Excerpta Medica

The American Journal of Surgery

The American Journal of Surgery 189 (2005) 229–235

Review

Locally recurrent breast cancer after conservation therapy

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Manuscript received January 30, 2004; revised manuscript July 16, 2004

Abstract

Background: Today, the majority of small invasive and noninvasive breast cancers are treated with breast conservation therapy (BCT). The incidence of local-regional recurrence (LRR) after BCT for stage 0, I, and II patients ranges between 5% and 22%.
Methods: A literature search for BCT, local recurrence, and regional recurrence was performed. Data from over 50 articles pertaining to the characteristics, risk factors, detection, management, and prognosis of these patients with LRR after BCT were collected and analyzed.
Results: Positive margins, high-grade ductal carcinoma in situ (DCIS), young age, and the absence of radiation therapy after BCT increase the risk for LRR. Prognosis at LRR is impacted by invasive versus noninvasive histology, size and stage, method of detection, and involvement of skin and/or axillary lymph nodes. The standard treatment is salvage mastectomy.
Conclusions: The prognosis for LRR after BCT is favorable compared with patients with postmastectomy chest wall recurrence.

Keywords: Breast cancer; Breast conservation therapy; Local recurrence; Regional recurrence

The majority of small invasive and noninvasive breast cancers are treated today by breast conservation therapy (BCT), which includes wide local excision and radiation treatment to the breast. Multiple prospective randomized clinical trials, including the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-04, B-06, and B-17 trials, and the Milan Institute Quandrantectomy versus Radical Mastectomy trial, showed no statistically significant difference in patient survival with mastectomy and breast conservation for small invasive and noninvasive carcinomas [1–10]. The incidence of local-regional recurrence (LRR) after BCT for stage 0, I, and II patients ranges between 5% and 22% [3,7,9,11]. The characteristics, risk factors, detection, management, and prognosis of patients with LRR after BCT are discussed in this collective review.

Characteristics of Local-Regional Recurrences

Although all LRR after BCT generally are grouped together, it is important to appreciate that there are several different types of recurrences that may reflect both cause and patient prognosis. The types of LRR are categorized by location of the breast recurrence in comparison with the primary treated breast carcinoma.

The most common type of LRR, present in 57% to 88% of patients [11–15], appears at the site of the primary breast cancer and probably represents incomplete resection of the initial carcinoma. The second type, which consists of approximately 22% to 28% of LRRs, is within the same quadrant but not directly at the site of the initial carcinoma. These are hypothesized to represent evolution of multifocal ductal carcinoma in situ (DCIS) since the time of the original surgery. The third type of recurrence is found within a different quadrant from the initial breast cancer. These remote LRRs are found in 10% to 12% of patients and likely represent a new primary breast cancer [12]. The fourth type of LRR is the rare radiation-induced carcinoma within the radiated treatment field of the initial primary carcinoma [12]. The fifth category of LRR is a diffuse or inflammatory recurrence, detected in less than 5% of patients (see Fig. 1) [13].

The majority of patients who sustain LRR do so within 2 years [16,17]. The greater the time interval between the initial diagnosis and the LRR, the more likely it is that the recurrence will be located in a remote area of the breast

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0002-9610/05/$ – see front matter
doi:10.1016/j.amjsurg.2004.07.039

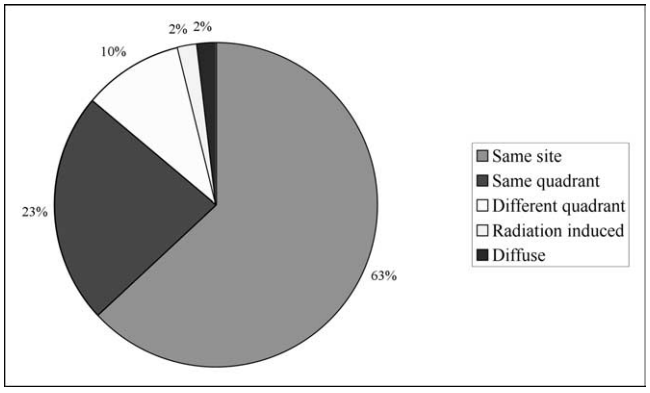

Fig. 1. Sites/types of LRR after BCT [12]. Adapted with permission.

[11,12,18]. Those patients with LRRs in the vicinity of the original tumor recurred an average of 33 months after BCT, versus those with a LRR in a distant location, who recurred an average of 75 months after BCT [15]. These data suggest a treatment failure with the early recurrences at the original site and the development of a new primary cancer, with the later recurrences in remote areas.

LRRs after BCT may be either invasive or in situ carcinoma. For women who initially were treated for invasive carcinoma, about 80% recur with invasive carcinoma, whereas the remainder have a DCIS recurrence [19]. In patients initially treated for DCIS, slightly more than half will recur with invasive breast carcinoma, while slightly less than half will have DCIS [20,21]. A small percentage of both invasive carcinoma and DCIS patients will be found to recur with either invasive lobular carcinoma or angiosarcoma [20].

Factors Associated With Increased Risk for Local Recurrence

Margin status

One of the most important predictors of increased risk for LRR is pathologic margin status after BCT. Margin status typically is described as negative, close, or positive. Controversy exists in the literature regarding the meaning of a close surgical margin, with definitions ranging from less than 1 cm to less than 1 mm. According to the NSABP, a margin is positive only if tumor cells are present at the inked surface. A close margin requires cancer cells to be within 1 mm of the inked margin and a negative margin implies that there is at least a 1-mm rim of normal parenchyma between the tumor and the margin. Positive margins are focal if observed in 3 or fewer power fields or diffuse if found in more than 3 power fields [22–25].

The majority of data show that close or positive margins result in an increased rate of LRR. In one series of 303 invasive breast cancers treated with BCT, patients with negative surgical margins had a 98% probability of local control at 10 years versus a probability of only 82% in those patients with close or positive margins ($P = .007$). Another study showed that patients with negative final margins had 100% local control versus 78% for those without negative margins ($P = .0001$) [23]. These data emphasize the importance of obtaining pathologic tumor-free margins at the time of resection or re-excision to optimize local control.

An extensive intraductal component (EIC) within an invasive breast cancer generally indicates a larger subclinical tumor burden and an increased likelihood of microscopically positive margins. When the margins are revised to a negative status, recurrence rates then decrease and become equivalent to women without an extensive EIC. In the presence of an EIC, negative margins strongly are recommended. Because revision of margins is equivalent to initial negative margins, it is important to recognize that these patients are not automatic mastectomy candidates [26].

Additionally, there are data to suggest BCT with a radiation boost to the surgical bed, in patients with a close or focally positive margin, generates equal or similar LRR rates as a negative margin [22,24,27]. Solin et al [22] compared nearly 700 women with invasive breast cancer and negative margins (>2 mm), positive margins, close margins (≤2 mm), or unknown margins after BCT. All underwent a similar dose of definitive irradiation. There was no significant difference among the groups for 5-year overall survival, no evidence of disease survival, or relapse-free survival. Park et al [27] showed, with 8 years of follow-up evaluation, the LRR for all patients with positive margins was 18% compared with 7% for those with negative margins. However, the patients with a close (defined here as <1 mm) margin had an equal rate of LRR to those with negative surgical margins. When the positive margins were analyzed further, those with a focally positive margin had an LRR of 14%, in contrast to the 27% LRR rate in those with extensively positive margins [27]. Thus, the actual amount of residual tumor in the excision bed is a significant predictor of increased recurrence.

Histology of the primary tumor

Pathologic characteristics of the tumor also affect the incidence of local recurrence. For more than 20 years, an EIC has been considered a risk factor for increased recurrence. Vicini et al [28] analyzed over 500 women with stage I or II breast cancer to determine the optimal extent of resection and found that an EIC was associated with a higher recurrence rate. For patients with EIC-positive (EIC+) tumors, the larger resections were associated with lower risks for recurrence when compared with the smaller-volume resections. However, for women with EIC-negative (EIC−) tumors, the risk for recurrence was not influenced by the resection volume. The conclusion was that a generous resection volume is more important for EIC+ than for EIC− breast cancers.

There are 4 main types of DCIS: papillary, cribiform,