Thoracic and Cardiovascular Surgery

Surgical Options in Malignant Pleural Mesothelioma: Extrapleural Pneumonectomy or Pleurectomy/Decortication

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Two operations have evolved for the surgical treatment of malignant pleural mesothelioma (MPM): extrapleural pneumonectomy (EPP) and pleurectomy/decortication (P/D). The goal of surgery in the multimodality treatment approach is to achieve a macroscopic complete resection, with adjuvant therapies directed at residual microscopic disease. Overall survival reported in a recent multicenter analysis of these two operations supports the use of P/D for early stage MPM provided that a complete resection is feasible; otherwise EPP will confer a survival advantage. For stage II disease, however, EPP demonstrates a possible advantage. The focus in stage III disease should remain on the ability to achieve macroscopic complete resection, rather than N2 disease. Patients with stage IV cancers have better survival if the lung is left in place.
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The role of extrapleural pneumonectomy (EPP) and pleurectomy/decortication (P/D) in the treatment of malignant pleural mesothelioma (MPM) is frequently misunderstood. EPP usually is defined as an en bloc resection of lung, pleura, pericardium, and diaphragm, whereas P/D involves resection of the parietal and visceral pleurae, pericardium, and diaphragm when necessary but spares the entire lung. These procedures are not interchangeable, and there are different factors that influence which procedure should be performed.

Most studies have exclusively included either P/D or EPP in conjunction with preoperative or postoperative chemotherapy, intrathoracic chemotherapy, postoperative external beam radiotherapy (external beam radiation therapy), intensity-modulated radiation therapy (IMRT), intraoperative radiotherapy, brachytherapy, photodynamic therapy, and a number of other novel adjuvants.[1-11] However, the decision to perform either EPP or P/D in multimodality studies has been based solely on surgical conjecture and bias rather than scientific data.

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Past studies have chosen endpoints, such as time to progression and patterns of recurrence, to justify a preferred procedure because numbers are too small to demonstrate statistically significant differences in survival.[12,13] However, these endpoints are fraught with inaccuracy because follow-up practices, definitions of progression of disease, and decisions to histologically document recurrence vary greatly and may not necessarily reflect ultimate survival. Therefore, we performed a large multicenter comparative study of 663 patients to investigate the outcome of EPP and P/D with survival as the primary endpoint.[14] The opinions expressed in this report are based primarily on the findings of this study.

Goals of Surgery

The primary goal of surgery is to remove all gross disease. This is termed an R1 resection or a macroscopic complete resection.[15] The fundamental premise is that resection of all gross disease will lead to prolonged survival. This assumption is based on findings which indicate that patients who have residual gross disease after surgery have worse survival than those who do not,[8,9] and selected patients after complete resection have prolonged survival.[3] However, a complete resection (R0) with surgery alone is theoretically unattainable owing to the inability to eradicate residual microscopic dis-

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ease (R1) regardless of whether an EPP or P/D is performed. Therefore, treatment has focused on R1 surgical resection in combination with radiation and/or chemotherapy in a multimodality setting.

The secondary goals of surgery are to obtain local control, evacuate pleural effusion, release an entrapped lung, improve ventilation/perfusion mismatch, and palliate pain from chest wall invasion. Because computed tomography and magnetic resonance imaging are notoriously inaccurate in defining the local extent of disease, surgeons are unable to decide on the most appropriate procedure until the time of thoracotomy.

Once the individual patient treatment goals are defined, functional status should determine the most appropriate procedure to perform. Prior talc pleurodesis does not preclude either EPP or P/D. The mortality of EPP and P/D ranges from 4% to 15% and 1% to 5%, respectively.[15] However, P/D is associated with less morbidity. Because there are different operative indications and clinical scenarios for each procedure, a prospective randomized trial to determine the superiority of one procedure over the other would be unreasonable. An equally absurd analogy would be to compare lobectomy to pneumonectomy in a randomized trial for lung cancer. The choice of procedure balances the morbidity and mortality of EPP or P/D based on extent of disease and the patient's functional status based on cardiopulmonary reserve.

Functional Status

Most MPM patients are in their fifth or sixth decade of life owing to the long latency period between asbestos exposure and disease development. A detailed physiological assessment is essential to ensure a safe surgical outcome. Pulmonary function testing should include a forced expiratory volume in 1 second, diffusion capacity, and, when indicated, a quantitative lung perfusion scan. Patients with postoperative predicted values of greater than 40% are considered acceptable for either EPP or P/D, whereas patients with values of less than 40% are acceptable only for P/D. Cardiac evaluation should demonstrate an ejection fraction of greater than 45% without reversible ischemia because right heart afterload is doubled after EPP. However, patients with poor cardiac function still may be candidates for P/D. Although there is a greater preference to perform a P/D in the setting of poor physiological function, this usually is performed at the expense of leaving gross tumor behind in patients with bulky disease that may otherwise be eradicated by EPP.

Intraoperative Findings

Minimal Disease

The American Joint Committee on Cancer Staging System divides the T1 descriptor into 2 categories: 1a describes a very early tumor that involves only the parietal pleura without mediastinal or diaphragmatic involvement and 1b describes an early but slightly more advanced tumor that involves all the pleural surfaces.[16] These are the best candidates for P/D but relatively few patients present with these operative findings.

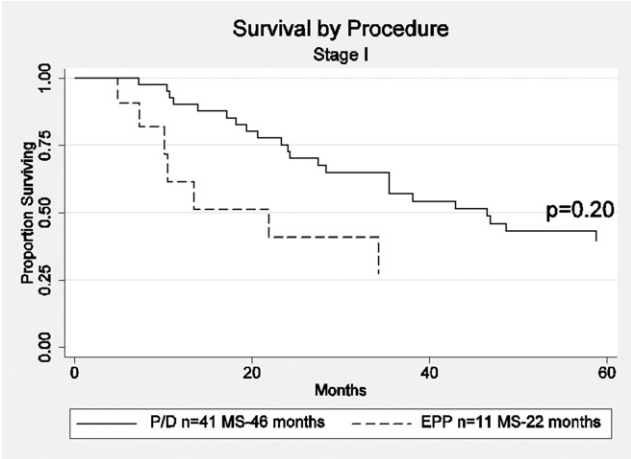

Figure 1 Kaplan-Meier survival curves of EPP and P/D for Stage I mesothelioma. (Reprinted with permission from Flores et al.[14])

The ideal operative scenario for P/D is a small amount of disease limited to the parietal pleura with only several, if any, foci of visceral pleural involvement. In this situation, after one resects the sixth rib the parietal pleura tears easily on dissection, and upon removing the pleural fluid, the surgeon finds a glistening pink visceral pleura free of disease or limited visceral pleural studding and spared fissures. P/D in this setting can be accomplished with a complete macroscopic resection.

Survival for stage I patients undergoing P/D and EPP is demonstrated in Figure 1. Factors that may influence outcome of P/D include lower mortality, lower postoperative adverse events, and greater lung capacity when relapse occurs. Proponents of P/D believe that it provides adequate cytoreduction, especially for patients with earlier stage tumors, is associated with a lower morbidity and mortality than EPP, and is an effective part of a multimodality treatment program in conjunction with therapies, such as photodynamic therapy, intrapleural and/or systemic chemotherapy, and IMRT.[4,5,7-11,17]

P/D should be performed by surgeons experienced in performing both procedures because the initial dissection is equivalent to that of an EPP. The P/D for mesothelioma is very different from the P/D for an empyema, and significant tumor can be left behind in inexperienced hands. Support for P/D also can be found in a recent study from a group that historically favored EPP. This study showed that P/D with intrathoracic chemotherapy for patients with compromised pulmonary function had surprisingly reasonable long-term survival results. However, operative mortality was 11% in this high-risk group.[5]

Bulky Disease

When the visceral and parietal pleural surfaces begin to fuse, the effusion may resolve or become loculated. This confluence of pleural surfaces designates a tumor as T2 and usually invades the underlying lung parenchyma. Typically, this

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