Effects of radiotherapy and surgery in early breast cancer: an overview of the randomized trials

Early Breast Cancer Trialists’ Collaborative Group

Authors' objectives
To perform a systematic overview of the results of randomised controlled trials (RCTs) of radiotherapy and surgery for early breast cancer.

Searching
Discussion with trialists and scrutiny of review articles was undertaken the systematic lists of trials prepared by the UICC (Geneva), NCI (Bethesda) and UKCCCR (London), and all current and previous proceedings of ASCO, AACR and UICC meetings were also reviewed; a computer-aided literature search was made; manufacturers were contacted.

Study selection
Study designs of evaluations included in the review
RCTs were included.

Specific interventions included in the review
Radiotherapy and surgical treatment of breast cancer.

Participants included in the review
Women with early breast cancer, in which all clinically apparent disease can be removed surgically, were included.

Outcomes assessed in the review
The outcomes assessed were: overall mortality, non-breast-cancer mortality and mortality excluding non-breast-cancer deaths; and rate of recurrence.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The inclusion criteria were as follows.

1. The trial started to enter patients before 1/1/1985.
2. The trial contained some properly randomised comparison.
3. The trial included at least two treatment groups that provided an unconfounded concurrently randomised comparison of different treatments.
4. The trial was not conducted in the USSR or Japan. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
Data on each individual patient were sought from investigators.

Methods of synthesis
How were the studies combined?
Peto's method (log rank analysis) was used to calculate overall odds ratio (OR), using the difference between the observed and the expected number, and its variance.

How were differences between studies investigated?
The chi-squared statistic was used to test heterogeneity among trials. Treatment effects of different subgroups were analysed separately.

Results of the review
There were 36 trials comparing radiotherapy plus surgery with the same surgery alone (17,273 women; 10 trials comparing more-extensive surgery with less-extensive surgery (4,818 women); and 18 trials comparing more-extensive surgery with less-extensive surgery plus radiotherapy (9,891 women).

Overall mortality was similar in patients treated with surgery plus radiotherapy or treated with surgery alone (40.3 versus 41.4%, p=0.5). Patients in the radiotherapy group had a lower risk of death due to breast cancer (OR 0.94, 95% confidence interval, CI: 0.88, 1.00; p=0.03) and a higher risk of death from other causes (OR 1.24, 95% CI: 1.09, 1.42; p=0.002). Isolated local recurrence was significantly lower in patients treated with surgery plus radiotherapy than in patients treated with surgery alone (6.7 versus 19.6%; OR 0.33). It was not possible to assess the effect of radiotherapy on distant recurrence.

Overall mortality was similar when more extensive surgery was compared with less extensive surgery (48.0 versus 50.1%; OR 0.97, p=0.4). The difference in isolated local recurrence between more and less extensive surgery was not significant.

No significant difference in total mortality was found when mastectomy was compared with breast-conserving surgery plus radiotherapy (22.9 versus 22.9%), or when axillary clearance was compared with radiotherapy (54.7 versus 54.9%).

Authors' conclusions
Some of the local therapies for breast cancer had substantially different effects on the rates of local recurrence (such as the reduced recurrence with the addition of radiotherapy to surgery) but there were no definite differences in overall survival at 10 years.

CRD commentary
The methods of this review (e.g., literature search, criteria for inclusion) have been described in previous publications.

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