

Pleuropneumonectomy: An Effective Treatment Modality for Malignant Pleural Mesothelioma?

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Preface

In Japan, asbestos was finally treated as a social issue in 2006, and a pleuropneumonectomy has been recently recognized as one of the effective treatments for malignant pleural mesothelioma.

A pleuropneumonectomy for this disease was first performed by Wörn in 1974,¹⁾ followed by other reports made by Butchart et al.,²⁾ Rusch et al.,³⁾ and Sugarbaker et al.⁴⁾ These reports include many problems, such as 1 surgical indications based on the clinical staging system, surgical techniques, and pre- and postoperative adjuvant therapy.

In this report, I review the results of a conventional pleuropneumonectomy and clarify the role of this aggressive approach in the multidisciplinary treatment of this disease.

1. Operative Method

Various textbooks have described the surgical techniques of a radical pleuropneumonectomy for the treatment of this disease,^{2,5,6)} but controversy still remains. The operation begins with a skin incision along the posterolateral side of the chest, and the blunt dissection is then started over the layer of endothoracic fascia beneath the bed of the 5th rib. The tumor that diffusely spread over the pleura hardly invaded beyond this elastic fascia, and a blunt dissection by the finger from the chest wall is easy to perform. On the other hand, when a small tumor extends to the parietal pleura in the early stage, we must dissect it carefully because it is impossible to perform an en block dissection of the parietal pleura, which has hard nodules among the soft normal pleura. There are various ranges for the excision line on the pericardium and the diaphragm.

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On the pericardium, which has three layers, it is possible to dissect the fibrous pericardium while leaving the endopericardium, but a complete resection of all layers of the pericardium is the basic approach used to make a radical resection. On the diaphragm, a superficial resection of the muscles is possible except for the tendon part which is composed of thick fibrous tissues. The resection of the diaphragm tends to be incomplete at the posterior part of the chest, which is the deepest and narrowest area of the pleural cavity. We therefore must make a wider operative field by extending the skin incision to the front of the chest, while cutting the anterior part of a few ribs. Rusch reported a second skin incision above the 10th intercostal space in order to resect the diaphragm⁵⁾; however, this method was not found to be very effective.

It is important to resect the chest wall around the drainage tube area because the tumor may spread along the tunnel of the tube. During the operation, we should keep in mind the need to perform an en block resection; otherwise the tumor cells may spread outside of the pleural cavity through the broken parietal pleura, pericardium, or diaphragm. To control the remnant tumor cells in the chest cavity, intrapleural chemotherapy,⁷⁾ photodynamic therapy,⁸⁾ and the hyperthermia⁹⁾ have previously been performed, but these trials have not yet been clearly proven to be effective in obtaining local control of this disease.

2. Results and Prognosis

The surgical results may improve as a result of recent advances in medical technology. However, the postoperative survival periods of a pleuropneumonectomy have been shown to be nearly the same during the past 40 years, i.e., the 2-year survival rates and the 5-year survival rates were as follows: Wörn (1974)¹⁾, 37% and 10%; Butchart et al. (1976),²⁾ 10% and 3%; Sugarbaker et al. (1999),⁴⁾ 38% and 15%; and Takagi et al. (2001)¹⁰⁾, 29.7% and 9.1% (Table 1). Sugarbaker et al.⁴⁾ reported that good results came from one epithelial-type case, which showed a negative cut margin and a negative finding for lymph node metastasis. Accurate indications are therefore necessary

Table 1. Results of a pleuropneumonectomy

Investigators	Year	No. of patients	Operative mortality (%)	2-year survival (%)	5-year survival (%)	Median survival (mo)
Wörn ¹⁾	1974	62	–	37	10	19
Butchart et al. ²⁾	1976	29	31	10	3	10
DaValle et al. ¹⁷⁾	1986	33	9	24	6	13
Allen et al. ¹⁸⁾	1994	40	8	23	10	13
Sugarbaker et al. ⁴⁾	1999	183	3.8	38	15	19
Rusch et al. ³⁾	2001	61	8	–	–	17
Takagi et al. ¹⁰⁾	2001	116	6	30	9	12

to obtain good results during a pleuropneumonectomy. The large majority of patients with malignant pleural mesothelioma died of locoregional failure despite aggressive therapy. Baldini et al.¹¹⁾ reported the patterns of postoperative failure to include ipsilateral hemithorax (35%), followed by the abdomen (26%), contralateral hemithorax (17%), and other distant sites (8%).

3. Postoperative Adjuvant Therapy

Most patients showed local recurrence in the ipsilateral hemithorax after a surgical resection,⁹⁾ and the various types of adjuvant therapy are the key to the strategy of improving patient survival by means of a pleuropneumonectomy. Sugarbaker et al.⁴⁾ reported good results with multimodality treatment combined with radiotherapy and systemic chemotherapy in 183 cases after a pleuropneumonectomy, i.e., the 2-year survival rate was 38% and the 5-year survival rate was 15%. The survival rate in this series improved to 68% at 2 years and to 46% at 5 years in the epithelial-type cases with a free resected margin. Postoperative radiation therapy for hemithorax in stages I and II is recommended, based on the findings of reports³⁾ from the Memorial Sloan-Kettering Cancer Center, which showed an 8.7% local recurrence rate and an excellent median survival period of 33.8 months.

4. Postoperative Complications

A pleuropneumonectomy is a highly invasive surgical procedure, and its mortality and morbidity rates remain high. Sugarbaker et al.¹²⁾ reported that the mortality rate was low (3.4%), but that the morbidity rate was high (60.4%) in 328 cases, even in 2/3 of the cases that demonstrated stages I and II disease. According to the progress of pleural mesothelioma, the surgical risks associated with this procedure are considered to be high, and the number of postoperative complications are also expected to in-

crease. Stewart et al.¹³⁾ reported the risk factors of complications to be induction chemotherapy, right-sided procedures, and prolonged operations.

The causes of death are respiratory failure, myocardial failure, and pulmonary embolus.¹⁴⁾

Conclusions

The answer to the question in the title of this paper is “Yes,” but the main purpose of performing a pleuropneumonectomy for the treatment of malignant pleural mesothelioma is to obtain a macroscopic radical resection instead of only a palliative resection.¹⁵⁾ The results of this operation alone are limited because of the high local recurrence rates. Furthermore, the postoperative complications will increase in the advanced stages. We therefore should discuss the indications for this procedure when treating patients with stage I and II disease according to an accurate staging system, induction therapy¹⁶⁾ for the radical resection, and postoperative chemoradiation therapy⁴⁾ to obtain good results. Further, we should pay attention to the major complications that are associated with this aggressive surgery. On the other hand, we also must elucidate the natural history of this disease to determine the effectiveness of various kinds of therapy. We believe that a precise analysis of the accumulated data from many institutes will help us to improve the results of this operation.

References

1. Wörn H. Möglichkeiten und Ergebnisse der chirurgischen Behandlung des malignen Pleuramesotheliomas. *Thoraxchir Vask Chir* 1974; **22**: 391–3.
2. Butchart EG, Ashcroft T, Barnsley WC, Holden MP. Pleuropneumonectomy in the management of diffuse malignant mesothelioma of the pleura. Experience with 29 patients. *Thorax* 1976; **31**: 15–24.
3. Rusch VW, Rosenzweig K, Venkatraman E, Leon L,

- Raben A, et al. A phase II trial of surgical resection and adjuvant high-dose hemithoracic radiation for malignant pleural mesothelioma. *J Thorac Cardiovasc Surg* 2001; **122**: 788–95.
4. Sugarbaker DJ, Flores RM, Jaklitsch MT, Richards WG, Strauss GM, et al. Resection margins, extrapleural nodal status, and cell type determine postoperative long-term survival in trimodality therapy of malignant pleural mesothelioma. Resection in 183 patients. *J Thorac Cardiovasc Surg* 1999; **117**: 54–65.
 5. Rusch VW. Mesothelioma and less common tumors. In: Pearson FG, Clement AH, Deslauriers J, et al, eds.; Thoracic Surgery, First Edition. New York: Churchill Livingstone, 1995; pp 1083–105.
 6. Michael YC, David JS. Technique of extrapleural pneumonectomy for diffuse malignant pleural mesothelioma. In: Shields TW, ed.; General Thoracic Surgery, Sixth Edition. Lippincott Williams & Wilkins, 2004; pp 922–9.
 7. Rusch VW, Niedzwiecki D, Tao Y, Menendez-Botet C, Dnistrian A, et al. Intrapleural cisplatin and mitomycin for malignant mesothelioma following pleurectomy: pharmacokinetic studies. *J Clin Oncol* 1992; **10**: 1001–6.
 8. Pass HI, DeLaney TF, Tochner Z, Smith PE, Temeck BK, et al. Intrapleural photodynamic therapy: results of a phase I trial. *Ann Surg Oncol* 1994; **1**: 28–37.
 9. Ratto GB, Civalleri D, Esposito M, Spessa E, Alloisio A, et al. Pleural space perfusion with cisplatin in the multimodality treatment of malignant mesothelioma: a feasibility and pharmacokinetic study. *J Thorac Cardiovasc Surg* 1999; **117**: 759–65.
 10. Takagi K, Tsuchiya R, Watanabe Y. Surgical approach to pleural diffuse mesothelioma in Japan. *Lung Cancer* 2001; **31**: 57–65.
 11. Baldini EH, Recht A, Strauss GM, DeCamp MM Jr, Swanson SJ, et al. Patterns of failure after trimodality therapy for malignant pleural mesothelioma. *Ann Thorac Surg* 1997; **63**: 334–8.
 12. Sugarbaker DJ, Jaklitsch MT, Bueno R, Richards W, Lukanich J, et al. Prevention, early detection and management of complications after 328 consecutive extrapleural pneumonectomies. *J Thorac Cardiovasc Surg* 2004; **128**: 138–46.
 13. Stewart DJ, Martin-Ucar AE, Edwards JG, West K, Waller DA. Extra-pleural pneumonectomy for malignant pleural mesothelioma: the risks of induction chemotherapy, right-sided procedures and prolonged operations. *Eur J Cardiothorac Surg* 2005; **27**: 373–8.
 14. Pass HI, Pogrebniak HW. Malignant pleural mesothelioma. *Curr Probl Surg* 1993; **30**: 921–1012.
 15. Sugarbaker DJ. Macroscopic complete resection: the goal of primary surgery in multimodality therapy for pleural mesothelioma. *J Thorac Oncol* 2006; **1**: 175–6.
 16. Opitz I, Kestenholz P, Lardinois D, Muller M, Rousson V, et al. Incidence and management of complications after neoadjuvant chemotherapy followed by extrapleural pneumonectomy for malignant pleural mesothelioma. *Eur J Cardiothorac Surg* 2006; **29**: 579–84.
 17. DaValle MJ, Faber LP, Kittle CF, Jensik RJ. Extrapleural pneumonectomy for diffuse malignant mesothelioma. *Ann Thorac Surg* 1986; **42**: 612–8.
 18. Allen KB, Faber LP, Warren WH. Allen KB, Faber LP, Warren WH. *Chest Surg Clin N Am* 1994; **4**: 113–126.