EDITORIAL

How Should We Manage Breast Cancer in the Breast, or Buddy, Can You Paradigm?

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It is easy to define the goals of the best locoregional therapy for women with invasive or noninvasive breast cancer. These goals are quite obviously the best survival, the least disfigurement, and the least likelihood of significant systemic toxicity. What is not so easy to define are the optimal ways of achieving any one of these three goals without compromising any of the others. The good news is that, within the past decade, a variety of paradigm-shifting clinical trials have been completed that provide a significantly higher degree of confidence in the efficacy of some of the choices that we offer our patients. In part, this improved situation is based on an awareness that the achievement of each of these three goals is more independent than was previously thought. Unfortunately, not everyone accepts this as proven, given the fact that most invasive breast cancers in the United States are still managed by mastectomy.

Nearly a century ago, the Halstedian view of breast cancer (and, in fact, most malignancies) held that their growth was expansile and that dissemination occurred through locally accessible lymphatic channels. A direct corollary of this belief was that a large enough extirpative circle drawn around the tumor would totally remove it and cure the patient. This biological concept, combined with a far more advanced presentation of most breast cancers common years ago, achieved local control at the expense of very substantial disfigurement. Equally undeniably, many women treated in this way, albeit a minority in aggregate, survived for decades to die of other unrelated causes.

The development by Fisher et al. (/) of the notion that the predominant lethality of breast cancer was due to systemic hematogenous spread, which had generally occurred prior to local therapy, gave rise to the idea that local management might not have a very significant impact on survival. A series of randomized trials involving even less surgical treatment of the breast, with or without additional radiation therapy, have tended to support this notion; virtually all trials showed no decrement in survival associated with surgery that was limited first to the breast alone and later to the tumor and immediately surrounding tissue (I-6). What is also clear is that the removal of increasingly less breast tissue and the omission of radiation therapy all lead to increasing rates of local treatment failure within the breast. For example, in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-06 protocol (/), patients who received radiation therapy following lumpectomy had more than a threefold reduction in breast recurrences. Similarly, the Milan Cancer Institute trial (7), which compared quadrantectomy with tumorectomy, showed that the more extensive local surgery resulted in more than a threefold reduction in breast recurrences at the expense of greater disfigurement. On the basis of these and other studies, it is obvious that both increasing the extent of local breast surgery and adding adjuvant radiation therapy to the breast can more effectively "cure" breast cancer. Clearly, "cure" of breast cancer does not guarantee avoidance of systemic metastases and eventual death from breast cancer. On the other hand, it is certain that adequate local treatment of some breast cancers does result in the cure of patients who would otherwise eventually become incurable if left untreated. These arguments are well summarized in the current American Society of Clinical Oncology Karnofsky Memorial Lecture delivered by Hellman (8). Among many data that could be cited, the unequivocal improvement in survival produced by screening mammography establishes the fact that some breast cancers behave as localized diseases and if left alone long enough (the unscreened population) will have systemic recurrences (9).

The most important question, however, is whether or not any subset of patients in whom viable invasive or noninvasive breast cancer cells are retained in the breast following incomplete local therapy develop disseminated disease as a result of the failure to remove them. This issue is probably the single, most important scientific argument given for mastectomy following a diagnosis of noninvasive duct cell carcinoma of the breast. The article from the Milan Cancer Institute, appearing in this issue of the Journal (10), attempts to address this question. More than 2000 women sequentially treated with quadrantectomy and radiation therapy were assessed for either local or distant treatment failure; the prognostic variables predicting either and time to treatment failure were presented. These authors, as well as others (11-15), noted that some prognostic variables, such as age under 40 years and local lymphatic permeation, predicted for women with invasive or noninvasive breast cancer cells retained in the breast following incomplete local therapy develop disseminated disease as a result of the failure to remove them. This issue is probably the single, most important scientific argument given for mastectomy following a diagnosis of noninvasive duct cell carcinoma of the breast. The article from the Milan Cancer Institute, appearing in this issue of the Journal (10), attempts to address this question. More than 2000 women sequentially treated with quadrantectomy and radiation therapy were assessed for either local or distant treatment failure; the prognostic variables predicting either and time to treatment failure were presented. These authors, as well as others (11-15), noted that some prognostic variables, such as age under 40 years and local lymphatic permeation, predicted for both local treatment failure and distant disease. Other variables,

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See "Note" section following "References."
such as extensive intraductal component, appeared to be risk factors for local treatment failure with tumorectomy with or without radiation therapy. Paradoxically, in several studies, including the current study, axillary lymph node involvement predicted, as expected, for distant recurrences, but a lower in-breast recurrence rate. This divergent effect has been attributed to the synergistic effects of radiation therapy and chemotherapy on residual breast cancer.

So far, most studies have failed to suggest that residual viable breast cancer in the breast or axillary lymph nodes detected and treated at a later date has a negative impact on survival. It cannot be emphasized enough how counter-intuitive this finding is. How is it possible that 5 or more years of "exposure" to retained viable breast cancer cells cannot contribute to increased risk of dissemination and lethality? Some studies (16,17) have, in fact, suggested that radiation therapy (as compared with more or less surgery) can improve breast cancer survival. Nonetheless, in the Italian trial comparing quadrantectomy with tumorectomy, relapse rates were three times higher in the tumorectomy group, with no impact on survival (7). However, there were only 35 distant recurrences in each group, and the study did not have the duration of follow-up or the numbers of patients to detect modest changes in recurrence rates. Similarly, while the NSABP B-06 trial had remarkably divergent in-breast recurrence rates with lumpectomy versus lumpectomy with radiation treatment, distant disease-free survival has thus far been identical in both treatment arms (1). It can always be argued that neither this study nor any of the other randomized trials looking at surgical approaches that compared breast conservation with mastectomy have the power to detect some modest increase in lethality or distant disease-free recurrence as a result of less local treatment. Possibly, a meta-analysis might uncover such an effect, but this appears unlikely, since most of these studies have shown a minimal but statistically insignificant advantage for lumpectomy and radiation therapy as compared with mastectomy.

It is possible that studies of noninvasive breast cancer may provide the best answer to this question. This is because, with careful pathologic examination and verification of lack of invasion, one would expect survival rates approaching 100% with mastectomy. Increases in distant recurrences as a result of significantly less local control (e.g., lumpectomy versus lumpectomy plus radiation therapy; the design of the NSABP B-17 trial) may eventually, with long enough follow-up, suggest whether or not there is a small survival disadvantage because of poorer local control and retained viable breast cancer (18,19). Thus far, there are no data to suggest that failure to treat every breast cancer cell in the breast (proven empirically by recurrences within the same quadrant of the breast) has had any impact on survival. For this reason, it appears appropriate to emphasize the increasingly well established role for nonmastectomy management of invasive breast cancer for most patients. Furthermore, even if there is no apparent impact on survival, given the devastating psychological impact of in-breast recurrence and the likely requirement for mastectomy, adequate local therapy needs to be given a high priority with meticulous surgical and radiotherapeutic management combined with close correlative examinations by pathologists.

References


Note

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