Surgical management of malignant pleural mesothelioma: a systematic review and evidence summary
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CRD summary
This review assessed the surgical management of patients with malignant pleural mesothelioma. The authors found that there were insufficient data to draw conclusions about different types of surgery for malignant pleural mesothelioma. Despite the limitations of this review, overall, the authors’ conclusions reflect the poor quality of the included studies.

Authors’ objectives
To assess the surgical management of patients with malignant pleural mesothelioma, with a focus on extrapleural pneumonectomy (EPP) and pleurectomy (PL).

Searching
MEDLINE, EMBASE (1985 to February 2004), Cancerlit (1985 to October 2002) and the Cochrane Library (Issue 1, 2004) were searched using the reported search terms. The reference lists of selected studies and reviews were screened. Ongoing studies were sought from a named internet source, while two further named websites were searched for existing relevant evidence-based practice guidelines. Studies were only included if they were published in full in English. The reviewers excluded studies published before 1985 to limit the problems with changes in classification, staging and treatment over the years.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), systematic reviews, phase II trials, and prospective and retrospective cohort studies were eligible for inclusion.

Specific interventions included in the review
Studies of surgical resection were eligible for inclusion. The included studies used surgery (EPP, lobectomy and PL) with and without chemotherapy and/or radiotherapy and supportive care.

Participants included in the review
Studies of patients with malignant pleural mesothelioma were eligible for inclusion. Studies were excluded if most patients had other types of cancers. Some of the primary studies included patients with unresectable disease.

Outcomes assessed in the review
Studies were included if they assessed clinical or sub-clinical adverse effects, survival, recurrence rates, prognostic factors or quality of life.

How were decisions on the relevance of primary studies made?
Two reviewers selected studies and disagreements were resolved through discussion.

Assessment of study quality
Validity was not formally assessed, but aspects of validity were discussed: study design, selection criteria, comparability of the control groups where these existed, sample size and adequacy of reporting.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.
extraction. Where reported, the extracted data included the percentage of patients with each outcome of interest, and median survival and percentage survival at 2, 3 and 5 years.

**Methods of synthesis**

How were the studies combined?
The studies were grouped by type of surgery and study design (prospective or retrospective) and combined in a narrative.

How were differences between studies investigated?
Differences between the studies were discussed in the paper. Other differences were evident from the tables.

**Results of the review**

Thirty-two studies (n at least 3,370) were included. There were 12 prospective, non-controlled studies (n=778) and 18 retrospective studies (n=2,405); the other 2 studies used a mix of retrospective and prospective data (n at least 187).

Study validity.

Only case series and non-comparative phase II studies were identified. Methodological flaws included a lack of similar concurrent comparison groups and a lack of reporting of the time period used to measure survival.

Many studies used data from before 1985 and there was the possibility of overlapping data.

Studies of both EPP and PL (17 studies, n=2,152).

Prospective, non-controlled studies (8 studies, n=688): studies used a variety of different treatments in addition to surgery. Median survival for PL and EPP was reported in 3 studies: 14.5 to 22 months after PL and 9.4 to 14.7 months after EPP. Recurrence rates were reported in 3 studies: one study found that after a median of 33.7 months, 79% survived after PL and 69% after EPP; one study found local recurrence in 35% with PL and 0% with EPP, and distant recurrence in 4% and 25%, respectively; the third study found similar recurrence after PL (67%) and EPP (60%). Operative mortality was reported in 4 studies, and ranged from 0 to 3% after PL and 4 to 14% after EPP. Post-operative complications were reported in 6 studies. The most common complications were arrhythmia in 36 to 40% with EPP and 6 to 37.5% with either EPP or PL, and bronchopleural fistulae in 18% and 43% after EPP (based on 2 studies) and 3 to 8% after either EPP or PL (based on 2 studies).

Retrospective studies (9 studies, n=1,464): the studies collected data over 9 to 36 years and provided a low level of evidence.

Studies of EPP (3 studies, n at least 192).

Two studies using a mixture of retrospective and prospective data found similar median survival after EPP with or without adjuvant chemotherapy (18 to 19 months). One of these studies reported 30-day operative mortality of 3.8%. The other study was a small retrospective case series (n=5).

Studies of PL (12 studies, n=1,026).

Prospective, non-controlled studies (4 studies, n=90): all studies used intrapleural chemotherapy and most patients also received systemic chemotherapy post-operatively. All studies were small, and three did not include a concurrent comparison group and excluded patients after enrolment. Studies reported the excision of variable amounts of tumour. In one study patients diagnosed pre-operatively were given chemotherapy, while the others were not. Median survival ranged from 9 to 18.3 months. Retrospective studies (8 studies, n=936): the studies collected data over 5 to 21 years. Six studies reported using chemotherapy and/or radiotherapy as adjunctive treatment. Median survival ranged from 10.9 to 18.1 months (based on 7 studies).
Authors' conclusions
There were insufficient data to draw conclusions about surgery for malignant pleural mesothelioma.

CRD commentary
The review addressed a clear question that was defined in terms of the participants, intervention and outcomes; the criteria for study design were broad, which seemed appropriate for this topic. Several sources were searched and attempts were made to locate unpublished studies, thus minimising the possibility of publication bias. The restriction to English language studies might have led to language bias. Methods were used to minimise errors and bias in the study selection process, but it was unclear whether similar steps were taken in the extraction of data. Validity was not formally assessed, but methodological limitations of some studies were discussed.

Adequate information on the primary studies was provided in either tables or the text. In view of the differences among studies, a narrative synthesis with studies grouped by intervention and study design was appropriate. There were limitations to this review but, overall, the authors' conclusions reflect the poor quality of the included studies.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that future research should report methods used to select patients, operative morbidity and mortality, and quality of life. They also stated that all centres should start using one system for staging patients. They further stated that RCTs should be used to assess the effects of EPP in patients with a good prognosis and to assess PL for patients with a poorer prognosis.

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