UNIVERSITY OF MEDICINE AND PHARMACY
FROM TÂRGU-MUREŞ
DOCTORAL SCHOOL

CONTRIBUTIONS TO THE COMPLEX
MEDICO-SURGICAL TREATMENT OF
PLEURAL SPACE DISEASES

DOCTORAL THESIS

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Pleural diseases are still a problem of modern medicine, mainly due to the increasing number of patients and the results of the treatment, which are far from being good. A main characteristic of pleural diseases is the lack of randomized studies which can offer statistical arguments for a certain therapeutic approach; major pleural surgery remains reluctant to what is now called “evidence-based medicine” and is still performed on the basis of personal experience and local protocols. This Ph D thesis is based on the work and studies performed in Surgical Clinic IV University of Medicine and Pharmacy from Târgu-Mureș, Romania, which has a long tradition and some original contributions to the management of pleural disease.

PART 1 (GENERAL PART) is dedicated to the following subjects concerning the study of normal and diseased pleural space:

1.1. Embriology, anatomy and histology of the pleura
1.2. Physiology of the pleural space
1.3. Physiopathology of the pleural space – implications for surgery
1.4. Role of the cytokines in the pleural space
1.5. Paraclinic examinations in the diagnosis of pleural diseases (imagistics, thoracenthesis and examination of the pleural fluid, invasive and other explorations)
1.6. Indication for surgery and choice of the procedure in the main pleural diseases
1.7. Techniques for obliteration of the pleural cavities

Chapters 2.1 – 2.6 are focused on the aspects which are of special importance from the surgeon's point of view.

PART 2 (SPECIAL PART) is dedicated on different studies made on specific topics of pleural diseases. All the studies were made on patients treated by the same medico-surgical team in the Surgical Clinic IV University of Medicine and Pharmacy from Târgu-Mureș, Romania.

2.1. Actual problems of pleuro-pulmonary decortication is a critical study on 1204 patients who underwent decortication during 01.01.1985-31.05.2008; 93,9% of them presented with comorbidities and 56,4% required additional procedures, most of them on the lung parenchyma. The overall severe morbidity was 27,3%, resulting in a 7,1% mortality, the most important causes of postoperative exitus being the uncontrolled sepsis and the cardiac complications. Pleuro-pulmonary decortication remains the most performed major pleural procedure, with many advantages compared to the other techniques. Future developments are related to an earlier indication for surgery and performance of this procedure using less aggressive approaches, including VATS.

2.2. Thoracopleuroplasty associated with muscle transposition for pleural empyema – analysis of a personal series of 76 patients. The main aim of this association is to reduce the chest wall mutilation through a simple procedure and to improve the overall rate of success for chronic empyema. It is a personal series of 76 patients with chronic empyema with failure of less aggressive treatment and not amenable to lung decortication, in which we used a total of 148 muscle flaps (1,9/patient). The overall mortality was 6,3%, with an average ICU and postoperative hospitalisation of 3,5 and 32,7 days. Functional evaluation showed no difference between pre- and post-operative values of of VC (p=0,9299) and FEV1 (p=0,1047). Compared
with a group of 131 patients with thoracopleuroplasty without muscle transposition, the comparative study shows a lower recurrence rate (5.3% vs 9.2%, p=0.0410), no increase of morbidity (p>0.05 for all the major postoperative complications), a significant reduction of hospitalization – ICU (3.5 vs 8.3 days, p<0.0001), total (40.5 vs 75.3 days, p<0.0001) and postoperative (32.7 vs 52.3 days, p<0.0001) and a reduction in the number of the resected ribs – 5.3 vs 7.2 (p=0.0321).

2.3. Aspects of tactic and surgical technique in the use of muscle flaps in pleuro-pulmonary suppurations. Considering the controversies concerning the choice of certain flaps and the techniques of mobilization, we performed a detailed separate analysis on the use of each of the main flaps used in our group of 76 patients with thoracopleuromioplasty: serratus anterior (2.3.1.), pectoralis major and minor (2.3.2.) and latissimus dorsi (2.3.3.). Each flap has advantages and disadvantages and the techniques of mobilization used for intrathoracic transposition are quite different than those used in plastic and reconstructive surgery (including chest wall reconstruction). A comparative study on the use of different flaps / combination of flaps (2.3.4) shows no statistically significant difference in the outcome of these patients, supporting the idea that there is no “ideal” flap.

2.4. Thoracopleuroplasty and thoracopleuromioplasty in the treatment of suppurated residual cavities is a retrospective analysis of our experience with the use of space filling procedures on 44 patients with empyema after major thoracic procedures (except pneumonectomy). The overall morbidity was 61.4%, generating a mortality of 6.8%; the average ICU hospitalization was 36.3 days and the postoperative one was 36.3 days. The statistical analysis shows that the results are not influenced neither by the presence or absence of the bronchial fistula, nor by the type of the first procedure. Presence of TB (tuberculosis) appears as an important risk factor for some of the postoperative complications and for a prolonged hospitalization. The Kaplan-Meier survival curve suggest that if the patient survives the procedure, his late survival is influenced only by the other comorbidities.

2.5. Role of the thoraco-mediastinal plication in the treatment of post-pneumonectomy empyema is a retrospective analysis of 28 patients with thoraco-mediastinal plication performed for post-pneumonectomy empyema, which is considered the most severe postoperative complication in modern surgery. The overall mortality was 7.1%, with an average postoperative hospitalization of 31.3 days. Presence of the bronchial fistula does not have any impact on the postoperative course; analysis of the ventilatory functional tests showed no difference between the pre- and post-operative values of VC (p=0.9295) and FEV1 (p=0.7808). In patients with pneumonectomy for cancer, the Kaplan-Meier curve showes a median survival of 29 months, which justifies the medical and financial efforts.

2.6. Thoracopleuroplasty and muscular plombage as palliative “comfort” procedure in cases of empyema secondary to intrathoracic unresectable neoplasia is an analysis on a group of 11 patients, showing an increased rate of postoperative complications and a high mortality (18.2%), with a Kaplan-Meier median survival rate of 14 months. These results suggest a very limited role of this kind of surgery in patients with less aggressive forms of unresectable cancer, without major comorbidities and who understand and accept the risks associated with this aggressive treatment.
2.7. **Use of the muscle flaps in the treatment of postoperative empyema.** Use of the muscle flaps in patients with previous thoracotomy is a debated aspect. Based on our experience (12 patients – 25 flaps) we conclude that, although limited as volume and mobilization, their use after thoracotomy is still possible and maintains the main advantages of the method.

2.8. **Reevaluation of the Schede procedure.** Although it was the first successful procedure for empyema, the Schede procedure was almost abandoned due to some major disadvantages. Based on our experience (9 cases) we conclude that the principle of this procedure is a correct one but the indications of this procedure remain very few: hyperchronic suppurations, recurrences after other thoracoplasties or suspicion of neoplasia; modern conditions and some technical changes of the original technique (en-bloc parietectomy with the electrocautery, use of the muscle flaps and primary wound closure) allow good results.

2.9. **Pleuro-pulmonary decortication as the first stage in the solving of intra-abdominal suppurations with intrathoracic complications** is an analysis of a group of 18 patients with severe intrathoracic complications secondary to subdiaphragmatic suppurations who underwent decortication as the first stage of the treatment; this group is characterised by a high morbidity and mortality. Based on our experience, we made a change in the order of the operative steps, with the aim to reduce the operative shock and blood losses.

2.10. **Pleural lesions during urologic surgery** is an analysis of a group of 39 patients with pleural lesions occurring during urologic surgery. Most of them (37 patients) required only minor procedures – thoracentesis and tube thoracostomy; only 2 of them required thoracotomy and decortication (overinfected loculated urinothorax). The only risk factor for the development of these complications seems to be the approach used: the high and middle approach in endoscopic percutaneous surgery and the lombotomy through the bed of the 12th rib in open surgery. Most of these complications can be solved through minor procedures.

2.11. **Extrapleural hematoma – particular anatomo-clinical entity in thoracic surgery** is an analysis of a group of 8 patients admitted and treated for extrapleural hematoma in Surgical Clinic IV UMPh from Târgu-Mureș, Romania between 01.01.1985-01.01.2008. Our data show that the development of this lesion does not require a violent trauma; the diagnosis is difficult in the absence of a CT examination with i.v. contrast. Treatment requires solving of the associated lesions and careful hemostasis, which may be difficult due to the diffuse bleeding secondary to the decollation of the parietal pleura.

2.12. **Bacteriologic study on patients with pleural empyema undergoing major surgery.** Bacteriology of pleural empyema is still poorly described, which makes the choice of an antibiotic treatment a difficult problem. Our data on operated patients show the predominance of *Staphylococcus* (42,8%) and *Streptococcus* (34,5%), followed by *Pseudomonas* (21,4%), *Acinetobacter* (17,8%) and *E. coli* (14,3%); Klebsiella, *Enterobacteria* and *Enterococi* were encountered with an incidence between 5 and 10%; 44% of cultures remained sterile, the other ones having an average of 2,1 bacteria identified / patient. The antibiotic resistance showed interesting results (high antibiotic resistance in many currently used antibiotics); a careful monitorisation would allow improved local politics, with immediate clinical and economic impact.
2.13. Use of recombinant factor VII activated (rFVIIa) as hemostatic agent during major pleural surgery. We performed an analysis of a group of 53 non-hemophilia patients with major pleural surgery who received rFVIIa to control diffuse bleeding; the group includes 16 cirrhotic patients (classic contraindication for this kind of surgery). Most patients required only small doses (1.2 mg/60KUI-2.4 mg/120 KUI), which were not influenced by the type of surgical procedure. rFVIIa appears as an excellent hemostatic agent during major pleural surgery but the overall impact on morbidity and mortality requires further prospective randomised studies; the major disadvantage remains the high cost, which is in part compensated by the reduction of blood losses and avoidance of some complications.

The last 3 chapters are detailed case-reports, with particular clinical situations or procedures; all of them are dealing with rare situations, some of them being reported for the first time in our country: **pleural empyema in a stage C3 HIV/AIDS patient solved by 5 ribs thoracopleuroplasty (Botianu procedure) and muscular plombage (2.14.), eso-broncho-pleuro-cutaneous fistula with empyma necessitans and septic shock solved by 4 ribs posterior thoracopleuroplasty and open thoracic window (2.15) and embolisation of bronchial arteries associated with a complex thoracopleuro-mioplasty for solving a MDR giant cavity with bronchial fistula and massive recurrent hemoptisis (2.16).**

**ORIGINAL ASPECT OF THE THESIS**

- association of the muscle transposition with the Botianu thoracopleuroplasty (personal series):
  - some of the techniques were used for the first time in our country:
    - the serratus anterior muscle flap
    - the reversed latissimus dorsi muscle flap
  - compared with the published literature, our series contains the largest number of reversed latissimus dorsi muscle flaps used to treat empyema
  - the comparative study concerning the choice of the flap / combination of flaps for intrathoracic transposition used to treat only pleuro-pulmonary suppurations (the only study concerning only suppurated intrathoracic lesions);
  - compared to other published papers concerning the intrathoracic transposition of muscle flaps, our series has the largest proportion of TB (tuberculous) lesions (almost one half)
  - **study on the use of space-filling procedures (thoracopleuroplasty with or without muscle flaps) in special circumstances, each of them very debated in the literature:**
    - suppurated residual cavities
    - post-pneumonectomy empyema
    - as a palliative (“comfort”) procedure in cases of empyema secondary to unresectable intrathoracic neoplastic lesions
    - use of the muscle flaps in postoperative empyema (after previous thoracotomy)
    - **use of the muscle flaps associated with the Schede parietectomy** (first reported procedure in Romania), with a reevaluation of this procedure in modern conditions.
the pleuro-pulmonary decortication in cases of empyema secondary to intraabdominal suppurations with intrathoracic complications, with a change in the order of the operative steps with the aim of reducing the operative shock and the blood losses

-study of the pleural lesions occurring during urologic procedures, made from a thoracic surgeon's point of view

-study of the bacteriology of pleural empyema undergoing major surgery (types of bacteria and antibiotic resistance, with immediate clinical and economic implications)

-use of the recombinant factor VII activated (rFVIIa) in major pleural surgery (empyema + pleural tumors); on the moment when this study was started, it was the only one dedicated to the use of this new drug in this kind of surgery (“Best Poster Awards” finalist – CHEST 2005)

-thoracopleuromioplasty for a pleural empyema in an HIV/AIDS patient (national premiere).

-use of a combination of posterior thoracopleuroplasty with open thoracic window for an eso-broncho-pleuro-cutaneous fistula with empyema necessitans and septic shock

-first embolisation of bronchial arteries associated with a complex thoracopleuromioplasty for solving a MDR giant cavity with bronchial fistula and massive recurrent hemoptisis (national premiere).