Mesothelioma: Live to fight another day

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Central Message

In surgery for pleural mesothelioma, less is more. Preserving the lung, diaphragm, and pericardium, when possible, facilitates recovery and survival by helping patients live to fight another day.

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Ambrogi and colleagues¹ present another retrospective, single-center, 10-year experience with pleurectomy/decortication (P/D) followed by heated intraoperative chemotherapy (HIOC) for the treatment of malignant pleural mesothelioma (MPM). The study's strengths are inclusion of a full cohort (not only patients with favorable features), comprehensive data, and long-term follow-up (median >5 years). The authors should be commended for recognizing that margins are always positive in macroscopic complete resection of MPM, systematizing their intraoperative protocol, minimizing mortality/morbidity, and assuring that all patients received adjuvant therapy.

As in many retrospective cohort studies, weaknesses are largely due to small size. Attempts at multivariable regression yield hazards ratios with little clinical relevance (eg, a hazard ratio of 1.007) and/or confidence intervals with little reliability (eg, 95% confidence interval of 0.120-0.968), suggesting overfitting of models with too many predictors and too few events. The HIOC protocol is unusual, using a lower dose of cisplatin (80 mg/m²) than what demonstrated more efficacy in cisplatin-only regimens² and a choice of a double agent (epirubicin) that has not been investigated in prospective trials for HIOC in MPM.

The study confirms increasing consensus that lung preservation, ie, P/D or extended P/D (EPD), is paramount in MPM.³ Older studies excluded patients who died perioperatively⁴ or evaluated only patients with favorable prognostic features,⁵ circumventing intention-to-treat analysis, limiting the generalizability of results, and overestimating the benefit of extrapleural pneumonectomy (EPP). More recent studies have demonstrated similar overall survival for either procedure but lower operative, short-term, and 1-year mortality with P/D compared with EPP.⁶⁻⁸ The group of Ambrogi and colleagues¹ takes it one step further and advocates leaving the pericardium and diaphragm intact in all cases. Others have shown no difference in survival between P/D and EPD but were biased by tumor

invasiveness in the EPD group.⁹ Batirel and colleagues⁸ demonstrated that leaving small amounts of MPM behind did not reduce long-term survival, and the current study supports this too.

Leaving the pericardium and diaphragm intact may yield superior results by several mechanisms. With a quicker recovery, patients tolerate much-needed adjuvant therapy better and have more reserve to undergo additional treatment when MPM recurs, as data suggest most patients recur. With less extensive surgery, MPM patients live to fight another day. The results of the current study¹ suggest a possible additional mechanism—leaving the pericardium and diaphragm intact may prevent contamination of unaffected cavities. The update by Baldini and colleagues¹⁰ on patterns of MPM recurrence after EPP demonstrated 54% of 169 patients experienced recurrence in the ipsilateral chest or mediastinum and 39% in the abdomen, whereas only 2% of patients in the current study¹ experienced recurrence in the abdomen (and 8% in the diaphragm).

The study by Ambrogi and colleagues¹ is too small to draw definitive conclusions, but the key message is the report's biggest strength—in MPM surgery, less is more. There is a point of diminishing returns, and we must measure extent of resection against the goals of preserving function/quality of life, minimizing morbidity, and reducing mortality. Although there is still debate over the actual benefit of surgery in MPM, there is consensus that the patient must live to fight another day.

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