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Evidence-based Series #7-14-2: Section 1

Surgical Management of Malignant Pleural Mesothelioma: A Clinical Practice Guideline

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Question

What is the role of surgery (pleurectomy or extrapleural pneumonectomy) in the treatment of adults with malignant pleural mesothelioma?

Target Population

This evidence-based series applies to adult patients with diffuse or localized malignant pleural mesothelioma.

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

Key Evidence

- This series is based on eighteen studies involving both extrapleural pneumonectomy and pleurectomy (eight prospective and ten retrospective), four studies examining extrapleural

pneumonectomy only (two retrospective and two including both retrospective and prospective data), and twelve studies examining pleurectomy only (four prospective and eight retrospective). All but three studies also included adjuvant chemotherapy, radiotherapy or photodynamic therapy as part of the therapeutic regimen, making the assessment of the role of surgery impossible.

- Three prospective studies that involved both extrapleural pneumonectomy and pleurectomy, along with adjuvant chemotherapy, radiotherapy, or photodynamic therapy, directly compared the two surgical treatments (1-5). 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.
- Operative mortality for both types of surgery was reported in two non-controlled, comparative prospective studies (3-5) and in two non-controlled, non-comparative prospective studies (6,7). 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 (1); in a second study, the rates were 39% and 71%, respectively (6).
- 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 (8-11). Three of those studies also reported two-year survival (12% to 40%) and local recurrence rates (75% to 80%) for this combined-modality approach. Operative mortality was similar in two trials (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.
- Seven non-controlled prospective (1,2,4-7,12,13) and five retrospective case-series studies (14-18) explored the effect of prognostic factors on survival using multivariate analyses. Of the prospective studies, three were non-comparative studies (6,7,13), one had comparison groups that were not of interest (2), and three had relevant comparison groups but they assigned patients based on disease characteristics (1,4,5,12). 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 (9,19-21). 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.

Future Research

Future trials for malignant pleural mesothelioma should consist of randomized controlled trials examining extrapleural pneumonectomy for patients with good prognosis, pleurectomy for

patients with poorer prognosis, pleurodesis for patients with pleural effusions, and pleurectomy versus pleurodesis for palliation of symptoms of malignant pleural mesothelioma. Quality of life as an outcome should also be included in future surgical trials involving this disease.

Related Guidelines

- PEBC Evidence Summary #7-14-1 *Chemotherapy for Mesothelioma* (posted on the CCO Web site);
- PEBC Evidence-based Series #7-14-3 *Radiotherapy for Mesothelioma* (currently under development).

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