MÆDICA - a Journal of Clinical Medicine

ORIGINAL PAPERS

Minimally Invasive Surgical Treatment of Malignant Pleural Effusions

Adrian CIUCHE, MD[a]; Claudiu NISTOR, PhD[a]; Daniel PANTILE, MR[a]; Prof. Teodor HORVAT, PhD[b]

[a]Department of Thoracic Surgery, "Dr. Carol Davila" Central Emergency University Military Hospital Bucharest, Romania
[b]Clinic of Thoracic Surgery, "Alexandru Trestioreanu" Bucharest Oncologic Institute

I undersign, certificate that I do not have any financial or personal relationships that might bias the content of this work.

ABSTRACT

Introduction: *Usually the pleural cavity contains a small amount of liquid (approximately 10 ml). Pleural effusions appear when the liquid production rate overpasses the absorption rate with a greater amount of liquid inside the pleural cavity.*

Material and method: *Between January 1998 to December 2008 we conducted a study in order to establish the adequate surgical treatment for MPEs. Effective control of a recurrent malignant pleural effusion can greatly improve the quality of life of the cancer patient. The present review collects and examines the clinical results of minimally invasive techniques designed to treat this problem.*

Results and discussion: *Patients with MPEs were studied according to several criteria. In our study we observed the superiority of intraoperative talc poudrage, probably due to a more uniform distribution of talc particles over the pleural surface. Minimal pleurotomy with thoracic drainage and instillation of a talc suspension is also a safe and effective technique and should be employed when there are contraindications for the thoracoscopic minimally invasive procedure.*

Conclusions: *On the basis of comparisons involving effectiveness, morbidity, and convenience, we recommend the thoracoscopic insufflations of talc as a fine powder with pleural drainage as the procedure of choice.*

Keywords: malignant pleural effusions, thoracoscopic minimally invasive treatment

Address for correspondence:
Adrian Ciuche, Department of Thoracic Surgery, "Dr. Carol Davila" Central Emergency University Military Hospital, Calea Plevnei, Sector 1, Bucuresti, Romania. Tel.: +40 21 319 30 51; Fax: +40 21 319 30 30
e-mail: adi_ciuche@yahoo.com

INTRODUCTION

Usually the pleural cavity contains a small amount of liquid (approximately 10 ml) (1). Pleural effusions appear when the liquid production rate overpasses the absorption rate with a greater amount of liquid inside the pleural cavity.

Malignant pleural effusions (MPEs) represent common and debilitating complications of a wide array of malignancies that may be primary to the pleura or to other intra- or extrathoracic sites (2).

Moghissi states that there are two types of pleural effusions associated with neoplastic disease: Type I (real malignant pleural effusions – MPE) and Type II (paramalignant or paraneoplastic effusions) (3). The term MPE defines effusions that result from direct infiltration of the pleura by cancer cells. Effusions caused by indirect effects of cancers on the pleural space, such as obstruction of mediastinal lymph nodes, bronchial obstruction, pulmonary embolism, superior vena cava syndrome or decreased oncotic pressure, are termed paramalignant or paraneoplastic effusions (2). Type II pleural effusions are histologically characterized by the absence of neoplastic cells in pleural fluid, as well as in pleural biopsy fragments (3).

Common symptoms include dyspnea, cough and variable chest pain, which may be diffuse and severe as occurs with mesotheliomas or localized and occasionally pleuritic in nature.

A standard chest X-Ray can detect as little as 50 mL of pleural fluid as evidenced by blunting of the posterior costo-phrenic recess on the lateral views and 200 mL by obscuring the lateral recess on the postero-anterior view. Although there are many radiologic signs, standard radiographic findings, however, provide only suggestive evidence of MPE.

Chest ultrasonography can detect as little as 5 mL of pleural fluid and has a higher sensitivity when compared with standard chest X-Rays. Ultrasonographic findings are not sufficient to diagnose MPEs (2).

Contrast-enhanced chest CT has become the imaging modality of choice to detect pleural effusions and assist the differentiation between benign and malignant effusions detected by standard radiographs. Chest CT may also identify the primary neoplasm. Chest CT findings characteristic of malignant pleural disease include circumferential pleural thickening, nodular pleural thickening, parietal pleural thickening greater than 1 cm and mediastinal pleural involvement or evidence of a primary tumor (4).

Although limited experience exists with the use of PET with F-18 fluorodeoxyglucose (PET-FDG) for diagnosing malignant pleural thickening or effusions, PET-CT seems to perform well in differentiating benign from MPEs (5).

Treatment for malignant pleural effusions in based on exact knowledge of presence or absence of pleural metastases. If pleural metastases are not present the treatment is specific and addresses the primary tumor: if the primary neoplastic site is controlled, the neoplastic pleural effusion will disappear. In presence of pleural metastases large amounts of liquid can accumulate inside the pleural cavity leading to respiratory failure – non-specific treatment is required with exclusive purpose of draining the fluid in order to increase the patients' quality of life. Pleurodhesis aims to stop the accumulation of pleural fluid. This is achieved by creating fibrous adhesions inside the pleural cavity, between the parietal and visceral pleura. An important principle that has to be followed in order to achieve an effective pleurodhesis is the complete removal of the fluid inside the pleural cavity and a complete lung expansion before usage of talc (5). This creates pleural adhesions between the two flaps in contact. ❑

MATERIAL AND METHODS

Between January 1998 to December 2008 we conducted a study in order to establish the adequate surgical treatment for MPEs.

During this period of time 440 patients were diagnosed and treated for neoplastic pleural effusions. In Figure 1 and Table 1 it can be seen that malignant pleural effusions represent the second cause of pleural pathology in our series, accounting for almost one fourth of all pleural pathology, at a small gap behind pneumothorax, which is the most common pleural pathology (about 28% of pleural pathology). Pleural empyema stands for almost 16% of all the pathology addressed through thoracoscopic procedures, being the third most common pleural pathology.

Between January 1998 and December 2008 a total of 368 MPEs have been approached through minimally invasive procedures

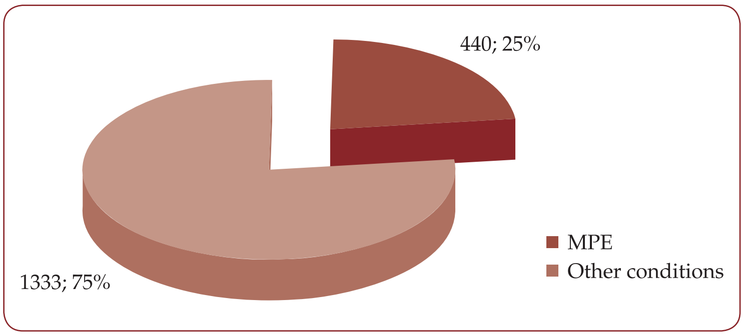


FIGURE 1. MPEs share of total cases

(363 patients underwent thoracoscopic procedures and 5 patients were subjected to VATS). The statistical analysis revealed a positive correlation between patients' age and the incidence of MPEs. Older patients, with a peak in the 6th and 7th decade, are more likely to have a malignant pleural effusion. Calculated value for Pearson correlation coefficient (r) was 0,205326, with a p-value less than 0.0001. Sex analysis showed similar prevalence on males and females, with a male:female ratio of 0.981.

Lung cancer was the most frequent known underlying condition for minimally invasive approached MPEs in our study (111 cases) (Table 2). ❑

Age decade	1	2	3	4	5	6	7	8	9	10
MPEs	0	3	0	17	49	104	113	65	16	1

TABLE 1. Comparative table of number of cases of minimally invasive addressed MPEs on decades of age

No.	Starting point	No of cases
1.	Unknown starting point	**117**
2.	Lung cancer	**111**
3.	Breast cancer	**48**
4.	Pleural mesothelioma	**41**
5.	Ovary cancer	**10**
6.	Colo-rectal cancer	**8**
7.	Mediastinal tumors	**7**
8.	Other cancers	**6**
9.	Lymphoma	**4**
10.	Renal cancer	**4**
11.	Hepatic cancer	**2**
12.	Cervical cancer	**2**
13.	Pancreas cancer	**2**
14.	Uterus cancer	**1**
15.	Malignant melanoma	**1**
16.	Larynx cancer	**1**
17.	Bladder cancer	**1**
18.	Tonsils cancer	**1**
19.	Hipopharynx cancer	**1**
	Total	**368**

TABLE 2. Hierarchy of primary cancers that generated the appearance of MPEs with minimally invasive surgical approach

STATISTICAL ANALYSIS

Patients with MPEs were then studied according to several criteria. Gender analysis showed similar prevalence on males and females, with a male:female ratio of 0.981 (Figure 2).

The statistical analysis revealed a positive correlation between patients' age and the incidence of MPEs. Older patients are more likely to have a malignant pleural effusion, while younger patients are more likely to have nonspecific inflammatory pleural effusion. Calculated value for Pearson correlation coefficient (r) was 0,205326, with a p-value less than 0.0001.

Figure 3 shows a progressive growth in minimally invasive approach (thoracoscopic and VATS) for neoplastic pleural effusions during the last years.

A comparative study between the two surgical approaches (minimally invasive versus open surgery) showed a greater prevalence of minimally invasive techniques for patients in the 6th, 7th and 8th decade and a greater prevalence of classical-surgery techniques for patients with extreme ages (very young and very old), mainly because of the more frequent use of minimal pleurotomy as single therapeutic gesture in these patients (Figure 4). Calculated value for Pearson correlation coefficient (r) was 0,183015, with a p-value less than 0.0001.

The statistical analysis performed on patients who received surgical treatment through minimally invasive techniques showed that thoracoscopy was carried mainly on older patients (with a peak in the 6th and 7th decade), while VATS was carried mainly on younger patients (with a peak in the 3rd decade). Calculated value for Pearson correlation coefficient (r) was 0,262171, with a p-value less than 0.0001.

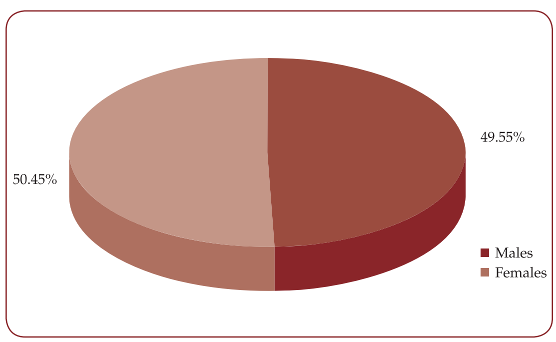
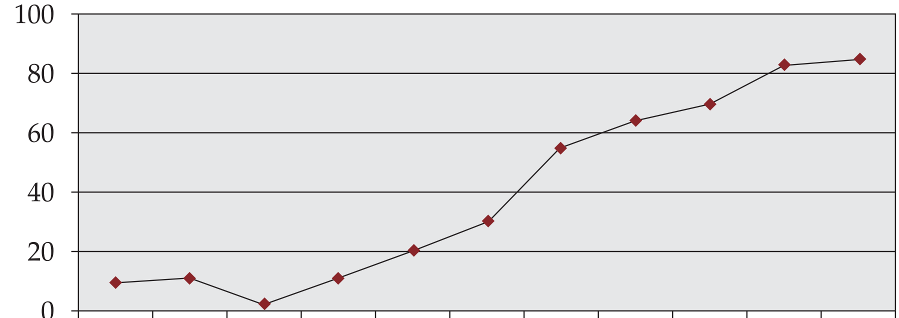
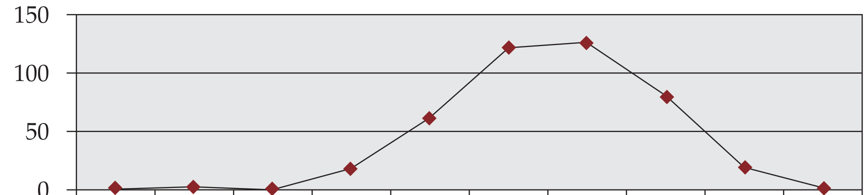


FIGURE 2. Patients' sex distribution



	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
MPE	9	11	2	11	20	30	55	64	70	83	85

FIGURE 3. Total number of MPEs during 1998-2008



Decade	1	2	3	4	5	6	7	8	9	10
MPE	1	2	3	4	5	6	7	8	9	10

FIGURE 4. MPE incidence according to age decade

We also tried to determine the most adequate surgical procedure for addressing MPEs and which is more adequate for non-malignant pleural effusions. The statistical analysis revealed that thoracoscopic procedures are more adequate for MPEs than VATS, while for non-malignant pleural effusion the more adequate procedure seems to be VATS. Calculated value for Pearson correlation coefficient (r) was 0.29798, with a p value less than 0.0001. Thoracoscopic pleurodhesis proved to have the lowest rate of pleural fluid relapse with the lowest rate of surgical complications and hospitalization. ❑

RESULTS AND DISCUSSIONS

After diagnosing an MPE through thoracentesis we keep the patient under observation for relapse of pleural fluid. If no pleural effusion relapses, the patient should be kept under further observation. If there is relapse of MPE, the patient should undergo thoracoscopic surgery, but only after establishing the assessment of his general condition, anesthetic and surgical risk. If the risks are considered too high, then minimal pleurotomy is indicated. If after either procedure complete lung expansion is obtained, then chemical pleurodhesis is recommended. If complete lung expansion is not achieved, then other therapeutical options should be considered (long-term chest catheter, pleuroperitoneal shunting, palliative repeated thoracentesis).

Intraoperative pleurodhesis is obtained through insufflation of a sclerotic agent (e.g. talc). Postoperative pleurodhesis consists of pleural instillation of a fibrotic solution through the drainage tube inserted into the pleural cavity (through minimal pleurotomy or thoracoscopic).

The agents used for pleurodhesis can be classified as cytostatic (they reduce tumor volume and as a result we have a decrease in pleural fluid) or as sclerotic agents (they reduce the pleural fluid relapse as a result of their pro-inflammatory, fibrogenetic effect with pleural space suppressing).

Bleomycin is now the most used pleural cytostatic agent, mainly because of his sclerotic effect. Ruckdeschel (6) realized a prospective study in which he compared the pleurodhesis

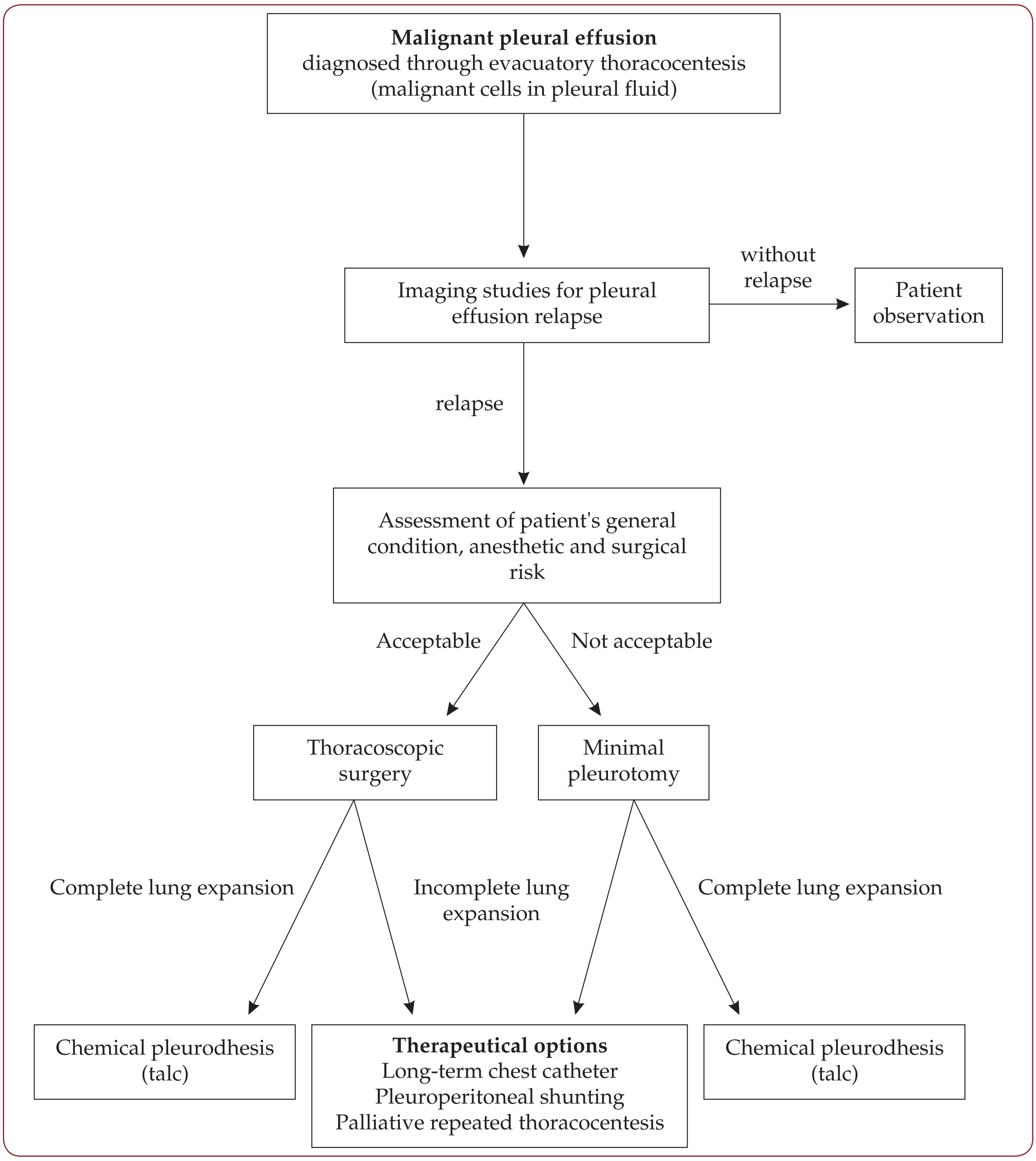


FIGURE 5. Management of malignant pleural effusions

obtained by the use of 1 gram of tetracycline with the pleurodhesis obtained by the usage of 60U of bleomycin. His study showed superior result for the use of bleomycin, regarding its sclerotic effect. He also observed that the patients on which he used bleomycin had less pleural pain after pleurodhesis. Usually well tolerated by the patients, sometimes bleomycin can have a nephrotoxic effect on patients with renal failure.

Several studies show similar efficiency (close to 90 %) in MPEs' treatment for poudrage (talc insufflations) and for drainage tube talc instillation (7).

In our study we observed the superiority of intraoperative talc poudrage, probably due to a more uniform distribution of talc particles over the pleural surface. By obtaining a fully expanded lung we avoided the risk of bacterial infection of talc powdered pleural cavities.

Thoracoscopic pleural biopsy can be performed under local or general anesthesia. It allows multiple, targeted biopsies of pleura, lung and mediastinum. Thoracoscopic pleural biopsy is indicated for relapsed MPEs, without histological diagnostic confirmation.

This diagnostic method is superior to cytological diagnosis from pleural fluid obtained through thoracentesis, with a sensibility of 80-100% (8).

Considering the results of our study, we propose the following algorithm for MPEs management (Figure 5). ❑

CONCLUSIONS

Minimally invasive surgery (Thoracoscopic surgery and VATS) is a safe and efficient method which can be used in order to diagnose and treat pleural effusions.

Minimally invasive diagnostic procedures have a specificity of 97-100%, while minimally invasive treatment procedures are efficient, with a small rate of failure.

Local anesthesia can be performed on conscious, cooperative patients, although optimal anesthesia in these cases is general anesthesia with selective intubation.

Drainage tubes can be removed quicker in thoracoscopic surgery compared to open thoracic surgery and the hospitalization time is significantly reduced.

Acute postoperative pain syndrome is significantly reduced in patients with minimally invasive approach, meaning a lower usage of analgesics.

Complications are rare (2% in literature, 2.49% in our study) and can be resolved without a mortality increase.

Lower hospitalization time, lower usage of analgesics and quicker recovery means significant reduction of hospitalization costs.

REFERENCES

1. **Sahn SA –** State of the art – the pleura. *Am Rev Respir Dis.* 1988;138:184-234.
2. **Heffner JE –** Diagnosis and management of malignant pleural effusions. *Respirology.* 2008;13:5-20.
3. **Moghissi K –** The malignant pleural effusion: tissue diagnosis and treatemnt. International Trends. In: Deslauriers J, Laquet KL. General Thoracic Surgery vol.6. St. Louis, Missouri: C. V. Mosby Company 1990: 397-408.
4. **Yilmaz U, Polat G, Sahin N, et al. –** CT in differential diagnosis of benign and malignant pleural disease. *Monaldi Arch. Chest Dis.* 2005;63:17-22.
5. **Horvat T, Ciuche A –** Pleureziile maligne. În Tratat de Chirurgie, vol IV Chirurgie Toracica, Editura Academiei Române 2008: 253-260.
6. **Ruckdeschel JC, Moores D, Lee JY, et al. –** Intrapleural therapy for malignant pleural effusions: a randomized comparison of bleomycin and tetracycline. *Chest.* 1991;100:1528-1535.
7. **Kinasewitz GT, Fishman AP –** Influence of alterations in Starling forces on visceral pleural fluid movement. *J Appl Physiol.* 1981;51:671
8. **Pepper JR –** Thoracoscopy in the diagnosis of pleural effusions and tumours. *Br J Dis Chest.* 1978;72:74.