Review: Postoperative radiotherapy decreases survival in early-stage non–small-cell lung cancer


Question

In patients with non–small-cell lung cancer (NSCLC), does the addition of postoperative radiotherapy increase survival?

Data sources

Studies were identified by searching MEDLINE and CANCERLIT using a modified version of the Cochrane Collaboration optimum search strategy. Hand searches were also done of meeting abstracts, reviews, specialist journals, and book bibliographies. Cancer trial registries were searched, and investigators were contacted.

Study selection

Studies were selected if they were randomised controlled trials that compared postoperative radiotherapy with no further treatment, the patients had NSCLC and had had complete surgical resection, the method of randomisation was blinded, orthovolt radiation was not used, and recruitment occurred between 1965 and 1995.

Commentary

The study from the PORT Meta-analysis Trialists Group is important because it concerns lung cancer, the leading cause of cancer death around the world. It may also help us learn more about the effects of irradiating the chest in other types of cancer, particularly breast cancer.

Surgery is the mainstay of therapy for early-stage lung cancer, although about 60% of patients still die of the disease. Because local relapse remains problematic, radiotherapy has been used postoperatively in an attempt to prevent it and to improve survival. This meta-analysis shows, using the techniques employed, that such radiation has had the opposite effect. The hazard ratio for death with radiotherapy was increased (by 21%), equivalent to a reduction in absolute survival from 55% to 48% at 2 years.

Based on the data provided, the increase in deaths associated with radiotherapy appears to be related to causes other than cancer. Data from randomised trials of radical surgery with or without radiation for breast cancer and rectal cancer also show a small but real excess of deaths not caused by cancer in the radiation groups (1, 2; R. Gray. Personal communication). In these studies the magnitude of the risk is not as great as in this meta-analysis, but undoubtedly a small excess of deaths is caused by the radiation. The larger risk seen in this meta-analysis may be related to acute or delayed radiation effect on the lungs or heart in patients with premorbid disease secondary to smoking or surgery.

Conventional postoperative radiotherapy no longer be recommended as routine therapy in lung cancer. If new therapeutic approaches are to be tested, they should be done in large randomised controlled trials. The fact that only 2000 patients were recruited for these trials over 3 decades, when there were about 20 million deaths from this disease, is a strong indictment of our failure to test therapies adequately in lung cancer.

Chris J. Wormald, WI Institute of Health Sciences Oxford, England, UK

References


The data extraction

Patient data were obtained from trial investigators on survival, recurrence, follow-up, treatment allocation, date of randomisation, age, sex, histological cell type, tumour stage, and performance status.

Main results

9 randomised controlled trials (2128 patients) were included; 3 trials were unpublished. Doses of postoperative radiotherapy ranged from 30 to 60 Gy, given in 10 to 30 fractions. No evidence existed for heterogeneity among trials. Overall survival was greater in patients who received surgery alone (P = 0.001) (Table). The hazard ratio for death with postoperative radiotherapy was 1.21 (95% CI 1.08 to 1.34). Overall recurrence-free survival was also greater for surgery alone (P = 0.018) (Table). The hazard ratio for local or distant recurrence or death was 1.13 (CI 1.02 to 1.26). Subgroup analyses showed that postoperative radiotherapy was more detrimental to survival among patients with earlier-stage disease (P for trend < 0.001) and lower nodal status (P for trend = 0.016).

Conclusion

Postoperative radiotherapy in patients with resected non–small-cell lung cancer adversely affects overall and recurrence-free survival, particularly for patients with stage 1 or stage 2 disease.


Postoperative radiotherapy vs surgery alone at 2 years for non–small-cell lung cancer

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Weighted event rates</th>
<th>RR (95% CI)</th>
<th>NNI (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Postoperative radiotherapy</td>
<td>Surgery alone</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>52%</td>
<td>45%</td>
<td>16% (7 to 22)</td>
</tr>
<tr>
<td>Recurrence or death</td>
<td>54%</td>
<td>50%</td>
<td>8% (2 to 16)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RRI, NNI, and CI calculations based on time-to-event data supplied by author.