Carcinoma of the Breast in the Geriatric Population

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- Adjuvant radiation therapy after partial mastectomy is the standard approach for the conservative treatment of carcinoma of the breast. However, a recent survey concluded that many physicians do not prescribe radiation therapy after lumpectomy when the patient is 70 years of age or older. The omission of radiation therapy has benefits both in terms of increased quality of life and major savings in cost. Retrospective data from Cooke and colleagues suggest that the omission of radiation therapy may be a sound approach, but prospective data are lacking.

Before we abandon a tested therapy on the basis of age and sporadic retrospective data, it would be prudent to test the suggested new treatment against the current state-of-the-art therapy in a prospective randomized trial. In 1994, the Cancer and Leukemia Group B (CALGB) began conducting a multi-institutional study of carcinoma of the breast in women who are older than 70 years of age. Recently, the Eastern Cooperative Oncology Group (ECOG) and the Radiation Therapy Oncology Group (RTOG) also agreed to participate. Patients who have clinically node-negative, estrogen-receptor positive or indeterminate tumors that are 2 cm or less and have undergone breast conservation therapy will be randomly assigned to receive either radiation therapy or no radiation therapy. All patients will receive tamoxifen (Nolvadex®) for five years.

Approximately 600 women will need to be involved in this study to answer the question of whether breast cancer patients who are older than age 70 years should receive radiation therapy. This article summarizes the rationale for this study and encourages surgeons to participate in the trial.

The risk of developing carcinoma of the breast increases with age. Within the same one-year interval, carcinoma of the breast develops in 1.5 of 1,000 women between the ages of 40 and 50 years compared with 3.75 of 1,000 women who are 71 years of age or older (Figure 1). As the life expectancy of the population in the U.S. increases, the absolute number of women older than 70 years of age with carcinoma of the breast can also be expected to increase in the next few decades. This projection emphasizes the importance of implementing prospective studies to assess the optimal treatment of elderly women with carcinoma of the breast.

The ten-year reanalysis of data from the National Surgical Adjuvant Breast and Bowel Project (NSABP) Protocol B-06 has shown that the choice of local therapy or the addition of radiation therapy to local therapy has no statistically significant effect on the survival rate of patients with carcinoma of the breast (Figure 2). However, while no advantage in survival is associated with the addition of radiation therapy to lumpectomy, the rate of local recurrence is affected. Patients treated by lumpectomy without radiation therapy have an incidence of local ipsilateral breast tumor recurrence of approximately 40% compared with approximately 10% when radiation therapy is given. The noticeably higher rate of ipsilateral breast tumor recurrence in patients who have not received radiation therapy has led most physicians to offer either lumpectomy plus radiation therapy or modified radical mastectomy as the standard treatment of invasive carcinoma of the breast.

The question remains as to whether or not certain subsets of patients have an intrinsically lower rate of local recurrence and, therefore, may not require radiation therapy. The geriatric population may rep-
Figure 1—The incidence of carcinoma of the breast is shown by age group.

Figure 2—NSABP Protocol B-06: Ten-year reanalysis.

Figure 3—Status by age: Five years after the diagnosis of carcinoma of the breast.

Figure 4—The effect of tamoxifen on ipsilateral breast tumor recurrence.

represent such a subgroup for the following reasons: (1) adjuvant radiation therapy is associated with no impact on the survival rate (or with an impact so small that it is not measurable in clinical trials); (2) biologic factors in older patients decrease the rate of ipsilateral breast tumor recurrence; (3) comorbid conditions and the resulting decreased life expectancy shorten the period in which an elderly patient is at risk of experiencing a recurrence; (4) adjuvant tamoxifen therapy diminishes the rate of ipsilateral breast tumor recurrence; and (5) preservation of the breast remains a viable option, even after local recurrence.

Discussion

- The Use of Adjuvant Radiation Therapy Is Not Associated with Any Measurable Impact on Survival—Four randomized trials have compared preservation of the breast with and without radiation therapy (Table 1). All of the trials showed that the addition of radiation therapy did not have a measurable impact on the survival rate.

- Biologic Factors in Older Patients Decrease the Rate of Ipsilateral Breast Tumor Recurrence—The findings of the Milan Trial III include the observation that recurrences of carcinoma of the breast decrease with increasing age. Patients younger than 45 years of age had a rate of 17.5% for ipsilateral breast tumor recurrence. Patients between the ages of 46 and 55 years had a rate of 8.7% for ipsilateral breast tumor recurrence, and patients older than 55 years of age had a rate of 3.8% for ipsilateral breast tumor recurrence. The overall trend of decreasing rates of recurrence with increasing age indicate that older patients may be at a decreased risk for local recur-
rence than premenopausal patients.

- Comorbid Conditions and the Risk of Experiencing a Recurrence—Comorbid conditions and a relatively decreased life expectancy shorten the period in which an elderly patient is at risk of experiencing a recurrence.13 Frequently, geriatric patients have serious comorbid conditions that diminish their life expectancy to a greater degree than the diagnosis of carcinoma of the breast. For example, a 70-year-old patient with carcinoma of the breast has an 8% risk of dying from the carcinoma and a 13% risk of dying from a comorbid disease within five years. In contrast, an 85-year-old woman has a 12% risk of dying from carcinoma of the breast and a 49% risk of dying from other causes within the same five-year period. This relationship deserves consideration when recommending both primary and adjuvant treatment (Figure 3).

- Adjuvant Tamoxifen Therapy Diminishes the Rate of Ipsilateral Breast Tumor Recurrence—Adjuvant tamoxifen therapy diminishes the rate of ipsilateral breast tumor recurrence. In the NSABP B-14 trial, patients who received tamoxifen had approximately a 50% decreased risk of experiencing ipsilateral breast tumor recurrence compared with patients who received a placebo (Figure 4).10 In this CALGB study, all patients will receive tamoxifen for five years because our understanding indicates that it is a safe and appropriate adjuvant therapy for most elderly patients with carcinoma of the breast. Most elderly patients with carcinoma of the breast have tumors that are estrogen-receptor positive.

The efficacy of tamoxifen in treating patients with estrogen-receptor positive, node-negative tumors was established in the NSABP B-14 trial.10 The National Institutes of Health (NIH) Consensus Conference of 1985 further established that tamoxifen therapy was appropriate in the treatment of estrogen-receptor positive, node-positive tumors.11 In addition, a role for tamoxifen in the treatment of patients with estrogen-receptor negative tumors was demonstrated in the 1992 meta-analysis.12 Among patients who were older than 50 years of age and who had estrogen-receptor negative tumors, a 16% reduction in both the odds of recurrence and death was observed.12

- Preservation of the Breast Remains a Viable Option, Even after Local Recurrence—Preservation of the breast often remains a viable option, even after local recurrence. A higher rate of ipsilateral breast tumor recurrence in the nonradiated group does not necessarily exclude preservation of the breast (Figure 5). Preservation of the breast after tumor recurrence has been assessed in three randomized trials. Liljegren and colleagues found that 11 of 37 patients (30%) who developed local recurrences could be treated with repeat lumpectomy followed by radiation therapy.6 Clark and
apy decrease the incidence of subsequent mastectomy? (2) Does radiation therapy decrease the rate of local recurrence beyond the benefit provided by tamoxifen therapy? (3) Do the rates of disease-free survival and overall survival differ between treatment groups?

The omission of adjuvant radiation therapy clearly decreases the morbidity associated with treatment, and the older patient is also spared the inconveniences associated with daily treatments. Despite these potential benefits, adjuvant radiation therapy is the established therapy for patients with carcinoma of the breast, including older women. The decision to withhold radiation therapy in elderly women who are capable of undergoing these treatments demands justification, which can only be provided by a well-controlled trial. The CALGB 9343 study is designed to address this important issue. Physicians who wish to participate in this trial should consult with one of the participating institutions of the CALGB, ECOG, or RTOG.

Table

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number of Patients</th>
<th>Years of Follow-Up</th>
<th>Radiation Therapy (%)</th>
<th>No Radiation Therapy (%)</th>
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<tr>
<td>Fisher and Anderson</td>
<td>930</td>
<td>10</td>
<td>71</td>
<td>65</td>
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<td>Liljegren et al</td>
<td>381</td>
<td>5</td>
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<tr>
<td>Veronesi et al</td>
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<td>No difference</td>
<td>No difference</td>
</tr>
<tr>
<td>Clark et al</td>
<td>837</td>
<td>3</td>
<td>91.1 to 96</td>
<td>90.5 to 96</td>
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Coworkers and Veronesi and colleagues demonstrated that the breast could be preserved in many women who experienced local recurrences.\(^5\)\(^7\) These studies indicate that for many women, the goal of preservation of the breast is not necessarily compromised by the omission of initial adjuvant radiation therapy (Figure 5).

Conclusion

The optimal management of carcinoma of the breast in elderly women has not been tested in a prospective manner. Only recently has evidence indicated that the response to therapy for carcinoma of the breast may be different in older and younger women and that these differences may be used to benefit older postmenopausal patients.

Protocol 9343 (Figure 6) of the CALGB (ECOG, RTOG intergroup study) is a prospective, randomized trial that is currently open for the enrollment of clinically node-negative patients with estrogen-receptor positive or indeterminate carcinoma of the breast, who are 70 years of age or older and who have been treated by lumpectomy followed by tamoxifen for five years. Patients are randomly assigned to either receive or not receive adjuvant radiation therapy. Patients are stratified by age and whether or not dissection of the lymph nodes was performed.

This study is designed to address the following issues: (1) Does radiation therapy decrease the incidence of subsequent mastectomy? (2) Does radiation therapy decrease the rate of local recurrence beyond the benefit provided by tamoxifen therapy? (3) Do the rates of disease-free survival and overall survival differ between treatment groups?

The omission of adjuvant radiation therapy clearly decreases the morbidity associated with treatment, and the older patient is also spared the inconveniences associated with daily treatments. Despite these potential benefits, adjuvant radiation therapy is the established therapy for patients with carcinoma of the breast, including older women. The decision to withhold radiation therapy in elderly women who are capable of undergoing these treatments demands justification, which can only be provided by a well-controlled trial. The CALGB 9343 study is designed to address this important issue. Physicians who wish to participate in this trial should consult with one of the participating institutions of the CALGB, ECOG, or RTOG.

References