The Oncologic Safety and Practicality of Breast Conservation Surgery in Large Breast Tumors 5 Centimeters or More

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Abstract

The surgical management of large breast cancers is controversial. Improvements in neoadjuvant chemotherapy along with utilisation of oncoplastic surgical techniques have enabled breast conservation in women with larger breast cancers. This study demonstrates oncologic equivalence of BCS and mastectomy for tumors ≥ 5 cms. The re-excision was higher in this cohort in comparison to smaller tumors in other studies. Extensive DCIS was a risk factor for inadequate margins.

Background: Surgery remains a therapeutic strategy for women with breast cancer, and long-term outcomes for breast conservation surgery (BCS) and radiotherapy are equivalent to those for mastectomy. To date, there are few published data assessing the oncologic safety and practicality of BCS in women with large breast cancers ≥ 5 cm. The current study compares survival outcomes for women with breast cancer ≥ 5 cm undergoing BCS or mastectomy. **Methods:** All women undergoing surgery for breast cancer ≥ 5 cm between January 2004 and December 2011 were included in this study. Kaplan–Meier survival curves statistically compared the overall survival (OS), disease-free survival (DFS), and local recurrence-free survival (LRFS) in the BCS and mastectomy groups. Statistical analysis involved chi-square analysis and *t* test. The mean length of follow-up was 55.25 months (range, 6-115 months). **Results:** A total of 217 women had surgery for tumors ≥ 5 cm (BCS in 51, mastectomy in 166). There was no statistical difference in the OS, DFS, and LRFS between groups ($P = .439$; 95% confidence interval, 0.114-0.347). The re-excision rate of women undergoing BCS was 45.1%, with 65.2% of women undergoing a completion mastectomy. Extensive ductal carcinoma in situ represented the only significant risk factor associated with inadequate margins ($P = .021$). Larger tumor size was associated with a greater risk of local recurrence ($P = .039$). **Conclusions:** This study is one of the largest studies to date to report BCS + radiotherapy as a safe oncologic treatment option for women with large breast cancers. However, the higher re-excision rate advocates a need to investigate ways to improve patient selection.

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Introduction

Surgery remains the cornerstone in the management of breast cancer. The surgical approach to breast cancer has undergone a dramatic paradigm shift over the past 2 decades.[1] Historically, Halsted's mastectomy was the sole treatment option; however, limited prognostic advantages from more aggressive surgery and improved understanding of molecular biogenesis resulted in an increase in breast conservation methods.[2,3] Scientific support for this transition derives from multiple landmark randomized prospective trials demonstrating oncologic equivalence of breast conservation surgery (BCS) and radiotherapy in comparison with mastectomy for early-stage breast cancer.[4-8] The outcomes from these early trials are reinforced by longer follow-up studies.[9-12] Breast cancer I remains the most common cause of cancer-related deaths in women.[13] The incidence of breast cancer is continually increasing with a 2% per annum predicted increase over the next 10 years and a greater increase in the younger population.[14] Advancements in diagnostics and improved multimodality treatments options have improved 5-year survival in women with breast cancer[15]; therefore, younger

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women are living longer with breast cancer. Subsequently, there is an endeavor to achieve a genuine match between optimal oncologic outcome and maintaining a patient's quality of life. This can be accomplished with BCS because it offers improved cosmetic outcome and generally a better quality of life in comparison with a mastectomy for early-stage breast cancer.[16] Improvements in neoadjuvant chemotherapy and adoption of oncoplastic surgical techniques have accommodated the expansion of BCS to larger breast tumors.[17] Conventionally, these women were treated with a mastectomy because it is difficult to achieve the basis of BCS, an adequate histologic margin with favorable postoperative breast cosmesis.

Few studies have demonstrated the oncologic safety of BCS for larger breast tumors. However, these studies are hampered by short-term follow-up,[18] smaller tumor size < 5 cm,[19] and no emphasis of clear histologic margins.[20] Inadequate surgical margins represent a high risk for adverse outcomes from BCS,[21] and with tumor size a risk factor for re-excision,[22] the feasibility of BCS in these larger tumors needs to be evaluated.

There are concerns regarding the oncologic safety and practicality of BCS in tumors ≥ 5 cm. The purpose of this study is 2-fold: (1) to compare overall survival (OS), disease-free survival (DFS), and local recurrence-free survival (LRFS) in women undergoing BCS or mastectomy for breast tumors ≥ 5 cm; and (2) to assess risk factors associated with inadequate margins in women undergoing BCS for large tumors while assessing the percentage of residual breast cancer in the re-excision specimens.

Patients and Methods

Patients

All women undergoing surgery for breast cancer ≥ 5 cm at a single university designated breast cancer provider between January 2004 and December 2011 were prospectively recorded into a comprehensive breast cancer database. Two groups of patients were identified within this cohort. The first group included women who had BCS + radiotherapy, and the second group included women who underwent mastectomy $\pm$ radiotherapy. Breast cancer diagnosis was confirmed histologically by a core needle biopsy, after initial history, clinical examination, and radiology in the breast clinic. Women with a confirmed histologic diagnosis were discussed at a multidisciplinary meeting and managed accordingly by neoadjuvant chemotherapy or immediate surgery (BCS or mastectomy). Pathologic tumor sizes of ≥ 5 cm (largest diameter) were included, corresponding to the American Joint Committee on Cancer classification of T3 or T4 (except T4d).[23] Patients with proven metastatic disease were omitted from the study (n = 24). Metastatic disease was excluded through history, clinical examination, chest radiograph, computed tomography-Thorax/abdomen/pelvis/brain, or bone scan if indicated.

Surgery

BCS was performed if clinical assessment and review of radiology imaging suggested that a circumferential adequate histologic margin could be achieved while maintaining good cosmetic outcome. Women demonstrating multifocal tumors or any contraindication to radiotherapy underwent a mastectomy. Macroscopic margins of at least 1 cm were obtained intraoperatively. The resected specimens from the breast were placed in 10% formalin, sliced serially at 5-mm intervals, embedded in paraffin, and sectioned and stained with hematoxylin–eosin. Complete axillary dissection (level I + level II or level III) was performed on women with positive sentinel node or confirmed axillary nodal involvement preoperatively. All resected specimens were discussed at a multidisciplinary meeting. Inadequate margins were divided into positive margins (tumor cells located a resected margin) or close margins (tumor cells located > 0 to ≤ 2 mm from resected margin).[24] Women with inadequate margins underwent a targeted cavity shave or a completion mastectomy depending on the residual breast volume, nature of the margin involvement, age of the patient, and prognostic features of the breast tumor.

Neoadjuvant Chemotherapy

All women were discussed at the multidisciplinary meeting before commencement of neoadjuvant chemotherapy. A variety of multimodality chemotherapy regimens were given at Galway University Hospital, depending on patient characteristics, tumor bulk, and hormonal status. A common neoadjuvant regimen was doxorubicin (90 mg/m^2 given over 48 hours every 3 weeks for 4 cycles). Only women who had a breast tumor size ≥ 5 cm post-neoadjuvant chemotherapy were included in this study. Triple negatives were administered Epirubicin Cyclophosphamide and Docetaxel (epirubicin 90 mg/m^2, cyclophosphamide 600 mg/m^2, d1, 21 days a cycle for 4 cycles, followed by docetaxel 80 mg/m^2, d1, 21 days a cycle for 4 cycles). Granulocyte colony stimulating factor support was given to all patients. Trastuzumab was given to Her^{2+} breast tumors over a 12-month period, in conjunction with chemotherapy. An initial loading dose of 4 mg/kg was given, followed by 2 mg/kg weekly for the first 3 months and then 6 mg/kg monthly for the remaining 12 months. Tamoxifen (10 mg twice daily for 5 years) was administered to all ER$^+$/PR$^+$ tumors.

Radiotherapy

Women in both groups underwent a radiotherapy regimen of 50 Gy in 28 fractions (1.8 Gy per fraction) over a $5^1/_2$ -week period, 4 to 6 weeks postsurgery. Women with > 4 nodes positive in the axilla received targeted radiotherapy to axilla. Women with 1 to 3 axillary nodes were discussed at a multidisciplinary meeting assessing their suitability for radiotherapy to the axilla.

Follow-Up

A clear multidisciplinary management plan was outlined for all women. Women with adequate margins and no surgical complications were followed up for 6 months for the first year with clinical examination. After the first year, this was extended to a yearly clinical examination and mammogram. Patients with involved axillary nodes were followed up by the oncologist every 4 months. Local recurrence (LR) was defined as the reappearance of histologically similar breast cancer in the ipsilateral breast.

Statistical Analysis

Data were categorized for statistical analysis. The chi-square test and t test were used to analyze breast cancer prognostic factors between the BCS and mastectomy groups. The starting date for survival analysis was the date of the initial tumor biopsy, with