Annals of Surgical Oncology, **6**(1):17–18
Published by Lippincott Williams & Wilkins

Editorial

A Survival Benefit From Axillary Dissection: Was Halsted Correct?

Monica Morrow, MD

Breast surgery in general, and axillary dissection in particular, have come to be regarded by many as staging procedures that are useful for maintaining local control but do not affect survival. This is a far cry from the Halstedian concept of meticulous radical surgery for the cure of breast cancer that governed surgical thinking in the United States until the 1970s. Acceptance of axillary surgery as a staging, rather than a therapeutic, modality resulted from clinical observations that most women with axillary node metastases treated with surgery alone die of breast cancer, and the demonstration that adjuvant systemic chemotherapy improves survival in women with node-positive breast cancer. The most direct articulation of this new role for surgery came from Bernard Fisher, who stated "breast cancer is a systemic disease involving a complex spectrum of host-tumor interactions and variations in effective local treatment are unlikely to affect survival substantially."[1] This "systemic disease" hypothesis dominated our thinking about breast cancer management from the 1970s to the 1990s, with a number of beneficial results. Most notable among these were the development of breast-conserving therapy and the recognition that node-negative breast cancer did not always imply a good prognosis for the disease.

However, a number of recent clinical observations have led to a resurgence of interest in the potential therapeutic role of aggressive local therapy of breast cancer. As one of these reanalyses, Orr presents a meta-analysis of the impact of axillary dissection on survival in this issue of the *Annals of Surgical Oncology*.[2] The technique of meta-analysis has become extremely popular, but when evaluating the results of such analyses, it is important to remember that their validity is determined by the quality of the studies included in the analysis and their relevance to current practice. In this regard, there are several important points to consider about the studies cited in Orr's analysis. Of the 2936 patients, approximately 21% were from the Guy's I and II trials. These studies compared patients treated by radical mastectomy to those treated by wide local excision and an inadequate dose of breast irradiation.[3] A systematic plan of surgical salvage was not followed for patients who relapsed in the breast or the axilla. If one presumes that untreated metastases in the axilla can serve as the source of additional metastases and result in decreased survival, it is equally biologically plausible that uncontrolled local failure in the breast can act in the same fashion. Thus, it is difficult to conclude much more from these two trials than that inadequate local therapy with inadequate salvage therapy has the potential to decrease survival. This general concept, that inadequate local therapy does have an impact on survival, is consistent with the idea that axillary dissection could affect survival, but it is not proof.

The patients for whom axillary dissection often is considered least beneficial are those with small cancers at lowest risk for axillary node metastases, usually T1 lesions, particularly those 1.0 cm or less in size. It is difficult to imagine how the removal of histologically normal nodes would alter survival. For this reason, the authors' analysis of Stage I patients is of particular interest. However, it is incorrectly stated that the B04 and Guy's II trials included only Stage I patients. Both studies included T2 and T3a tumors in their eligibility criteria,[3,4] and these larger tumors would be expected to have a higher risk of nodal metastases than would T1 lesions. The Stage I analysis appears to be an analysis of clinically node-negative breast cancers, and no conclusions can be drawn from it regarding the benefit of axillary dissection in Stage I patients as defined by the TNM staging system (tumor less than or equal to 2.0 cm in size, clinically node-negative).

Received October 14, 1998; accepted October 16, 1998.
From the Department of Surgery, Northwestern University Medical School, Chicago, IL 60611-3010
Address correspondence to: Monica Morrow, MD, Division of General Surgery, Dept. of Surgery, Northwestern University Medical School, Tarry 11–703, 300 East Superior St., Chicago, IL 60611-3010.

The biology underlying Orr's contention that axillary dissection is therapeutic is not clearly articulated. For example, he seems to believe that whereas treatment of axillary nodes is important, treatment of the internal mammary nodes is not. This allows inclusion in the meta-analysis of patients who had extended radical mastectomy. But why should nodal metastases at one site, but not another, alter survival? The internal mammary lymph nodes contain metastases in at least 30% of axillary node-positive patients, and are the only site of nodal metastases in 5% of breast cancer patients.[5] The prognosis conferred by metastases to the internal mammary nodes is similar to that seen with isolated axillary metastases, and metastases at both nodal sites are associated with a poorer prognosis than are metastases at either site alone. Studies of extended radical mastectomy were not large enough to detect a 5% difference in survival even if one existed, so perhaps a meta-analysis is warranted.

When viewed in isolation, it would be difficult for me to say that this meta-analysis clearly demonstrated a survival benefit for axillary dissection. However, other data validate the underlying assumption that local therapy does affect the natural history of some breast cancers. If all breast cancers were systemic from the time they became clinically recognizable, screening mammography should have no effect on survival, yet studies clearly demonstrate a 30% reduction in mortality in women aged 50 and older who are screened. The recent Danish[6] and British Columbia trials,[7] in which postmastectomy radiotherapy was given to the chest wall, axilla, internal mammary node fields, and supraclavicular node fields of patients with axillary metastases demonstrate a survival benefit when compared to treatment with mastectomy alone. In addition, studies of the long-term outcome of patients with small breast cancers metastatic to 1 to 3 axillary nodes demonstrate that two-thirds of these patients survive after locoregional therapy alone.[8] What remains is to define the group of patients who are likely to obtain a survival benefit from aggressive local regional therapy. As mentioned previously, the survival of women with node-negative disease will not be changed by axillary dissection. In women with large tumors and multiple positive nodes, the risk of systemic disease is high, and local therapy is unlikely to affect survival. However, axillary dissection in this group is worthwhile to maintain local control. It is the patient with a more limited regional tumor burden—1 to 3 positive nodes and a small primary tumor—in whom locoregional therapy has the greatest likelihood of improving survival. Sentinel node biopsy, by allowing the reliable identification of nodal metastases, eliminates axillary dissection for patients who will not benefit because of the absence of metastases. For the patient with metastases to the sentinel node, dissection of the remaining nodes remains standard practice, even if the patient has been staged as needing chemotherapy. New clinical trials with the power to detect a small survival benefit for axillary dissection are being developed to provide definitive answers to the questions raised by this meta-analysis regarding the therapeutic role of axillary dissection in node-positive breast cancer.

REFERENCES

1. Fisher B. Laboratory and clinical research in breast cancer–a personal adventure: The David A Karnovsky Memorial Lecture. *Cancer Res* 1980;40:3863–74.
2. Orr RK. The impact of prophylactic axillary node dissection on breast cancer survival–a Bayesian meta-analysis. *Ann Surg Oncol* 1999;6:109–16.
3. Hayward JL *The Guy's Hospital trials on breast conservation*. In: Harris JR, Hellman S, Silen W, eds. *Conservative management of breast cancer. New surgical and radiotherapeutic techniques*. New York: JB Lippincott, 1983:77–90.
4. Fisher B, Redmond C, Fisher ER, et al. Ten-year results of a randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *N Engl J Med* 1985;312: 674–81.
5. Morrow M, Foster RS. Staging of breast cancers. A new rationale for internal mammary node biopsy. *Arch Surg* 1981;116:748–51.
6. Overgaard M, Hansen PS, Overgaard J, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. *N Engl J Med* 1997;337:949–55.
7. Ragaz J, Jackson SM, Le N, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. *N Engl J Med* 1997;337:956–62.
8. Quiet CA, Ferguson DJ, Weichselbaum RR, et al. Natural history of node-positive breast cancer. The curability of small cancers with limited number of positive nodes. *J Clin Oncol* 1996;14:3105–11.