CORRESPONDENCE

Re: Breast-Conserving Surgery With or Without Radiotherapy: Pooled-Analysis for Risks of Ipsilateral Breast Tumor Recurrence and Mortality

In a recent article in the Journal, Vinh-Hung and Verschraegen (1) provided a valuable pooled analysis of randomized trials of postoperative radiotherapy after breast-conserving surgery. They reported a small increase in breast cancer mortality and a substantial risk of local recurrence from the omission of breast radiotherapy. These important observations should not be interpreted to imply that all patients require breast radiotherapy after breast-conserving surgery and appropriate systemic therapy. We believe, however, that in contrast to younger patients, there are insufficient data to draw this conclusion in older patients. Indeed, the U.S. National Institutes of Health, in its 2000 consensus statement for breast cancer (2), makes no specific recommendation on adjuvant therapy for patients aged 70 years or older because of the paucity of data for this group of patients. Of the 15 randomized trials assessing the role of breast radiotherapy or its omission included in the pooled analysis by Vinh-Hung (1), only three (Uppsala-Orebro, Tokyo, and the Cancer and Leukemia Group B [CALGB]) included patients over age 70. In this older group of patients, there are competing risks of mortality from predominantly vascular causes and breast cancer. National Institutes of Health (NIH) consensus development panels on breast cancer (3) provided better insight into several age-related issues. One issue is that the extreme difficulty in following up older patients may have led earlier studies to mistakenly conclude a lower risk of recurrence. The updated report revealed substantially improved registration of deaths and recurrences—55 deaths were reported (39 deaths with no radiotherapy, 25 deaths with radiotherapy), and a statistically nonsignificant 19% excess relative risk of mortality from omitting radiotherapy (4). The updated report also showed statistically significantly poorer in-breast and poorer locoregional recurrence-free survivals in the absence of radiotherapy (2).

Although elderly patients are under-represented in clinical trials, the relationship between age and survival in breast cancer is now well established. All large studies concur that the effect of age is biphasic: high mortality in younger women, lowest in menopausal women, and then increasing again with age (Tai P: personal communication). To provide a concrete representation of the biphasic relationship and to obtain quantitative estimates of the risks associated with age, consider a cohort of low-risk patients who have a primary
breast carcinoma 2 cm or less in diameter, and a status of pN0 (axillary dissection) selected from the Surveillance, Epidemiology, and End Results (SEER) database, for diagnostic years 1988–1997 (4). Figure 1 shows counts and rates of death in this cohort as a function of age. The average follow-up was 7.8 years. Despite the short follow-up period and the overall low breast cancer–specific death rate, the biphasic shape is immediately apparent: high breast cancer death rates in patients younger than 50 years and a small but steady increase in patients aged 50 years or older (Fig. 1, D). This biphasic relationship clarifies how breast cancer can be misperceived as being indolent in older patients. Group comparisons indicate that postmenopausal patients, as a group, have a lower risk of breast cancer death than younger premenopausal patients (Fig. 1, D). But by each successive year of age within their group, the older postmenopausal patients have a greater risk of dying of breast cancer than do younger postmenopausal patients (Fig. 1, D), which shows that older age is not associated with lower risk.

Should we infer from the unremitting risk that all patients, regardless of age, should receive adjuvant radiotherapy? Kunkler et al. draw attention to the importance of competing risks of death. Figure 1, E, shows an exponential increase of non–breast cancer deaths with age. Figure 1, F, shows the corresponding odds of non–breast cancer death. At age 60 years, the odds of death from breast cancer versus other causes are 1:2.5. At age 65 years, the odds are still substantial: 1:3.5. At age 70 years, the odds are 1:5. At age 80 years, the odds are 1:10. Considering mortality only, these odds suggest that it is reasonable to propose that low-risk older patients participate in the PRIME II trial. But taking local recurrences into account, if patients are considered fit for surgery, then it is unclear why they should be denied the chance to have radiotherapy to reduce their risk of recurrence. The evidence of risk reduction is strong, and improvements that will benefit low-risk and fragile patients are within reach (5).

Shouldn’t the priority be to enroll these patients in trials of alternatives to conventional radiotherapy, whether it be short-course (6) or intra-operative radiotherapy (7)?

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REFERENCES


NOTES

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