

Radiation Improves Overall Survival After Mastectomy in Women with Node-Positive Breast Cancer

Ragaz J, Olivotto AO, Spinelli JJ, et al. Locoregional radiation therapy in patients with high-risk breast cancer receiving adjuvant chemotherapy: 20-year results of the British Columbia Randomized Trial. *J Natl Cancer Inst* 2005;97:116–26.

Study Overview

Objective. To assess the role of locoregional radiation following modified radical mastectomy in women with node-positive breast cancer.

Design. Randomized prospective trial with intention-to-treat analysis.

Setting and participants. From 1979 to 1986, 318 premenopausal women with breast cancer with pathologically positive axillary lymph nodes after a modified radical mastectomy were randomized to either locoregional radiation or no additional treatment. All patients received adjuvant chemotherapy with cyclophosphamide, methotrexate, and 5-fluorouracil. Radiation therapy was given by a multifield technique to include the chest wall, axilla, supraclavicular, and internal mammary regions. Patients with positive estrogen receptor status underwent a second random assignment to radiation-induced oophorectomy plus prednisone versus no hormonal manipulation.

Main outcome measures. Event-free survival, disease-free survival, systemic disease-free survival, breast cancer-specific survival, overall survival, and locoregional recurrence.

Main results. Baseline characteristics between groups were similar. At 20-year follow-up, 191 patients had experienced a breast cancer relapse, and 190 patients had died (170 from breast cancer and 20 from other causes). For patients assigned to chemotherapy alone compared with patients assigned to chemotherapy and radiation therapy, event-free survival at 20 years was 25% versus 38%, respectively (relative risk, 0.70 [95% confidence interval, 0.54–0.92]; $P = 0.009$). As well, breast cancer-free survival was 30% versus 48%, respectively ($P = 0.001$). Twenty-year breast cancer-specific survival was 38% versus 53%, respectively ($P = 0.008$), and overall survival was 37% versus 47%, respectively ($P = 0.03$). Additionally, the impact of radiation therapy for all survival outcomes in the subgroup with 1 to 3 involved axillary nodes was similar to that in the subgroup with more than 4 nodes involved. The long-term toxicities associated with

radiation were 3 (1.8%) cardiac deaths in the chemotherapy and radiation arm compared with 1 (0.6%) in patients treated with chemotherapy alone ($P = 0.622$). Radiation was associated with increased arm edema.

Conclusion. High-risk breast cancer treated with modified radical mastectomy followed by treatment with radiation and adjuvant chemotherapy leads to improved survival compared with chemotherapy alone.

Commentary

Over 150,000 women are diagnosed with invasive breast cancer each year. The majority will be lifelong survivors after undergoing primary therapy with either modified radical mastectomy or breast-conserving surgery plus radiation. Women with node-positive breast cancer are at increased risk for tumor recurrence after primary therapy and benefit from adjuvant chemotherapy and, if hormone receptor-positive, selective estrogen receptor modulators.

Radiation therapy plays an important role in local breast cancer treatment in eradication of occult residual disease. It has proven to reduce local recurrence after breast-conserving surgery and is a standard of care in this setting, although improvement in overall survival has not been seen in a randomized study [1]. Postmastectomy radiation has been more controversial. For women with high-risk disease, postmastectomy radiation has been proven to reduce local recurrence [2]; however, effects on mortality have varied. In 1997, Ragaz et al reported improved disease-free survival and a trend towards improved overall survival with postmastectomy radiation in 318 Canadian premenopausal women with node-positive breast cancer [3].

In the current article, Ragaz and colleagues present updated 20-year data from their postmastectomy radiation study. Similar to the initial publication, radiation was associated with improvements in local recurrence and disease-free survival. More important, overall survival was significantly improved in the radiation cohort—an effect observed in both the 1 to 3 node-positive and 4 or greater node-positive patient groups.

These findings are important and add to a growing body of evidence that radiation improves both local recurrence

rates and overall survival after mastectomy. This trial was well-designed and follow-up is now at 20 years. However, this study's limitations should still be considered. First, the radiation technique (rapid fractionation) is not commonly used in the United States. As well, the fields of treatment differ from standard practice in the United States (where the internal mammary field is often excluded). Additionally, the adjuvant chemotherapy regimen used is now likely considered to be inferior to more modern regimens, and the use of adjuvant hormonal ablation was limited. These concerns raise the question of how applicable these results are to standard practice in the United States. Nonetheless, these data suggest that postmastectomy radiation should be considered a part of standard practice. Randomized trials are in progress.

Applications for Clinical Practice

Postmastectomy radiation is currently recommended for women with breast cancer at high-risk for recurrence,

including those with tumors > 5 cm or involving the chest wall or skin, inflammatory breast cancer, or at least 4 axillary nodes involved.

—Review by David R. Spiegel, MD

References

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