Extrapleural Pneumonectomy for Pleural Malignancies

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KEYWORDS

• Extrapleural pneumonectomy • Nonsmall cell lung cancer • Malignant pleural effusion
• Pleural carcinomatosis

KEY POINTS

- Extrapleural pneumonectomy (EPP) is a radical procedure involving en bloc resection of the lung with parietal and visceral pleurae, and usually ipsilateral diaphragm and pericardium.
- EPP was initially described in the treatment of refractory tuberculosis and is currently more commonly employed in the treatment of malignant pleural mesothelioma.
- Several centers have successfully performed EPP in the context of treatment of pleural dissemination of nonmesothelioma malignancies, including thymoma and nonsmall cell lung cancer (NSCLC).
- Patients with stage IV NSCLC caused by malignant pleural effusion without mediastinal nodal or distant metastases may be considered for EPP following induction chemotherapy.

INTRODUCTION

Extrapleural pneumonectomy (EPP) is a radical procedure involving resection of the lung, visceral and parietal pleura, and, generally, the ipsilateral diaphragm and pericardium, with reconstruction of the latter two. Historically, this procedure has been employed to treat infection (tuberculosis) and diffuse malignant pleural mesothelioma. EPP may also have a role in select cases in the treatment of pleural dissemination of nonmesothelioma malignancies, such as nonsmall cell lung cancer (NSCLC), thymoma, and other tumors.

HISTORY

Irving Sarot was the first to describe the technique of EPP in the mid-20th century, as performed at the Mount Sinai Hospital in New York City.[1] He reported individual cases and results for 23 patients whose tuberculous infection of the chest was either not amenable to or had failed other treatments, such as thoracoplasty or collapse therapy. Sarot concluded that the extrapleural dissection "extend (ed) the range of excisional surgeries," enabling safe resection even in the case of empyema and total pleural symphysis. In 1976, Butchart and colleagues[2] at the University of New Castle were the first to report employing EPP to treat patients with malignant pleural mesothelioma. Operative mortality in Butchart's series was 31% and considered prohibitive, leading many physicians to question the role of EPP in treating patients with pleural mesothelioma. Nevertheless, Butchart concluded that if the complication and perioperative death rates could be reduced, the procedure could be indicated for certain types of disease. He emphasized that appropriate preoperative cardiopulmonary evaluation and careful intra- and

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postoperative management were critical to reducing operative morbidity and mortality for EPP.

In the two decades that followed Butchart's series, improvements in preoperative patient selection, intraoperative technique and anesthesia, and postoperative recognition and management of complications[3] reduced the mortality of EPP to rates under 4%.[4] Modern series describing results of EPP in pleural mesothelioma patients report postoperative mortality of 2.2% to 7%.[5–9] Currently, EPP and the lung-sparing alternative, extended pleurectomy/decortication, are considered by many to have a critical role in the multimodality treatment of malignant pleural mesothelioma.[10]

PLEURAL DISSEMINATION OF MALIGNANCY

Whereas malignant pleural mesothelioma represents a primary tumor of the pleura, many malignancies, including lung, colon, breast, thymoma, sarcoma, and others, metastasize to the pleura. Reduced mortality and morbidity of the modern EPP technique have led surgeons to explore the role of this procedure in the management of pleural dissemination of other tumors (**Table 1**). Flores and colleagues[11] reported a small series of 4 pediatric patients who underwent EPP, only 1 of whom had pleural mesothelioma.

Thymoma

Thymoma in particular has a tendency toward pleural spread, and several groups have described their experience with extended resection, including EPP, for locally advanced disease.[12] Wright described the Massachusetts General Hospital experience with 5 patients who underwent EPP for stage IVa thymoma.[13] There were no postoperative deaths and one major complication (tamponade requiring removal of the pericardial patch); 5-year survival was 53% (95% confidence interval [CI] 25%–75%). In another retrospective study, Huang and colleagues[14] reported Memorial Sloan-Kettering Cancer Center's series of 18 patients undergoing extended resection for stage IVa thymoma following induction chemotherapy, including 4 patients who underwent EPP and adjuvant radiation. There were no postoperative deaths, and 5-year survival for the group (including other types of extended resection) was 78%. Ishikawa and colleagues[15] at the Tochigi Cancer Center published another report of 11 patients undergoing similar extended resection for stage IVa or IVb thymoma, with 4 patients undergoing EPP. There were no postoperative deaths, and 5-year survival was 75%.

Sarcoma

Pleural dissemination of sarcoma is difficult to treat in general and with surgery in particular. There are only rare reports in the literature describing EPP for sarcoma. In a two-patient series (1 chondrosarcoma and 1 hemangiopericytoma), 1 patient died of disease 2 years after EPP, and the other was alive 4.5 years after EPP (and 1 year following limited chest wall resection for recurrence).[16] In a more comprehensive series of patients undergoing EPP for pleural dissemination of various malignancies, Sugarbaker and colleagues[17] reported that 10 patients with sarcoma experienced a median survival of 3.7 months. Although we offer EPP in selected healthy sarcoma patients with limited or no alternative therapeutic options, we are less enthusiastic about performing EPP for this disease.

PLEURAL DISSEMINATION OF NONSMALL CELL LUNG CANCER

Nonsmall Cell Lung Cancer Staging

Like other malignancies, NSCLC may metastasize to the pleura, resulting in malignant pleural effusion. The TNM NSCLC staging system in the Sixth Edition of the American Joint Committee on Cancer (AJCC) described malignant pleural effusion without other metastases as T4M0 or stage IIIb NSCLC,[18] with many clinicians referring to this as "wet IIIb" lung cancer to distinguish it from stage IIIb patients with contralateral mediastinal or supraclavicular nodal disease. In the Seventh edition, however, malignant pleural effusion was upstaged to M1 (M1a in contrast to M1b, which represents distant metastases) or stage IV NSCLC.[19] The International Association for the Study of Lung Cancer (IASLC) Staging Committee based this change on data suggesting the survival of patients with malignant pleural effusion was similar to that of patients with distant metastases and significantly worse than that of patients with other types of T4 tumors. Five-year survival for the 471 patients with malignant pleural effusion in the IASLC database was 2%, compared with 14% in the 418 patients with other types of T4 tumors ($P<.0001$).[20]

Mediastinal Nodal Disease

The status of the mediastinal nodes markedly affects prognosis for patients with stage IV NSCLC caused by pleural dissemination. This is supported by analysis of the IASLC data, although the staging committee did not specifically compare patients with and without nodal disease. Five-year survival for the 87 N0 patients with pleural dissemination