International Journal of Radiation Oncology biology • physics

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Clinical Investigation: Breast Cancer

Impact of Margin Status on Local Recurrence After Mastectomy for Ductal Carcinoma In Situ

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Received Jun 13, 2012, and in revised form Jul 25, 2012. Accepted for publication Jul 30, 2012

Summary

We reviewed the records of 142 women who underwent mastectomy and no radiation therapy for ductal carcinoma in situ (DCIS). There were very few local recurrences among patients with close margins (≤2 mm; 1/23, 4.3%) or positive margins (1/21, 4.8%) and none in the 98 patients with negative margins. This is the largest series of patients with DCIS and positive mastectomy margins, and it suggests a sufficiently low rate of local recurrence such that postmastectomy radiation therapy is likely not warranted.

Purpose: To examine the rate of local recurrence according to the margin status for patients with pure ductal carcinoma in situ (DCIS) treated by mastectomy.

Methods and Materials: One hundred forty-five consecutive women who underwent mastectomy with or without radiation therapy for DCIS from 1998 to 2005 were included in this retrospective analysis. Only patients with pure DCIS were eligible; patients with microinvasion were excluded. The primary endpoint was local recurrence, defined as recurrence on the chest wall; regional and distant recurrences were secondary endpoints. Outcomes were analyzed according to margin status (positive, close (≤2 mm), or negative), location of the closest margin (superficial, deep, or both), nuclear grade, necrosis, receptor status, type of mastectomy, and receipt of hormonal therapy.

Results: The primary cohort consisted of 142 patients who did not receive postmastectomy radiation therapy (PMRT). For those patients, the median follow-up time was 7.6 years (range, 0.6-13.0 years). Twenty-one patients (15%) had a positive margin, and 23 patients (16%) had a close (≤2 mm) margin. The deep margin was close in 14 patients and positive in 6 patients. The superficial margin was close in 13 patients and positive in 19 patients. One patient experienced an isolated invasive chest wall recurrence, and 1 patient had simultaneous chest wall, regional nodal, and distant metastases. The crude rates of chest wall recurrence were 2/142 (1.4%) for all patients, 1/21 (4.8%) for those with positive margins, 1/23 (4.3%) for those with close margins, and 0/98 for patients with negative margins. PMRT was given as part of the initial treatment to 3 patients, 1 of whom had an isolated chest wall recurrence.

Conclusions: Mastectomy for pure DCIS resulted in a low rate of local or distant recurrences. Even with positive or close mastectomy margins, the rates of chest wall recurrences were so low that PMRT is likely not warranted. © 2013 Elsevier Inc.

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Conflict of interest: none.

Int J Radiation Oncol Biol Phys, Vol. 85, No. 4, pp. 948–952, 2013
0360-3016/$ - see front matter
http://dx.doi.org/10.1016/j.ijrobp.2012.07.2377

Introduction

Patients who are treated with mastectomy for ductal carcinoma in situ (DCIS) generally do not require further local treatment because their risk of a chest wall recurrence is low (1). A positive surgical margin suggests the possibility of persistent malignant cells in the remaining breast or subcutaneous tissue, which could potentially lead to a higher risk of local recurrence (LR). If this is true, patients with such margins after mastectomy for DCIS may benefit from further local therapy such as postmastectomy radiation therapy (PMRT). However, the risk of recurrence on the chest wall for patients with a positive or close mastectomy margin remains unclear.

The status of the resection margin is an important factor in determining local recurrence (LR) in patients with DCIS treated with breast-conserving therapy, presumably from carcinoma remaining in the adjacent breast tissue (2-6). However, treatment by mastectomy differs from breast conserving therapy in important ways that may result in a lower risk of a chest wall recurrence despite a positive or close margin. First, the pectoralis fascia is, in general, removed with the breast tissue at the time of mastectomy. The pectoralis fascia likely serves as an anatomic barrier for DCIS cells, which, by definition, are confined to the basement membrane and lack the ability to penetrate this fascia. Similarly, DCIS cells lack the ability to penetrate lymphatic vessels or dermis and are therefore very unlikely to remain in the skin of the chest wall after mastectomy.

Because of the concern for a higher rate of LR with a close or positive mastectomy margin, some advocate PMRT for these patients (7, 8). However, to our knowledge, no clinical trials have examined the role of PMRT in the setting of positive or close margins, and the data from single institutions reporting the outcomes in these patients are limited and conflicting (9). In particular, the number of patients with positive margins in prior series has been small, and the status of the superficial margin is rarely reported. We sought to clarify the risk of chest wall and regional recurrence in patients with pure DCIS with close or positive mastectomy margins in a series of consecutive patients treated at our institution whose superficial and deep mastectomy margins were closely examined.

Methods and Materials

We retrospectively reviewed the medical records of 887 consecutive women who underwent mastectomy between January 1998 and December 2005 at Faulkner Hospital, a community affiliate of the Dana-Farber Cancer Institute. The study cohort consists of 145 of these women with pure DCIS without microinvasion, with no history of prior malignancy (except nonmelanoma skin cancer), and with at least 6 months of follow-up. The study was approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board.

Age at mastectomy, receipt of hormonal therapy, and type of mastectomy were abstracted from the patients' clinic notes and operative reports. Nuclear grade; presence or absence of necrosis; and estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER-2/neu) status were obtained from the pathology reports of the patients' biopsies, lumpectomy specimens, and mastectomy specimens. We included patients who had received PMRT as part of their initial treatment in this report to avoid bias in the outcomes based on our institution's practice patterns.

A positive margin was defined as DCIS at a final inked mastectomy resection margin. A close margin was defined as in situ disease $\leq$2 mm from a final inked mastectomy resection margin. Both the superficial and deep margins were inked at the time of mastectomy. Follow-up time was measured from the date of mastectomy to the last known confirmed date of breast cancer disease status.

The primary endpoint of this study was LR, was defined as recurrence on the ipsilateral chest wall or subcutaneous tissues. The secondary endpoints were regional recurrence or distant metastasis. A regional recurrence was defined as disease recurrence in the ipsilateral nodal regions, including axillary, supraclavicular, or internal mammary lymph nodes.

Although follow-up was at the direction of the treating surgeon, in general, patients were seen by their surgeon every 6 months for the first 2 years, then yearly for the subsequent 3 years. After 5 years, patients were typically seen yearly by either their treating surgeon or their primary care physician. The primary form of surveillance was physical examination.

Results

The median age of the cohort was 52 years (range, 27-82). Three patients (2%) received PMRT as part of their initial treatment and were considered separately from those who did not. The 142 patients with pure DCIS who did not receive PMRT constituted the primary cohort; their characteristics are listed in Table 1 and are as follows. Twenty-one patients (15%) had a positive margin and 23 patients (16%) had a close ($\leq$2 mm) margin. The deep margin was positive in 6 patients and close in 14 patients. The superficial margin was positive in 19 patients and close in 13 patients. If a patient had 1 positive margin and 1 close margin (n=4), this patient was grouped together with those who had positive margins. The median width of the close margin was 1 mm (range 0.5-2 mm). The extent of involvement (focal vs broad) of the positive or close margin was not routinely recorded in the pathology reports, and therefore could not be reported upon. Forty-three percent of patients had nuclear grade 3 and 35% had necrosis. A skin-sparing mastectomy was performed in 83 patients (58%), all of whom had breast reconstruction. Axillary surgery was performed in 69 patients (49%): 30 had sentinel lymph node biopsy only and 39 had an axillary dissection with a median of 9 nodes removed. No axillary nodes contained tumor. Adjuvant endocrine therapy (tamoxifen, aromatase inhibitor, or oophorectomy) was given to 13% of patients.

The median follow-up time was 7.6 years (range, 0.6-13.0 years). Outcomes are reported in Table 2. The crude rates of chest wall recurrence were 2/142 (1.4%) for all patients, 2/44 (4.5%) for patients with close or positive margins, 1/21 (4.8%) for those with positive margins, and 1/23 (4.3%) for those with close margins. Two of the 61 patients (3.3%) with grade 3 disease and 2/83 (2.4%) of those who underwent skin-sparing mastectomy developed a chest wall recurrence. Because there were only 2 events in this cohort, we did not think it would be accurate to report univariate or multivariate analyses of prognostic factors for chest wall recurrence.

Only 1 patient had an isolated LR on the chest wall. This patient initially presented with multifocal, extensive high nuclear grade DCIS with a focally close (1 mm) deep margin and had no adjuvant therapy. Two years later, she developed a chest wall nodule detected