT setting triple negative are associated with higher locoregional rate [32]. Evaluating our patients molecular subtype not affected the local ( $p = 0.25$ ) or locoregional ( $p = 0.35$ ) recurrence, and did not affected the pathologic complete response (PCR) ( $p = 0.51$ ), even different pathologic response rate. The PCR occurred in 50% Her positive, 31.6% triple negative, 23.1% Luminal/her positive and 22.5% luminal/her negative.

Radiotherapy is a standard treatment after BCS, decreasing local

recurrence [2]. Unfortunately two patients in the control group were not submitted to radiotherapy. One because rapid disease progression, and the other refused radiotherapy because panic syndrome, but she did not developed recurrence. Although this condition occurred, it did not affected the local ( $p = 0.20$ ), locoregional ( $p = 0.24$ ) recurrence or overall survival ( $p = 0.10$ ).

BCS in LABC has several characteristics that call for OS criteria to be reevaluated [7,20]. It must be associated with clear margins [33] and adjuvant breast radiotherapy [1,2,24]. Therefore, the present study seeks not only to show that OS is feasible in LABC, but that the recurrence rate is similar to that of patients undergoing conventional treatment for LABC. Candidates initially selected for LABC and BCS were those with no involvement of the skin or chest wall, absence of multicentric disease or extensive microcalcifications, tumors smaller than 5 cm, unfavorable tumor location, no contraindications to radiotherapy and negative margins, with contraindications for inflammatory carcinoma [34]. Patients with N2-3 lymph nodes, residual tumor >2 cm, and presence of lymphovascular embolization should be evaluated with caution because there is a higher risk of local recurrence [16,35], but it was not considered in the indication of our cases. A limitation of BCS in LABC is extensive resection, which can lead to large breast deformity,

especially in the case of superior pole tumors. Tumor/breast volume ratio, tumor location and the need for skin resection are OS indications and they were used in this case-series for selecting the surgical treatment [36]. Evaluating our patients we must inform that the indication of the surgery was based on breast-tumor relation, clinical aspects, radiological and post-NC evaluation. T3 patients was selected based on breast-tumor relation, allowing safety for large tumor resection with free margins. Only localized clinical T4 was selected. Patients with local disease progressing during chemotherapy were not submitted to BCS. Radiologic evaluation was performed in all patients and tumor markup was performed. When possible, our group option is to resect all area previous to NC [20], a fact that led to a high free surgical margins. In the presence of positive margin during operative and post-operative period, 2 patients with LABC were submitted to mastectomy, and they were not included in this study. BCS is feasible in LABC, even for initial tumors with an average size of 5.3 cm (range 2–8.5 cm), provided that they are associated with a free surgical margin averaging 12 mm (range 1–40 mm) [21], thus expanding the indication criteria initially established in such a way that the presence of localized skin infiltration, localized multifocal disease and the favorable breast/tumor ratio that allows resection of the entire tumor area [20,21].

In LABC, adequate pre- and postoperative radiological clinical evaluation [37,38], marking of the tumor bed [39], intraoperative frozen-section examination, pretreatment resection of the entire tumor area, and good clinical and pathological response are factors that contribute positively to good outcomes. The type of tumor fragmentation also has an influence on resection, with 14.3% cases of microscopic multifocal disease, which is only detected by the removal of the entire surgical specimen [21]. In patients undergoing NCT, the local recurrence rates were 11.2% at 5.3 years in the service's case series [21] and 19% at 4.6 years [40], and estimated to be 21.5% at 20 years [41]. This rate is influenced by follow-up time, type of chemotherapy used, complete pathological response rate, tumor size, lymph node status [15,21], the use of radiotherapy [2], and method of recurrence evaluation [21].

OS is a recent procedure, and most case-series use tumors approximately 3 cm in size [6,7] and have recurrence rates of up to 7% [3–6]. However, there is a variable follow-up time of 1–74 months [4], with an average of 37.1 months [5]. Rietjens et al. evaluated the long-term results of OS ( $n = 148$ ) for tumors averaging 2.2 cm, with 84.5% smaller than 3 cm and 40.5% N0. Over an average follow-up of 74 months, the authors observed no recurrence for pT1 tumors, but five recurrences for pT2–3 tumors (8.4%) [10]. Fituosi et al. evaluated OS ( $n = 540$ ) using various selection criteria, with an average tumor size of 29 mm (4–100 mm), 18.9% with close or involved margins and 93 (17.2%) subjected to NCT, with an average of 49 months follow-up and 6.8% of recurrence rate [6].

Evaluating retrospective case-control study, Chakavorty et al. separated cases only by surgical technique, with 440 undergoing conventional surgery and 150 OS. In patients undergoing OS, the average tumor size was 21 mm, and the average weight of the surgical specimen was 67 g, values that were higher than those of patients undergoing conventional surgery. A total of 25% received NCT. OS was associated with greater tumor size, greater specimen weight and lower rate of re-excision. With an average of 28 months' follow-up, the 6-year local recurrence were 4.3% in OS and 3.7% in patients undergoing conventional treatment [11]. Down et al. studied 121 patients undergoing conventional surgery and 37 having OS. OS was related to larger tumor diameter (2.39 cm), greater weight of the resected specimen (average 231.1 g) and greater margin distance (14.3 cm), a fact that led to lower surgical re-excision rates in the group undergoing OS (5.4%). However, this

study did not evaluate recurrence rates, and the minimum average follow-up was 22.1 months in the control group [12].

Mazouni et al. performed a case-control study of patients undergoing NCT and BCS, with 214 patients undergoing standard treatment and 45 OS. A total of 25.8% were T3/T4 tumors, and 44.8% had metastatic lymph node disease prior to NCT. Anthracycline, cyclophosphamide and 5FU with or without docetaxel were used. The average tumor size was 40 mm, and excised volume were greater in patients undergoing OS. The local recurrence rate was 5% [22] vs. 4% at 46 months. The groups did not differ with respect to response to NCT, and no differences were observed between groups regarding recurrence, metastasis, or survival [22].

Silverstein et al. [24] introduced the term "Extreme oncoplasty (EO)" for patients whose initial option was mastectomy but they were submitted to OS and BCS. They reported 66 patients with large tumors, 77 mm mean size, lower margins, higher re-excision rate and similar recurrence, than patients with lower size tumors submitted to OS ( $n = 245$ ). The main limitation of the study is a limited follow up (24 months). They consider that OS and BCS improve the quality of life, and although local recurrence would be higher, it will have a little impact on survival. Using the single criteria of size ( $>5$  cm), 61.4% of our patients represents EO and all were LABC. A higher recurrence observed in our study probably was associated to the higher follow up and tumors characteristics.

Cutress et al. [9] evaluated some criteria related to safety for OS and considered that in BCS, the recurrence rate should not exceed that in patients undergoing standard treatment [9], which was observed in our case series through both chi-square analysis ( $p = 0.712$ ) and analysis of recurrence-free survival ( $p = 0.646$ ). Comparing similar groups and observing similar results, we consider that on the same conditions, OS is feasible, giving the same results related to BCS in LABC.

Santos et al. [42] performed a cross sectional study evaluating patients who underwent OS ( $n = 57$ ) or lumpectomy ( $n = 65$ ). They performed a cosmetic evaluation using the Garbay scale and the BCCT.core software. They observed that excellent aesthetic results were more frequent in the OS group. Losken et al. [5] performed a meta-analysis comparing OS and BCS, observing that OS was associated with higher weight, lower positive margins, lower re-excision surgeries and better cosmetic satisfaction (89.5% OS x 82.9% BCS), but the mean size for OS was 2.7 cm and for BCS was 1.2 cm. Our group mean diameter was 5.26 cm, observing high surgical weight (307.4 g) and high margin distance (16.4 mm). Unfortunately it was a retrospective study and a cosmetic evaluation was not performed and would not be able. 25.6% of the patients died, a fact that was influenced by advanced clinical stage at diagnosis and long follow up.

De Lorenzi et al. [23] performed a matched case-control study, evaluating 454 patients submitted to OS and 908 control, followed by 7.2 years, observing that the OS and DFS were similar between the groups. The matching was based on age, year of surgery and tumor size. Although it represents the large matched case-control published series, only 10 patients in the OS group (2.2%) was pT3–4, and patients with neoadjuvant chemotherapy were excluded for the analysis. Our publication represents the large matched case-control study performed in LABC, submitted to NCT with long follow up, a fact that may decrease possible biases, and strengthens the use of OS, in this selected group of patients. The main limitation of this study is that it is retrospective study, but there is no prospective study with large tumors submitted to OS. The OS indications are related to the patient, tumor size and breast characteristics, making difficult to perform prospective studies. The present case-control study was matched to reduce possible biases. The average size was 5.25 cm, and the average weight was 241.5 g. There was a longer follow-up (67.13

months), the local recurrence rate was 11.2%, and there were no differences between groups in terms of tumor size, follow-up and recurrence rate, with only the weight of the surgical specimens being higher in patients undergoing OS, which reinforces the indication for the use of OS in LABC patients undergoing NCT. This study demonstrates the validity of OS for larger tumors in LABC patients undergoing NCT, with acceptable proportional recurrence rates.

## 5. Conclusion

The present study shows that OS is a feasibility procedure for LABC patients undergoing NCT. It is a safety procedure for LABC, offering the similar oncologic results observed in patients submitted to classic BCS.

## Ethical approval

The project was approved by the Research Ethics Committee under protocol number 135/2008.

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## Author contribution

RACV participated from the study design, submission to Ethics Committee, cases selection, surgery, data analysis and written version.

GFAC participated from the data review, data analysis and written version.

CSN performed the pathological review and review the final version.

MAM performed the pathological review and review the final version.

MMB participated from the study design, data analysis and review the final version.

MAAKF participated from the study design, data analysis and review the final version.

## Conflict of interest

The authors declare no conflicts of interest.

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## Guarantor

René A C Vieira is the guarantor.

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