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Multiple re-excisions versus mastectomy in patients with persistent residual disease following breast conservation surgery

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Abstract

Background: Persistently involved margins following breast conservation surgery (BCS) create a diagnostic dilemma regarding the recommendation of further BCS or mastectomy.
Methods: A retrospective review of 276 breast cancer patients who underwent BCS and required additional surgical treatment between 1990–2002 was performed.
Results: For treatment of persistently involved margins, 63% of subjects underwent re-excision the first time, 49% the second time, and 37% the third time. The incidence of residual carcinoma increased linearly with the number of initially involved margins ($P = .03$). Ductal carcinoma-in-situ (DCIS) or infiltrating lobular carcinoma (IFLC) primary histology was associated with a higher rate of residual cancer compared to invasive ductal carcinoma (IFDC) (62% vs. 69% vs. 54%, respectively, $P = .56$). A trend towards an increased risk of residual cancer in primary tumors ≥2 cm versus tumors under 2 cm was also evident (63%% vs. 50%, respectively, $P = .38$).
Conclusions: Approximately half of patients repeatedly selected BCS over mastectomy. It is important to realistically discuss the probability of definitive resection with patients who are undergoing breast conservation with re-excision.

Keywords: Breast conservation surgery; Breast conservation therapy; Residual cancer; Re-excision; Margins

Today, the majority of early invasive and noninvasive breast cancers are treated with breast conservation surgery (BCS). Numerous studies have shown that involved margins correlate with higher rates of local recurrence [1–4]. Thus, positive or close margins on final pathology generally warrant re-excision prior to adjuvant radiation therapy.

Persistently involved re-excision margins create a diagnostic dilemma for clinicians regarding recommendations for further surgical therapy. Current surgical practice requires that close or positive margins of the initial biopsy specimen undergo re-excision in an attempt to clear residual disease. If the margins continue to be involved following primary re-excision, additional surgery is usually recommended; however, other than patient preference and habitus, no clear guidelines exist as to whether the next procedure should be the resection of additional margins or a mastectomy.

In the literature, the frequency of residual invasive or in situ carcinoma in re-excision specimens ranges from 32% to 63% [5,6]. In a previous study, we identified factors that correlate with residual cancer in the primary re-excision specimen [5]. These included large tumor size, high tumor grade, young patient age, the presence and increased number of positive surgical margins, and single-color versus 6-color specimen inking. This current analysis moves a step further to help clinicians and patients choose multiple re-

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excisions versus mastectomy. Here we analyze histopathologic and treatment factors among patients who underwent initial BCS and at least 1 additional procedure (re-excision or mastectomy) for persistently involved margins.

Materials and Methods

A retrospective review of 276 breast cancer patients who underwent BCS and required additional surgical treatment between 1990 and 2002 was performed. Eighty-three of the 276 patients underwent a diagnostic procedure (fine-needle aspirate or stereotactic core biopsy) prior to definitive excision; 193 patients had an excisional biopsy with or without needle guidance as both a diagnostic and definitive procedure. The specimen margins were classified as close, positive, or not determined following initial excision. For this study, a positive margin was declared if there were cancer cells at the inked edge of the specimen. Close margins were defined as cancer cells within 1 mm of the inked specimen edge. The surgical specimens were addressed as 6 potential margins (anterior, posterior, superior, inferior, medial, and lateral). All subjects underwent at least 1 re-excision. Patients with persistently involved margins after the primary re-excision underwent further procedures including secondary/tertiary re-excision or mastectomy.

Patients were stratified by number and type of procedures performed and then grouped by the presence or absence of persistent cancer in the re-excised specimens. A patient was classified with residual disease if invasive or intraductal carcinoma was identified in the re-excision or mastectomy specimen. In some cases, initial excision was performed at an outside institution. However, all re-excisions and mastectomies were performed at our institution. All outside pathology slides were reviewed by an attending pathologist from our institution.

Chi-square analysis (or Fisher's Exact test) was used to explore factors that may predict residual cancer: initial margin status; tumor size, grade, and histology; number of involved margins; family history; hormonal markers; age; lymph node involvement; detection of mass in biopsy specimen; and method of initial excision (cautery vs. blade). Because the patient sample size became smaller for patients with third or fourth procedures, we did not perform multivariate analysis as the model results would be unstable and imprecise. As a result, we relied on χ^2 univariate analysis to suggest potential predictors for residual cancer. These analyses are only exploratory and should be interpreted with caution due to the issue of multiple comparisons. Because 12 comparisons were performed, the significance level used to evaluate statistical significance for these analyses was changed from alpha = .05 (2-sided) to alpha = .05/12 = .004 (2-sided). All statistical analyses were performed using SAS Version 9.1 (SAS Institute, Cary, NC).

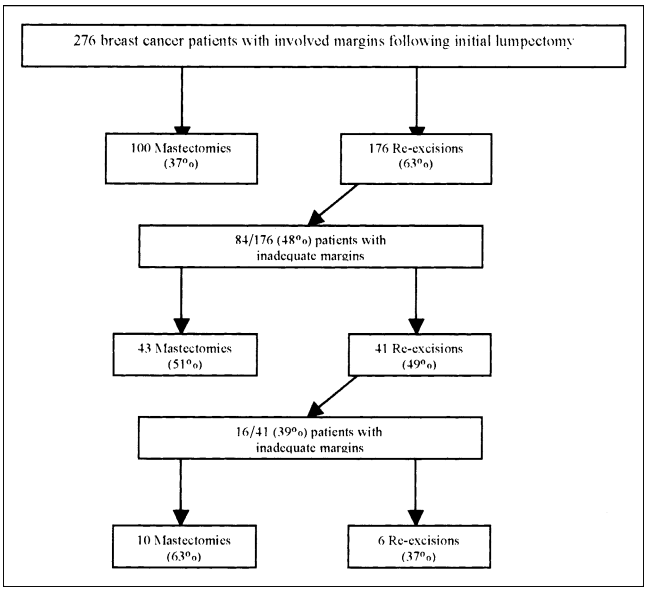

Fig. 1. Treatment course of 276 breast cancer patients who required multiple re-excisions or mastectomy following initial breast conservation with inadequate margins.

Results

Of the 276 patients who had BCS and required additional surgery due to involved (positive, close, or undetermined) margins, 176 (63%) chose re-excision while 100 (37%) opted for a mastectomy (Fig. 1). Overall, residual cancer was found in 63% (175/276) of the specimens. Separating by procedure, the rate of residual cancer was 58% (102/176) in the re-excision group versus 73% (73/100) in the mastectomy group ($P = .01$).

Of the 176 patients who underwent primary re-excision, 84 patients (48%) underwent a third procedure, either secondary re-excision or mastectomy, for persistently involved margins. In this group of 84 patients requiring further surgery, 41 (49%) chose a secondary re-excision versus 43 (51%) who opted for a mastectomy. Overall, residual cancer was found in 58% (49/84) of these specimens from patients undergoing a third surgical procedure. Separating by type of surgery, the rate of residual cancer was 54% (22/41) in the re-excision group versus 63% (27/43) in the mastectomy group ($P = .40$).

Of the 41 patients that underwent a secondary re-excision, 16 (39%) were then required to undergo a fourth procedure, either tertiary re-excision or mastectomy, for continued margin involvement. Of this group, 37% (6/16) chose to undergo a tertiary re-excision while the remaining 63% (10/16) had mastectomies. When the pathology for these 16 patients was examined, 63% (10/16) had residual cancer found in the surgical specimen.

Because the sample size was small for the subset of patients with 3 or more surgical procedures (n = 84), the resultant statistical power for evaluating potential associations was low. Furthermore, only P values $<.004$ were