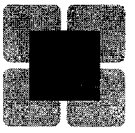

WILLIAM S. WILKE, MD, EDITOR

UNRESOLVED QUESTIONS IN BREAST CANCER THERAPY

The issue of whether to treat early breast cancer with modified radical mastectomy or radical mastectomy has long been controversial. However, studies in the last 20 years have shown no difference in survival between the two treatment modalities. The primary difference is the improved cosmetic result with the modified radical approach. Modified radical mastectomy also makes it easier to perform immediate breast reconstructive surgery. A major controversy today concerns the selection of patients for adjuvant chemotherapy and hormonal therapy, and when to initiate these modalities.

The role of local radiation therapy depends on circumstances as well as patient preferences regarding breast preservation. Given the widespread media coverage of breast disease and its treatment, more women request preoperative evaluation by all three traditional disciplines (surgery, radiotherapy, and chemotherapy), as well as reconstructive surgery. In most cases, however, the patient's first contact is with a general surgeon.

SURGERY

The surgical treatment of breast cancer today includes a number of options: total removal of the breast with or without immediate reconstruction, or breast conservation surgery removing only the tumor with a margin of normal tissue around it. In both cases, lymph nodes are removed from the axilla for staging and prevention of local recurrence. The choice of treatment depends on a number of factors, including tumor size, location, histology, and evidence of multicentricity on mammography. A family history of breast cancer (early onset, bilaterality) may also influence treatment choices.

The preferred approach at the Cleveland Clinic for tumors ≤2 cm located peripherally in the breast is partial mastectomy (removal of tumor and surrounding breast tissue). This approach has been criticized because of the multicentric nature of breast cancer in 25% to 75% of patients. If the foci are noninvasive, they have no effect on survival, although they may lead to later local recurrence.

Factors known to be important in prognosis include the number of lymph nodes involved, delay in treatment, tumor size and histologic type, and estrogen receptor status. The type of operation is not a significant prognostic factor. Patients with cervical lymph node involvement cannot be cured surgically and are candidates for radiation therapy.

A 60-month follow-up at the Cleveland Clinic showed that 75% of patients treated surgically at stage I remained free of recurrence, but the problem remains of recurrence in patients with early disease, regardless of the type of operation used.

RADIOTHERAPY

Radiotherapy has limited ability to control recurrence. Early breast tumors may be associated with a 20% incidence of distant metastases; therefore, local control is a separate goal from that of prolonging survival through prevention of metastases.

Improvements in surgical techniques and pathologic analysis have led to more patients being considered for breast-conserving operations. In addition, major improvements in the precision, dosimetry, and long-term complications of radiation therapy allow more women with early breast cancer to consider excision, either by lumpectomy with margins, or partial mastectomy followed by radiation therapy to the breast.

Certain characteristics in patients with early breast cancer (stage I or II, T1N0-T1N1/T2N0) suggest that breast-conserving surgery followed by radiation therapy is appropriate. These characteristics include the following: primary tumor <4 cm clinically or by mammography; single, well-defined tumor with focal, not diffuse, microcalcifications on mammography; small to moderately large breasts; or eccentrically located tumors, which make it difficult to achieve surgically negative margins or acceptable cosmetic results with mastectomy.

Conservative surgery plus irradiation is not an appropriate option for patients with large breasts, a large tumor relative to the size of the breast, multiple gross malignant tumors, or widespread microcalcifications.

Survival following conservative surgery and radiation is comparable to that observed following radical mastectomy. In either case, 90% of relapses occur within 5 years of treatment. Survival in node-positive patients is significantly less. Even with chemotherapy, the rate of disease-free survival in these patients is 58% to 71%.

Most relapses occur within the original tumor bed or in the radiation boost field margins. Those that occur elsewhere in the breast represent new primary tumors. Most relapses in the breast or the chest wall occur within 2 years of treatment; later relapses are rare.

CHEMOTHERAPY

In most patients, systemic recurrence is a more significant problem than achieving local control, and it is essentially a fatal event. In 1985, the National Institutes of Health (NIH) Consensus Statement on the Treatment of Early-Stage Breast Cancer recommended that premenopausal node-positive women receive adjuvant chemotherapy. It further stated that chemotherapy should be considered for postmenopausal women with positive axillary nodes and negative hormone receptors, but this is not recommended as standard practice. Even so, most oncologists use chemotherapy in this group because subsets of postmenopausal patients may benefit.

Based on clinical trials involving thousands of women, tamoxifen is the treatment of choice for postmenopausal women with positive axillary nodes and positive estrogen receptors. Although the standard duration of tamoxifen therapy is 5 years, some continue it indefinitely. The role of chemotherapy in this group of patients continues to be investigated.

The appropriate timing of the administration of the major treatment modalities for breast cancer—surgery, radiotherapy, chemotherapy, and hormone therapy—is an issue being re-examined in ongoing clinical trials. It may be that our current approach to breast cancer will be changed by these studies.

In 1985, adjuvant therapy was not generally recommended for women with negative nodes, except for certain high-risk patients. Since then, several important trials have indicated that adjuvant therapy may benefit a larger population of patients. In one trial, node-negative patients were treated with surgery plus placebo or surgery plus tamoxifen. The tamoxifen patients showed improved relapse-free survival, regardless of menopausal status.

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SUGGESTED READING

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Bohmert HH, Leis HP Jr, Jackson IT, eds. Breast cancer: conservative and reconstructive surgery. New York: Thieme Medical Publishers Inc., 1989.

Harris JR, Hellman S, Henderson IC, et al. Breast diseases. Philadelphia: J.B. Lippincott Co., 1987.

IMPROVED LABORATORY DIAGNOSIS OF SEPTICEMIA

The incidence of septicemia increased by 139% from 1979 (73.6 per 100,000) to 1987 (175.9 per 100,000). It is now the 13th leading cause of death in the United States, with an annual cost of $5 to $10 billion. The increase probably reflects several factors: (1) improved medical technology, which in turn may have increased the number of immunocompromised patients at risk for septicemia; (2) the more frequent use of invasive devices; and (3) better diagnostic ability. Given these numbers, it is timely to review the clinical characteristics of septicemia, and the methods of accurate diagnosis.

CHARACTERISTICS OF BACTEREMIAS AND CANDIDEMIAS

Bacteremias and candidemias are classified as transient, intermittent, and continuous, with distinguishing characteristics that influence the number and timing of blood cultures. Transient bacteremias occur commonly after manipulation or instrumentation of infected tissue or colonized mucosal surfaces, and early in the course of a localized infection. Intermittent bacteremias typically occur in the presence of an undrained focus of infection. Continuous bacteremia is characteristic of endovascular infection, such as infective endocarditis.

The sensitivity of a single blood culture ranges from 80% to 90%, increasing to 90% to >95% with two cultures, depending on whether the analyses include