Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials


CRD summary
This review found that after mastectomy and axillary dissection, radiotherapy reduced both recurrence and breast cancer mortality in women with one to three positive lymph nodes, even when systemic therapy was given. Despite reporting limitations, the collaborative nature of the review and use of individual participant data suggest that the results and the authors' conclusions are likely to be reliable.

Authors' objectives
To assess the benefit of radiotherapy after mastectomy and axillary dissection in women with breast cancer with only one to three positive lymph nodes.

Searching
As this was a re-analysis of an existing review search details were not presented and were reported in previous publications (see Other Publications of Related Interest). It appeared that databases were searched and that an international collaboration of trialists was used to identify all relevant published and unpublished trials.

Study selection
Eligible trials were of adjuvant radiotherapy versus no radiotherapy with the same surgery after mastectomy for invasive breast cancer. Trials dates had to start before 2000. Outcomes investigated included time to breast cancer mortality, time to any recurrence and time to locoregional and distant recurrence.

All trials used radiotherapy that included the chest wall, supraclavicular or axillary fossa and internal mammary chain. 72% of the participants had pathologically node-positive disease and 20% had node-negative disease. Details of the types of radiotherapy used were presented.

The authors did not report on how many reviewers performed the study selection.

Assessment of study quality
The authors did not report any assessment of study quality or of the quality of the individual participant data (IPD).

Data extraction
The review extracted IPD for all women in the included trials. It appeared that data on time to each outcome were extracted. Data were extracted on whether women had pathologically node-negative or node-positive disease and on the number of positive nodes. Women were classed as having axillary dissection if the trial protocol required removal of axillary lymph nodes at least levels I and II or if the median number of nodes removed was 10 or more; otherwise women were classified as having axillary sampling.

The authors did not report how many reviewers performed the data extraction.

Methods of synthesis
Meta-analyses were used to combine data. Details were not presented but were reported in previous publications. It appeared that a log-rank method was used to estimate summary relative risks with 95% coincidence intervals for each outcome with up to 10 years of follow-up. Analyses were stratified by trial, follow-up year, age and pathological node status.

Results of the review
Twenty-two trials were included. Participants totalled 8,135 women and 3,786 of these had axillary dissection up to level II with positive nodes. Median follow-up time was 9.4 years.
In 700 women with axillary dissection but no positive nodes, radiotherapy had no statistically significant effect on locoregional recurrence, overall recurrence or cancer mortality but did increase overall mortality (RR 1.23, 95% CI 1.02 to 1.49).

In 1,314 women with axillary dissection and one to three positive nodes, radiotherapy reduced locoregional recurrence, overall recurrence (RR 0.68, 95% CI 0.57 to 0.82) and cancer mortality (RR 0.80, 95% CI 0.67 to 0.95). Results were similar in the subset of trials where women were given systemic therapy.

In 1,772 women with axillary dissection and four or more positive nodes, radiotherapy reduced locoregional recurrence, overall recurrence (RR 0.79, 95% CI 0.69 to 0.90) and cancer mortality (RR 0.87, 95% CI 0.77 to 0.99).

Other results were presented (including for women with axillary sampling).

**Authors’ conclusions**

After mastectomy and axillary dissection, radiotherapy reduced both recurrence and breast cancer mortality in women with one to three positive lymph nodes, even when systemic therapy was given.

**CRD commentary**

This large updated re-analysis of an IPD review addressed a relevant research question with suitable inclusion criteria. As this was an update, reporting of review processes in this paper were limited. Search details were not presented but it appeared that effort was taken to identify all relevant published and unpublished trials. Whether action was taken to prevent reviewer error and bias was not reported but it is probable that such action was taken. Study quality was not reported but the included studies were probably good quality randomised trials. Trials were combined in meta-analyses but details of the methods used were not fully reported.

Despite substantial limitations in reporting, the collaborative nature of the review and its use of individual participant data suggest that the results and the authors’ conclusions are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors noted that in many countries where women were at lower risk of recurrence, absolute gains might be smaller but proportional gains might be larger because of more effective radiotherapy. They also suggested that the chest wall was an important target in postmastectomy radiotherapy.

**Research:** The authors noted that a trial of radiotherapy to the chest wall and trials of regional node irradiation were underway.

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