



Complete Summary

GUIDELINE TITLE

Surgical management of malignant pleural mesothelioma: a clinical practice guideline.

BIBLIOGRAPHIC SOURCE(S)

Maziak DE, Gagliardi A, Haynes AE, Mackay JA, Evans WK, Lung Cancer Disease Site Group. Surgical management of malignant pleural mesothelioma: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2005 Aug 9. Various p. (Evidence-based series; no. 7-14-2). [43 references]

GUIDELINE STATUS

This is the current release of the guideline.

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

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SCOPE

DISEASE/CONDITION(S)

Malignant pleural mesothelioma

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology
Pulmonary Medicine
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the role of surgery (pleurectomy or extrapleural pneumonectomy) in the treatment of adults with malignant pleural mesothelioma

TARGET POPULATION

Adult patients with diffuse or localized malignant pleural mesothelioma

INTERVENTIONS AND PRACTICES CONSIDERED

1. Pleurectomy
2. Extrapleural pneumonectomy

MAJOR OUTCOMES CONSIDERED

- Operative morbidity and mortality
- Recurrence rates
- Survival rates

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

Literature Search Strategy

MEDLINE and CANCERLIT databases were searched from 1985 through July 2005, using the Medical Subject Headings "mesothelioma/surgery" and "lung neoplasms/surgery" and the keyword or text word "mesothelioma" in combination with "surgery," "pleurectomy," "decortication," "pneumonectomy," and "resection". Similar terms were used to search the Cochrane Library 2002, Issue 4 for

additional clinical trials. These terms were then combined with the search terms for the following study designs: practice guidelines, meta-analyses, systematic reviews, randomized controlled trials, and clinical trials. The search was limited to 1985 onwards because the classification and staging of pleural mesothelioma have varied tremendously over time, and it is difficult to compare data from early trials with that of trials that are more recent.

Ongoing clinical trials were identified using the Physician Data Query (PDQ) database at http://www.cancer.gov/search/clinical_trials/. Relevant articles were selected and reviewed by two reviewers, and 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 (<http://mdm.ca/cpgsnew/cpgs/index.asp>) and the National Guideline Clearinghouse (<http://www.guideline.gov>) were searched for existing evidence-based practice guidelines.

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they were:

1. Randomized controlled trials (RCTs), systematic reviews (including meta-analyses or practice guidelines), phase II trials, or prospective or retrospective cohort studies examining the role of surgical resection for malignant pleural mesothelioma
2. Trials reporting clinical or sub-clinical adverse effects on the topics mentioned above

Exclusion Criteria

1. Trials where the majority of patients were being treated for conditions other than malignant pleural mesothelioma
2. Papers published before 1985
3. Abstract publications
4. Letters and editorials describing trial results
5. Papers published in a language other than English

NUMBER OF SOURCE DOCUMENTS

18 studies (eight non-controlled prospective, of which only four were comparative, and 10 retrospective case series) involving both pleurectomy (PL) and extrapleural pneumonectomy (EPP); four studies (two retrospective case series and two including both retrospective and prospective case-series data) examining EPP only; and four prospective non-comparative studies plus eight retrospective case series studies examining PL only were identified.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

A statistical synthesis of the evidence was not conducted because no randomized trials involving surgical treatment for mesothelioma were identified and the prospective and retrospective studies included a variety of adjuvant treatments.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Program in Evidence-based Care (PEBC) reports consist of a comprehensive systematic review of the clinical evidence on a specific cancer care topic, an interpretation of and consensus agreement on that evidence by Disease Site Groups and Guideline Development Groups, the resulting clinical recommendations and an external review by Ontario clinicians in the province for whom the topic is relevant.

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 reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A draft evidence summary version of this series was reviewed by Ontario practitioners. Any changes made to the report as a result of practitioner feedback are described in the original report. Practitioner feedback was obtained through a mailed survey of 111 practitioners in Ontario (31 surgeons, 36 medical oncologists, 23 radiation oncologists, 20 respirologists, and 1 hematologist). The survey consisted of items evaluating the methods, results, and interpretive

summary. Written comments were invited. The practitioner feedback survey was mailed out on June 5, 2003. Follow up reminders were sent out at two weeks (postcard) and four weeks (complete package mailed again). The Lung Disease Site Group (DSG) reviewed the results of the survey.

The evidence summary report was circulated to members of the Practice Guidelines Coordinating Committee (PGCC) for review and approval. Eight of thirteen members of the PGCC returned ballots. Three PGCC members approved the evidence-based series report as written, and five members approved the report conditional on the Lung Disease Site Group addressing specific concerns.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Because of the lack of sufficient high-quality evidence on the surgical management of mesothelioma, the Lung Cancer Disease Site Group opinion is that:

- The role of surgery in the management of malignant pleural mesothelioma cannot be precisely defined. Specifically, the lack of randomised controlled clinical trials makes it impossible to determine whether the use of extrapleural pneumonectomy or pleurectomy improves the survival of patients with malignant pleural mesothelioma or effectively palliates the symptoms of the disease.
- In patients who undergo surgery, combined with chemotherapy and/or radiotherapy, multivariate analysis shows that longer survival is associated with small, epithelial-type, node-negative pleural mesotheliomas.
- This Evidence Summary is confined to the surgical management of malignant pleural mesothelioma. Please refer to Evidence Summary Report #7-14-1 and the Evidence-based Series #7-14-3, to be released shortly, for opinions on the use of systemic therapy and radiation therapy in this disease.
- There is a need for future studies of the role of surgery in the treatment of mesothelioma to include evaluations of quality of life.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by non-controlled prospective studies (including comparative studies), and retrospective case series.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Three prospective studies that involved both extrapleural pneumonectomy and pleurectomy, along with adjuvant chemotherapy, radiotherapy, or photodynamic therapy, directly compared the two surgical treatments. Longer survival was reported with pleurectomy in all three studies; however, caution must be exercised in interpreting those comparisons because the patients were not randomly allocated to the surgical procedure, and thus survival outcomes may have been influenced by pre-surgery patient characteristics.
- Median survival was reported in four non-controlled, non-comparative prospective studies examining pleurectomy combined with intrapleural chemotherapy (13 to 27 patients per study) and was 9 months, 11.5 months, and 18.3 months in those four studies. Three of those studies also reported two-year survival (12% to 40%) and local recurrence rates (75% to 80%) for this combined-modality approach.
- Seven non-controlled prospective and five retrospective case-series studies explored the effect of prognostic factors on survival using multivariate analyses. Of the prospective studies, three were non-comparative studies, one had comparison groups that were not of interest and three had relevant comparison groups but they assigned patients based on disease characteristics. Seven of those studies included treatment type as a potential prognostic variable; three specifically examined the type of surgery. The factors most commonly associated with longer survival included epithelial-type mesothelioma (five studies), earlier stage of disease (five studies), use of adjuvant or combined modality treatment (five studies), and good performance status (four studies). Factors adversely associated with survival included high pre-treatment platelet count (three studies), positive nodal status (two studies), larger preoperative tumour volume (two studies), and larger postoperative residual tumour volume (one study). The type of surgery did not have a significant impact on survival in any of the three studies that examined that association.
- Two prospective and two retrospective non-comparative surgical studies, three including adjuvant chemotherapy or radiotherapy, reported the palliation of signs or symptoms of malignant mesothelioma following treatment. Pleural fluid control improved in 98% of 50 patients and 96% of 54 patients; the recurrence of pleural effusion was prevented in 80% of 20 patients; dyspnea improved in 47% of 20 patients and 100% of 37 patients; and pain improved in 21% of 19 patients and 85% of 71 patients. However, none of the studies described the methods of symptom assessment in detail.

POTENTIAL HARMS

- Operative mortality for both types of surgery was reported in two non-controlled, comparative prospective studies and in two non-controlled, non-comparative prospective studies. Operative mortality ranged from 0% (two studies) to 3% (one study) following pleurectomy and from 4% to 14% following extrapleural pneumonectomy. In one study, operative morbidity was 5% following pleurectomy and 18% to 36% following extrapleural pneumonectomy; in a second study, the rates were 39% and 71%, respectively.
- Operative mortality was similar in two non-controlled, non-comparative prospective studies examining pleurectomy combined with intrapleural chemotherapy (one patient death in each study), although morbidity varied

between 8% and 44% and included hemorrhage, renal toxicity, cardiac events, air leaks, and wound infections.

QUALIFYING STATEMENTS

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Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the evidence-based series is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding their content or use or application and disclaims any 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

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ADAPTATION

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

DATE RELEASED

2005 Aug 9

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is 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

The members of the Lung Disease Site Group (DSG) disclosed potential conflicts of interest relating to the topic of this evidence-based series. No potential conflicts were declared.

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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:

- Surgical management of malignant pleural mesothelioma. Evidence-Based Series report. Toronto (ON): Cancer Care Ontario (CCO), 2005 Aug 9. Various p. (Practice guideline; no. 7-14-2: Section 1. 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 24, 2006. The information was verified by the guideline developer on February 23, 2006.

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