

# Current Treatment of Mesothelioma

## Extrapleural Pneumonectomy Versus Pleurectomy/Decortication



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### KEYWORDS

• Malignant pleural mesothelioma • Extrapleural pneumonectomy • Pleurectomy decortication

### KEY POINTS

- Extrapleural pneumonectomy (EPP) entails en bloc resection of the lung, parietal and visceral pleurae, diaphragm, and pericardium.
- Pleurectomy decortication (P/D), either radical or extended, removes the parietal and visceral pleurae, including resection of the diaphragm and/or pericardium if involved, but preserves the underlying lung.
- Thorough preoperative evaluation of the patient's physiology allows for appropriate intraoperative decisions regarding EPP versus P/D.
- P/D is associated with better short-term outcomes than EPP in the form of perioperative morbidity and mortality.

### INTRODUCTION

Although controversial, the role of surgical resection in malignant pleural mesothelioma (MPM) is based on the principle of macroscopic resection of a solid tumor with adjuvant therapy to treat micrometastatic disease. Cancer-directed surgery for MPM is associated with a 5-year survival rate of 15%.<sup>1–3</sup> Two operations have been developed in this context: (1) extrapleural pneumonectomy (EPP), which involves the en bloc resection of the lung, parietal and visceral pleurae, diaphragm, and pericardium; and (2) radical or extended pleurectomy/decortication (P/D), which involves removal of the parietal and visceral pleurae, including resection of the diaphragm and/or pericardium if involved with tumor, but

always preservation of the underlying lung. Various patient-specific and even surgeon-specific or center-specific factors may influence which operation is performed. Most studies evaluating the surgical treatment of MPM have focused exclusively on either EPP or P/D, performed as part of multimodality therapy with numerous adjuvant treatments, including preoperative or postoperative chemotherapy, intracavitary chemotherapy or photodynamic therapy, preoperative or postoperative external beam radiation, and now immunologic therapy.<sup>4–9</sup> Results of single-center studies have been biased in favor of one or the other procedure and, consequently, there has been little evidence driving the decision of which operation to perform for individual patients.

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Conflict of Interest: The authors have nothing to disclose.

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## THE CASE FOR SURGERY IN TREATMENT OF MALIGNANT PLEURAL MESOTHELIOMA

Although there is no defined standard treatment for MPM, most studies in the literature support the use of curative intent surgery in the context of multimodality therapy.<sup>10–13</sup> Surgical resection is offered to more than 40% of MPM patients seen at large tertiary referral centers.<sup>14</sup> In the general population, however, fewer patients are offered cancer-directed surgery. Flores and colleagues<sup>15</sup> reported that cancer-directed surgery was performed in only 22% of 5937 patients with MPM in the Surveillance, Epidemiology and End Results (SEER) dataset between 1990 and 2004. Patients who underwent surgery experienced a median overall survival of 11 months (compared with 7 months without,  $P < .0001$ ) and cancer-directed surgery was an independent predictor of improved survival (hazard ratio, 0.68; 95% CI, 0.63–0.74). In a more recent comprehensive SEER analysis of 13,734 white and black MPM patients diagnosed between 1973 and 2009, cancer-directed surgery was predictive of longer survival.<sup>1</sup>

Left untreated, the median overall survival of patients with MPM is 7 months.<sup>11</sup> Many clinicians support treatment with surgery-based multimodality therapy for patients with favorable disease characteristics. Prognostic factors associated with longer survival are epithelial histology, female gender, and earlier stage. In 1 retrospective study of 945 patients, epithelial histology, female gender, earlier stage, lack of smoking or asbestos exposure, and left-sided disease were associated with longer survival.<sup>16</sup> Women experience longer survival compared with men, but this finding has been more consistent for younger women and those with epithelial tumors. Women under the age of 50 with early stage MPM demonstrated a median survival of greater than 30 months in a retrospective study of patients undergoing EPP for MPM.<sup>10</sup> In another SEER analysis of 14,229 MPM patients diagnosed in the United States between 1973 and 2009, female gender was a significant predictor of longer survival, independent of age, stage, race, and treatment (adjusted hazard ratio, 0.78; 95% CI, 0.75–0.82).<sup>12</sup> For men and women, higher stage disease and nonepithelial histology are associated with lesser survival.<sup>10,16</sup>

### OPTIONS FOR SURGERY

#### *Extrapleural Pneumonectomy*

Irving Sarot<sup>17</sup> first described the surgical technique of EPP in his mid-20th century case series of patients with tuberculosis treated at the Mount Sinai Hospital in New York City. Butchart and

colleagues<sup>18</sup> published the first series of EPP as treatment for patients with MPM in 1976, with a perioperative mortality rate of 31%. Butchart and associates emphasized that this technique may be indicated for certain types of tumors and, thus, adequate preoperative cardiopulmonary evaluation and careful perioperative management of patients were mandated.

In the decades that followed Butchart and co-workers' series, improvements in patient preoperative risk stratification, operative technique, anesthesia, monitoring, and early identification of complications reduced the mortality of EPP to rates less than 4%.<sup>2,19</sup> Modern series describing results of EPP for MPM report postoperative mortality of 2.2% to 7%.<sup>11,20–23</sup>

#### *Preoperative evaluation for extrapleural pneumonectomy*

Patients diagnosed with MPM who are considered for EPP are staged with PET computed tomography to evaluate for nodal or distant metastases. The level of PET avidity of the pleural tumor has been shown to correlate with survival, with greater avidity associated with lesser survival.<sup>24</sup> Enlarged and/or PET-avid mediastinal lymph nodes are evaluated with endobronchial ultrasonography or cervical mediastinoscopy. Although some centers perform routine staging mediastinoscopy in all patients, others have abandoned this because of the variable nodal drainage of the pleura with unpredictable pattern of nodal metastases and the lack of sensitivity of cervical mediastinoscopy for detecting extrapleural nodal spread in MPM.<sup>25,26</sup> Chest MRI is often performed to evaluate for diffuse chest wall, transdiaphragmatic, or transmediastinal invasion of tumor.<sup>27</sup> The presence of transdiaphragmatic extension of tumor and/or ascites warrants further evaluation with staging laparoscopy because intraabdominal tumor would preclude surgical resection.

The remaining preoperative evaluation is to determine the patient's ability to tolerate EPP.<sup>11</sup> Pulmonary function tests, including spirometry and diffusion lung capacity, should be performed. Quantitative ventilation/perfusion scan ("split function" test) is routinely done to assess perfusion to the affected lung. The product of the proportion of perfusion to the contralateral lung (which will remain after pneumonectomy) and the forced expiratory volume in 1 second is the predicted postoperative forced expiratory volume in 1 second. Although many clinicians recommend a value of at least 800 mL for pneumonectomy, the added morbidity of extrapleural, diaphragmatic, and pericardial resection have led most surgeons to consider a higher level, such as 1.2 L, for all but

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