

RESEARCH ARTICLE

Oncoplastic Breast Conserving Surgery with Nipple-areolar Preservation for Centrally Located Breast Cancer: a Retrospective Cohort Study

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Abstract

A comparison was made of survival outcomes of oncoplastic breast conserving therapy (oBCT) with nipple-areolar (NAC) preservation in women with centrally located breast cancer (CLBC) undergoing modified radical mastectomy (MRM) in China in a matched retrospective cohort study. We used a database including patients who received oBCT (n=91) or MRM (n=182) from 2003 to 2013 in our hospital. Matching was conducted according to five variables: age at diagnosis, axillary lymph node status, hormone receptor status, human epidermal growth factor-like receptor 2 status (HER-2) and tumor stage. The match ratio was 1:2. Median follow-up times for the oBCT and MRM groups were 83 and 81 months, respectively. There were no significant differences in 87-month overall, local, or distant recurrence-free survival between patients with oBCT and MRM (89% vs. 90%; 93% vs. 95%; 91% vs. 92%;). For appropriate breast cancer patients, oBCT for CLBC is oncologically safe, oncoplastic techniques improving cosmetic outcomes.

Keywords: Oncoplastic breast conserving surgery - nipple-areolar preservation - centrally located breast cancer.

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Introduction

Although oncoplastic breast conserving therapy (oBCT) has become a commonly used treatment for breast cancer (Spear SL et al., 2003), there has been concern over its use for centrally located tumors. It is accepted that a central lumpectomy with resection of the nipple-areolar complex (NAC) correlates with poor aesthetic outcomes. Also, there is little data to support central lumpectomy without resection of the NAC as an equal alternative to mastectomy in regard to oncological outcomes. In this study, we investigate oncological outcomes of patients with centrally located breast cancer (CLBC) treated with oBCT with NAC preservation compared with mastectomy.

Materials and Methods

Inclusion Criteria

We retrospectively analyzed our data including 91 patients with CLBC treated with oBCT with NAC preservation from Jan 2003 until Sep 2013 at the Department of Surgery, Jiangsu Cancer Hospital. Patients received clinical examination, ultrasonic detection, and mammography and/or Magnetic Resonance Imaging (MRI) before operation to exclude patients with multifocal diseases. Central tumors were defined as within 2 cm of the areolar margin. All patients received resection-free margins (>1mm). The choice of oncoplastic technique was

based on the tumor-to-breast size ratio, and the latissimus dorsi flap was used for breast reconstruction in patients with small to medium-sized breasts.

To compare the oBCT with the classical therapy methods in breast cancer patients, we conducted a matched retrospective cohort study with a match ratio of 1:2. Patients in the control group received modified radical mastectomy (MRM). Controls were matched according to five variables considered to have a major impact on chances of local recurrence, distant metastasis, and the survival rates: *i)* Age at diagnosis: ≥ 50 years, < 50 years. *ii)* Tumour size: Tis, T1, T2. *iii)* Axillary lymph node status: 0, 1–3. *iv)* Hormone receptor status: positive, negative. *v)* Her-2 status: positive, negative.

Adjuvant therapy

All the oBCT patients underwent a level I and II axillary lymph node dissection. Radiotherapy was given to the oBCT group. Adjuvant chemotherapy regimes were given to the invasive breast cancer patients according to NCCN guidelines. The human epidermal growth factor receptor-2 (HER2) was considered negative when immunohistochemical (IHC) staining was negative or 1+, and positive when IHC staining was 3+, or HER2 gene amplification was identified by fluorescence in situ hybridization (FISH). In cases of HER2 2+, FISH was performed to determine HER2 positivity. In both groups, the patients with HER-2-positive would take Herceptin

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for 1 year according to NCCN guidelines, and the patients with hormone receptor-positive would take tamoxifen for 5 years.

Results

A total of 91 oBCT patients and matched 182 MRM patients were included in this study. The primary surgical treatment for 91 patients with central tumors was oncoplastic breast conserving surgery with nipple-areolar preservation and the latissimus dorsiflap was used for breast oncoplastic. All the matched 182 patients underwent mastectomy, and the characteristics of both two groups are listed in Table 1.

Table 1. Patient characteristics

	oBCT	MRM	Significant
Age			
≥50 years	11 (12.09%)	22 (12.09%)	
<50 years	80 (87.91%)	160 (87.91%)	
Follow-up time			
Median time	83 months	81 months	NS
Tumor stage			
Tis	8 (8.79%)	16 (8.79%)	
T1	72 (79.12%)	144 (79.12%)	
T2	11 (12.09%)	22 (12.09%)	
Hormone receptor			
Negative	27 (29.7%)	54 (29.7%)	
Positive	64 (70.3%)	128 (70.3%)	
HER-2			
Negative	63 (69.23%)	126 (69.23%)	
Positive	15 (16.48%)	30 (16.48%)	
Not reported	13 (14.29%)	26 (14.29%)	
Lymph node status			
0	75 (82.42%)	150 (82.42%)	
1-3	16 (17.58%)	32 (17.58%)	
Histology			
DCIS	12 (13.19%)	26 (14.29%)	NS
IDC	61 (67.03%)	122 (67.03%)	
ILC	6 (6.59%)	11 (6.04%)	
Other	12 (13.19%)	22 (12.09%)	
Total	91	182	

*oBCT, breast conservative therapy, MRM, modified radical mastectomy, HER-2, human epidermal growth factor receptor-2, DCIS, ductal carcinoma in situ, IDC, infiltrating ductal carcinoma, ILC, infiltrating lobular carcinoma, NS, not significant

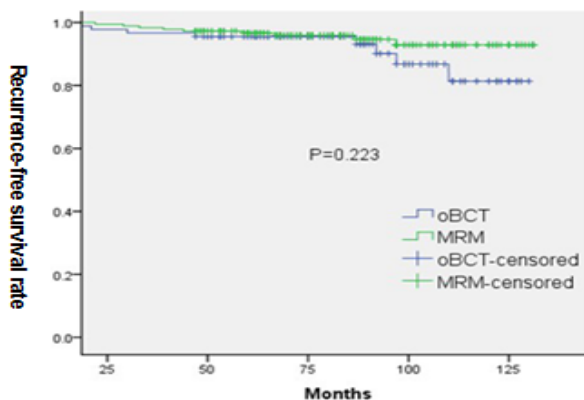


Figure 1. Kaplan-Meier Analysis Showing the Local recurrence-free Survival at 87 months in Modified Radical Mastectomy Patients and Breast Conservative Treatment Patients (p=0.223)

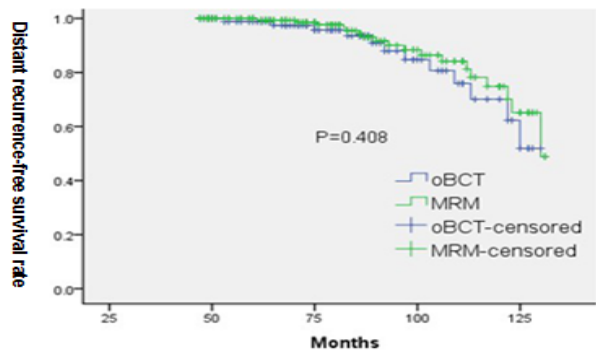


Figure 2. Kaplan-Meier analysis Showing the Overall Survival at 87 months in Modified Radical Mastectomy Patients and Breast Conservative Treatment Patients (p=0.408)

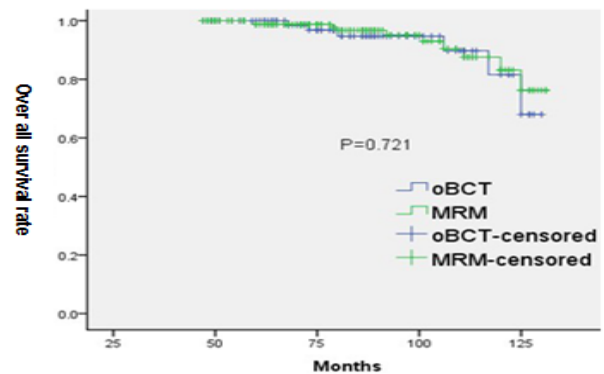


Figure 3. Kaplan-Meier Analysis showing the Overall Survival at 87 months in Modified Radical Mastectomy Patients and Breast conservative Treatment Patients (p=0.721)

The median follow-up time was 83 months in BCT and 81 months in MRM. There were no significant differences between the two treatments. The 87-month local recurrence-free survival rate was 93 % in the BCT group and 95 % in the MRM group (p=.223) (Figure 1). The 87-month distant recurrence-free survival rate was 91 % in the BCT group and 92% in the MRM group (p=.408) (Figure 2). The overall survival rates at 87 months in the BCT and MRM patients were 89% and 90%, respectively (P=0.721) (Figure 3).

Discussion

The present study is a matched retrospective analysis of oBCT with nipple-areolar preservation for CLBC, focusing on disease-free and overall survival. All patients with preservation of the NAC must obtain a negative surgical margin. The technique of oBCT involves the rotation of a latissimus dorsi flap and results in an immediate breast reconstruction with simultaneous excision of the tumor. In our study, we did not find statistical differences in overall survival and disease free survival between patients who received oBCT and MRM group.

The current study demonstrates that selected patients with central breast cancers treated with NAC-sparing conservative surgery have similar results as patients undergoing mastectomy.

There are relatively many contraindications to NAC-sparing conservative management of CLBC with early stage, because of the concern of occult nipple involvement (Parry RG et al., 1977). This challenge is supported by the low rates of NAC involvement in selected patients (Rusby JE et al., 2008; Brachtel EF et al., 2009). Patients undergoing conservative surgery for central tumors left with a central defect to the breast would be an undesirable aesthetic outcome and should be avoided. The cosmetic result in central tumors treated with lumpectomy and nipple-areolar preservation has been studied. Dale et al, evaluated 25 patients with retroareolar tumors all treated with breast-conserving therapy consisting of nipple-areolar preservation, demonstrated a 4% local recurrence rate at 48-month follow-up (Dale et al., 1996). Simmons et al, evaluated 63 central tumors and 36 retroareolar tumors treated with lumpectomy versus mastectomy and showed no difference at 5 years in relapse-free survival between these groups (Simmons et al., 2001). Gerber et al, were the first to describe preservation of the NAC in a small nonrandomized study in which they compared standard simple mastectomy, Skin-sparing mastectomy, and subcutaneous mastectomy, with similar local recurrence rates of 8%, 6%, and 5%, respectively. Survival was not statistically different in all groups, with a mean follow-up of 59 months (Gerber et al., 2003).

These published investigations provide information on the safety of oBCT for CLBC. However, there is little data on the safety of NAC preservation during breast-conserving therapy for central breast carcinomas. We compared the effects of oBCT and MRM on breast cancer patients in our hospital by the matched cohort study. We tried to use five variables to minimize the differences of the patients' clinical and pathological characteristics between the two groups. We found that oBCT is a good alternative surgical treatment modality for appropriately selected Chinese breast cancer patients. Our results were in line with that of a study by Fitzal et al (Fitzal et al., 2008).

Multiple randomized trials have demonstrated that breast-conserving therapy with partial mastectomy and radiotherapy provides survival equivalent to that seen with mastectomy for patients with early-stage breast cancer (Fisher et al., 2002; Arriagada et al., 2003; Poggi et al., 2003; Blichert-Toft et al., 2008). However, some studies have suggested that breast-conserving therapy is associated with higher local recurrence (Van Dongen et al., 2000; Veronesi et al., 2002; Sun Meng-Qing et al., 2013; Jia et al., 2014), and the result is similar to ours. There is a significant difference in a 125-month local recurrence-free survival between the two treatments groups (89% vs 82%; $p=0.04$).

In conclusion, this study demonstrates no significant difference in overall, local, or distant recurrence-free survival between oBCT and MRM. We suggest oBCT with NAC preservation to be a reasonable treatment option for selected patients with central breast cancers.

References

Arriagada R, Le MG, Guinebreteiere JM, et al (2003). Late local recurrences in a randomised trial comparing conservative

treatment with total mastectomy in early breast cancer patients. *Ann Oncol*, **14**, 1617-22.

Blichert-Toft M, Nielsen M, During M, et al (2008). Long-term results of breast conserving surgery vs. mastectomy for early stage invasive breast cancer: 20-year follow-up of the Danish randomized dbcg-82TM protocol. *Acta Oncol*, **47**, 672-81.

Brachtel EF, Rusby JE, Michaelson JS, et al (2009). Occult nipple involvement in breast cancer: clinicopathologic findings in 316 consecutive mastectomy specimens. *J Clin Oncol*, **27**, 4948-54.

Dale PS, Giuliano AE (1996). Nipple-areolar preservation during breast-conserving therapy for subareolar breast carcinomas. *Arch Surg*, **131**, 430-3.

Fisher B, Anderson S, Bryant J, et al (2002). Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med*, **347**, 233-41.

Fitzal F, Mittlboeck M, Trischler H, et al (2008). Breast-conserving therapy for centrally located breast cancer. *Ann Surg*, **247**, 470-6.

Gerber B, Krause A, Reimer T, et al (2003). Skin-sparing mastectomy with conservation of the nipple-areola complex and autologous reconstruction is an oncologically safe procedure. *Ann Surg*, **238**, 120-7.

Jia WJ, Jia HX, Feng HY, et al (2014). HER2-enriched tumors have the highest risk of local recurrence in Chinese patients treated with breast conservation therapy. *Asian Pac J Cancer Prev*, **15**, 315-20.

Parry RG, Cochran TC, Wolford FG (1977). When is there nipple involvement in carcinoma of the breast? *Plast Reconstr Surg*, **59**, 535-7.

Poggi MM, Danforth DN, Sciuto LC, et al (2003). Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. *Cancer*, **98**, 697-702.

Rusby JE, Brachtel EF, Othus M, et al (2008). Development and validation of a model predictive of occult nipple involvement in women undergoing mastectomy. *Br J Surg*, **95**, 1356-61.

Simmons RM, Brennan MB, Christos P, Sckolnick M, Osborne M (2001). Recurrence rates in patients with central or retroareolar breast cancers treated with mastectomy or lumpectomy. *Am J Surg*, **182**, 325-9.

Spear SL, Pelletiere CV, Wolfe AJ, et al (2003). Experience with reduction mammoplasty combined with breast conservation therapy in the treatment of breast cancer. *Plast Reconstr Surg*, **111**, 1102-9.

Sun Meng-Qing, Meng Ai-Feng, Huang Xin-En, Wang Mei-Xiang (2013). Comparison of psychological influence on breast cancer patients between breast-conserving surgery and modified radical mastectomy. *Asian Pac J Cancer Prev*, **14**, 149-52.

Van Dongen JA, Voogd AC, Fentiman IS, et al (2000). Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. *J Natl Cancer Inst*, **92**, 1143-50.

Veronesi U, Cascinelli N, Mariani L, et al (2002). Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med*, **347**, 1227-32.