Radiotherapy is Necessary for Breast Cancer Patients with 1-3 Positive Nodes

Studies have shown that postmastectomy radiotherapy (PMRT) can reduce the risks of recurrence and mortality in breast cancer patients with node-positive disease, especially in those with ≥4 positive nodes (1,2). Randomized data from the DBCG 82 b & c trials have proved that PMRT for node positive patients improves the 15-year overall survival by approximately 10% ($P = 0.015$) (1). Overgaard et al. reported a randomized trial of radiotherapy after mastectomy in 1708 high-risk premenopausal women, showing that the 10-year disease-free survival rates are 46% for the women treated with radiotherapy plus CMF (cyclophosphamide, methotrexate and fluorouracil) and 34% for those treated with CMF only ($P < 0.001$), with a similar magnitude of benefit in 10-year overall survival from 45% without PMRT to 54 % with PMRT ($P < 0.001$) (2). However, none of them has systematically discussed the benefit of PMRT for breast cancer patients with 1-3 positive nodes, and it still remains a debate whether breast cancer patients with a comparatively low risk benefit from PMRT (3).

Given this issue, we conducted a study for the effect of PMRT on breast cancer patients with 1-3 positive nodes (4). We focused on the patients with T1-T2 tumors and 1-3 positive nodes because the patients with T2≥3 are necessary to receive radiotherapy in spite of the number of positive nodes. Three electronic databases were systematically quarried for published studies evaluating the effects of PMRT on breast cancer patients with 1-3 positive lymph nodes. A total of 334 articles were initially identified, and ten studies with 3432 patients were included ultimately. Our analyses have shown that the pooled relative risk (RR) for locoregional recurrence rate (LRR) with PMRT is 0.348 (95% CI = 0.254 to 0.477), suggesting a significant benefit for PMRT to decrease the risk of LRR in patients with T1-T2 tumors and 1-3 positive nodes ($P < 0.05$). Furthermore, the RR is 0.330 (95% CI = 0.171 to 0.639) for T1, N1-3+ tumors; and 0.226 (95% CI = 0.121 to 0.424) for T2, N1-3+ tumors. Our study has revealed a significant reduction of LRR in patients with T1-T2 tumors with 1-3 positive nodes after treatment with PMRT; and the magnitude of the LRR risk reduction is slightly greater for larger tumors.

After the publication of our meta-analysis, the Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) has recently published a meta-analysis which has also discussed the effect of PMRT on breast cancer with 1-3 positive nodes (5). In this meta-analysis, PMRT has been shown to be able to reduce the LRR (2P < 0.00001), overall recurrence (RR = 0.68, 95% CI = 0.57 to 0.82, 2P = 0.00006), and mortality (RR = 0.80, 95% CI = 0.67 to 0.95, 2P = 0.01), no matter whether or not systemic therapy is given. When the patients with 1-3 positive nodes after axillary dissection were analyzed who were in trials in which the policy was to give systemic therapy, PMRT could also reduce the rates of overall recurrence (RR = 0.67, 95% CI = 0.55–0.82, 2P = 0.00009) and mortality (RR = 0.78, 95% CI = 0.64–0.94, 2P = 0.01). What’s more, this study has proved that the benefit of PMRT is not significant between patients with 1 and those with 2-3 positive nodes.

In general, the EBCTCG’s results are consistent with our meta-analysis. Both studies have revealed that PMRT could significantly reduce the risks of LRR and mortality of breast cancer patients, and clearly suggested that PMRT should be considered similarly for patients with one to three involved axillary lymph nodes as it should be for those with four or more affected axillary lymph nodes.

As reported before, radiotherapy may increase the death rate which is not related to breast cancer, mainly by inducing cardiac diseases and secondary cancer (6). This potential outcome lowers the benefit of PMRT on breast cancer mortality after a long time follow-up, and for this reason, it still remains controversial whether the patients with low-risk breast cancer really benefit from PMRT although PMRT is of great value for those with high-risk breast cancer defined as tumor size ≥5cm and positive nodes ≥4 or positive margins (5). Both EBCTCG and us have demonstrated that breast cancer patients with 1-3 positive nodes could benefit from PMRT, thereby PMRT should be considered in the treatment of this subgroup of patients. However, both meta-analyses are retrospective and perspective multicenter randomized studies are needed to confirm whether breast cancer patients with 1-3 positive nodes can benefit from PMRT. Furthermore, we should notice that not all patients with 1-3 positive nodes can benefit from PMRT. Many other factors may influence the effect of PMRT such as micro-metastasis, lymphatic vessel invasion, extra-capsular lymph node involvement, etc. (6,7). What deserves to be mentioned is that gene analysis is becoming an important tool to diagnose and forecast prognosis of patients (7). High-throughput chip technology may be applied to identify by DNA typing the subgroups of patients who may benefit from PMRT, thus providing guidance to personalized treatment.

Based on statistical studies, the debate whether breast cancer patients should receive PMRT is coming to an end (8). What we researchers should focus on is to promote the development of modern radiotherapy techniques adding lesser burden to patients and having little long-term side effects.

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