



Complete Summary

GUIDELINE TITLE

Postoperative adjuvant radiation therapy in stage II or IIIA completely resected non-small cell lung cancer.

BIBLIOGRAPHIC SOURCE(S)

Lung Cancer Disease Site Group. Okawara G, Ung YC, Markman BR, Mackay JA, Evans WK. Postoperative adjuvant radiation therapy in stage II or IIIA completely resected non-small cell lung cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Aug [online update]. 15 p. (Practice guideline; no. 7-1-1). [14 references]

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SCOPE

DISEASE/CONDITION(S)

Stage II or IIIA non-small cell lung cancer (NSCLC)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Oncology
Pulmonary Medicine
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To evaluate the use of postoperative radiotherapy to improve survival in patients with completely resected pathologic stage II or IIIA non-small cell lung cancer
- To evaluate the use of postoperative radiotherapy in reducing the risk of local recurrence in patients with completely resected pathologic stage II or IIIA non-small cell lung cancer

TARGET POPULATION

Adults with completely resected pathologic stage II or IIIA non-small cell lung cancer (NSCLC)

INTERVENTIONS AND PRACTICES CONSIDERED

Postoperative radiotherapy

MAJOR OUTCOMES CONSIDERED

- Survival
- Local tumor recurrence

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE (1985 through June 2002), CANCERLIT (1985 through June 2002), and the Cochrane Library (2002 Issue 2) databases were searched. "Carcinoma, non-small-cell lung" (Medical subject heading [MeSH]) was combined with "radiotherapy, adjuvant" (MeSH), "surgery" (MeSH) and each of the following phrases used as text words: "non small cell lung cancer," "adjuvant," "resect," "surgery," "surgical." These terms were then combined with the search terms for the following study designs: practice guidelines, systematic reviews or meta-analyses, and randomized controlled trials. In addition, the Physician Data Query (PDQ) clinical trials database on the Internet (http://cancer.gov/search/clinical_trials/) and conference proceedings of the annual meetings of the American Society of Clinical Oncology (1997 through 2001) and the American Society for Therapeutic Radiology and Oncology (1999 through 2001) were searched for reports of new or ongoing trials. Relevant articles and abstracts were selected and reviewed by two members of the Lung Disease Site Group and methodologists. The reference lists from these sources

were searched for additional trials, as were the reference lists from relevant review articles. The Canadian Medical Association Infobase and the National Guidelines Clearinghouse were searched for existing evidence-based practice guidelines.

August 2003 Update

The original literature search has been updated using MEDLINE (through August 2003), CANCERLIT (through October 2002), the Cochrane Library (Issue 3, 2003), and the proceedings of the annual meetings of the American Society of Clinical Oncology (2002-2003) and the American Society for Therapeutic Radiology and Oncology (2002).

Inclusion Criteria

Articles were selected for inclusion if they were fully published reports or published abstracts of meta-analyses or randomized controlled trials (RCTs) that compared adjuvant radiation therapy after surgery with surgery alone in patients with completely resected stage II or IIIA non-small cell lung cancer.

Exclusion Criteria

1. Papers lacking information on the stage distribution of the study population were excluded.
2. Papers published in a language other than English were not considered.

NUMBER OF SOURCE DOCUMENTS

One meta-analysis and one randomized controlled trial were reviewed.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The Lung Disease Site Group decided not to pool the results of trials of adjuvant radiotherapy compared with surgery alone in completely resected stage II or III non-small cell lung cancer because of the availability of a published meta-analysis

of individual patient data that compared those two treatment approaches in patients with stages I, II, or III non-small cell lung cancer.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The original recommendation regarding the role of postoperative radiotherapy in stage II and III non-small cell lung cancer (NSCLC) supported the use of postoperative radiotherapy in completely resected stage II and III non-small cell lung cancer because of evidence that it reduced local recurrence. Since the publication of the original guideline recommendation, important evidence has been reported in several papers that justified the revision of the guideline, particularly in relation to the role of postoperative radiotherapy. The consensus of the Lung Disease Site Group (DSG) was to discuss postoperative radiotherapy and postoperative chemotherapy with or without radiotherapy in two related guidelines. There was consensus among Lung DSG members on the greater importance and urgency of revising and updating the original recommendation on postoperative radiation in light of newly published data.

As in the original practice guideline, the literature review did not allow a clear separation between stage IIIA and IIIB disease. Therefore, the recommendations remain restricted to completely resected stage IIIA disease and do not address other subsets of stage III disease. The Lung DSG found that the completeness of resection is uncertain or unreported in many studies and they suggest that this should be reported in future research studies.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not included.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 110 practitioners in Ontario (40 medical oncologists, 21 radiation oncologists, 22 surgeons, 26 respirologists, and 1 hematologist). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendation and whether the draft recommendation should be approved as a

practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Lung Disease Site Group (DSG) reviewed the results of the survey.

Practice Guidelines Coordinating Committee Approval Process

The practice guideline report was circulated to members of the Practice Guidelines Coordinating Committee (PGCC) for review and approval. Ten of 11 members of the PGCC returned ballots. Six PGCC members approved the practice guideline report as written; one member approved the practice guideline as written and provided suggestions for consideration by the Lung DSG; and three members approved the practice guideline report conditional on the Lung DSG addressing specific concerns. The Lung DSG responded to the PGCC concerns and the guideline was subsequently approved.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- Postoperative radiation therapy is not recommended for use following complete resection of stage II non-small cell lung cancer.
- For stage IIIA disease, no definitive recommendation can be made for the use of postoperative radiotherapy, as a survival benefit has not been demonstrated and the data for improved local control is conflicting. The decision for postoperative radiotherapy must therefore be based on an individualized case assessment.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized controlled trials and meta-analyses.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

These guideline recommendations may aid physicians in making decisions concerning use of postoperative radiotherapy in the management of patients with stage II or IIIA completely resected non-small cell lung cancer.

POTENTIAL HARMS

- There is evidence from a meta-analysis of individual patient data from nine randomized controlled trials that postoperative thoracic irradiation in patients with completely resected non-small cell lung cancer significantly reduces overall survival (mortality hazard ratio, 1.21; 95% confidence interval, 1.08 to 1.34; $p=0.001$), with an absolute difference of 7% at two years (55% versus 48%). Of the three randomized controlled trials published after the meta-analysis, two of which also included data reported in the meta-analysis, one detected a survival advantage for patients treated with surgery alone compared with surgery followed by radiotherapy ($p=0.002$ log rank) and two detected no difference between the two treatments ($p=0.56$ and $p>0.05$).
- Subset analyses on data from the meta-analysis and one randomized controlled trial suggested that the detrimental effect associated with radiotherapy was greatest for patients with stage II disease. There was no clear evidence of an adverse effect or benefit for patients with stage III disease.
- Results from the meta-analysis detected a statistically significant difference in local recurrence-free survival (time to local recurrence or death) in favour of surgery alone (hazard ratio, 1.16; 95% confidence interval, 1.05 to 1.29; $p=0.005$). Three randomized controlled trials published after the meta-analysis also examined local recurrence rate. One did not detect a difference between treatments (relative risk, 0.85; 95% confidence interval, 0.64 to 1.14, $p=0.28$ log rank) and two detected an advantage for postoperative radiotherapy (both $p<0.01$).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Most reported trials involved radiation using cobalt-60 equipment which is no longer considered optimal for treatment in the majority of lung cancer patients. There is insufficient evidence to assess the effectiveness of postoperative radiotherapy with the use of newer equipment such as linear accelerators.
- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult these guidelines is expected to use independent medical judgement in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1997 Sep 15 (revised online 2003 Aug)

GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Lung Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the [Cancer Care Ontario Web site](#).

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Lung Cancer Disease Site Group disclosed potential conflict of interest information.

GUIDELINE STATUS

This is the current release of the guideline.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Postoperative adjuvant chemotherapy and/or radiation therapy in stage II or IIIA completely resected non-small cell lung cancer. Summary. Toronto (ON): Cancer Care Ontario. Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995; 13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 5, 1999. The information was verified by the guideline developer as of February 22, 1999. This NGC summary was updated by ECRI on December 17, 2001, June 23, 2003, and most recently on January 23, 2004. The most recently updated information was verified by the guideline developer as of February 23, 2004.

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