学 位 論 文 の 要 旨

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学 位 論 文 名　Role of 10-Gy Boost Radiation After Breast-conserving Surgery for Stage I-II Breast Cancer With a 5-mm Negative Margin

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論 文 内 容 の 要 旨

INTRODUCTION

Breast-conserving therapy (BCT) is a well-accepted method of treating early breast cancer, since major clinical trials have demonstrated that subsequent survival is equivalent to that after mastectomy. After breast-conserving surgery, postoperative irradiation of the breast has been reported to reduce ipsilateral tumor recurrence. However, it has not been established whether all patients should receive additional boost radiation to the site of tumor resection. In Japan, boost radiation is not always given to patients with negative resection margins because the criteria for deciding the surgical margin status are different from those used in the United States and Europe. In Japan, when the minimum distance between the invading edge of the cancer and the border of the resected specimen is greater than 5 mm, the surgical margin is defined as negative according to the 2005 Guidelines for Breast-conserving Therapy of The Japanese Breast Cancer Society (Study Group on a Protocol for Standard Breast-conserving Therapy). When the distance is ≤5 mm, the surgical margin is defined as positive. In the United States and Europe, on the other hand, a positive surgical margin is defined by the presence of invasive carcinoma or ductal carcinoma in situ at an inked margin. The present study was performed to evaluate the efficacy of a 10-Gy boost for stage I-II breast cancer with 5-mm tumor-free margins according to the Japanese guidelines. Accordingly, we performed a retrospective analysis of the long-term results obtained in patients treated at our institution.

MATERIALS AND METHODS

This was a retrospective cohort study, and the primary endpoint was local recurrence in the ipsilateral breast. Between July 1987 and August 2002, 137 patients with stage I-II breast cancer who received breast-conserving surgery at our institution and affiliated hospitals were referred to our department for postoperative radiotherapy. The median age of the subjects was 50 years, with a range of 27 to 83 years. The median follow-up period was 62 months from the date of surgery, with a range of 5 to 178 months. A total of 113 patients (82%) were followed for at least 36 months. The TNM classification of the UICC (2002) was used for tumor staging. All of the patients underwent breast-conserving surgery. When the minimum distance between the tumor edge and the border of the resected specimen was greater than 5 mm, the pathological diagnosis was a negative surgical margin according to the 2005 Guidelines for Breast-conserving Therapy of The Japanese Breast Cancer Society. When the width of the margin was ≤5 mm, it was defined as a positive surgical margin. All of the patients were reviewed and were confirmed to have negative surgical margins according to these guidelines. All patients received irradiation of the whole breast using opposed tangential fields and 4-MV photons delivered from a linear accelerator. The breast was irradiated to a total dose of 50 Gy in 25 fractions over 5 weeks. Then an additional 10 Gy (five fractions) boost was given to 79 patients using 6-12 MeV electrons (boost group), while 58 patients (no-boost group) received no further radiation. Overall survival, cause-specific survival, and disease-free survival were calculated from the time of surgery by the Kaplan-Meier method. To detect any bias between the groups with or without boost radiation, the χ^2 test was used to compare categorical variables and the t-test was used for continuous variables. Various possible prognostic factors for local recurrence (boost radiation, age, tumor size, axillary lymph node status, extensive intraductal component, hormone receptor status, menopausal status, surgical procedure, and chemotherapy) were evaluated by univariate analysis using the log-rank test and by multivariate analysis using the Cox proportional hazards model. To detect any subgroups showing a benefit of boost radiation, comparison was done by Yates' correction or Fisher exact test for adjustment of the χ^2 test.

RESULTS AND DISCUSSION

For the entire patient population, the 5-year overall survival, cause-specific survival, and

disease-free survival rates were 96.0%, 96.8%, and 94.2%, respectively. Local recurrence in the ipsilateral breast occurred in five patients, including one patient who had boost radiation, and four patients who did not. The 5-year local recurrence rates of the groups with or without boost irradiation were 1.61% and 1.92%, respectively. All five local recurrences were close to the site of tumor resection. All 5 patients underwent salvage surgery, with pathological evidence confirming recurrence. Local recurrence occurred within a median follow-up period of 94.0 months (range: 7.2-121.7 months) after initial surgery. Univariate analysis of the clinical and pathological parameters associated with local recurrence was performed. Boost radiation reduced the local recurrence rate, but the improvement was not significant according to the log-rank test ($p=0.070$). Age ($p=0.060$) and the presence of an extensive intraductal component ($p=0.090$) were most closely related to local failure, but there was no significant association between local recurrence and the tumor size, axillary lymph node status, hormone receptor status, surgical procedure, or chemotherapy. Multivariate analysis using the Cox proportional hazards model failed to detect any factors that were significantly associated with local control. Next, the local recurrence rates were compared between subgroups with or without various risk factors to detect any subgroups showing a benefit of boost radiation. However, subgroup analyses did not reveal any factors with a significant influence on local recurrence. The 5-year distant recurrence rate and cause-specific survival rate were respectively 2.63% and 97.6%, respectively, with boost radiation, and 6.18% and 96.4% respectively, without it. Both the distant recurrence and cause-specific survival rates did not show any significant differences between the boost and no-boost groups according to the log-rank test. There were no severe complications or impairment of the cosmetic outcome in either group. Although we had only a few patients with local failure, the follow-up period was also relatively short, so differences between the boost and no-boost groups may have been difficult to detect.

CONCLUSION

Boost radiation was performed on patients with stage I-II breast cancer with 5-mm negative margins according to the Japanese guidelines resulting in a tendency toward decreased local recurrence, but the improvement was not significant ($p=0.070$). A large randomized controlled study is necessary to establish more conclusive findings.