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A M E R I C A N C O L L E G E O F



P H Y S I C I A N S

Treatment of Sonographically Stratified Multiloculated Thoracic Empyema by Medical Thoracoscopy*

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Introduction: In cases of empyema, some form of intervention, either chest tube drainage, thoracoscopy, video-assisted thoracic surgery (VATS), or thoracotomy, with or without pleural fibrinolysis, is required. What the best approach is and when and how to intervene is a matter of debate.

Study objective: To analyze the safety and outcome of medical thoracoscopy in the treatment of multiloculated empyema.

Methods: We report a retrospective series of 127 patients with thoracic empyema treated with medical thoracoscopy from 1989 to 2003 in three hospitals in Switzerland and Italy. All patients had multiloculated empyema as identified by chest ultrasonography. In the absence of multiloculation, or in case of fibrothorax, simple chest tube drainage or surgical VATS/thoracotomy were performed, respectively.

Results: Mean age \pm SD was 58 ± 18 years (range, 9 to 93 years). In 47%, a microbiological diagnosis was made. Complications occurred in 9% of patients (subcutaneous emphysema, $n = 3$; air leak of 3 to 7 days, $n = 9$). No mortality was observed. Forty-nine percent of patients received postinterventional intrapleural fibrinolysis. Medical thoracoscopy was primarily successful in 91% of cases. In four patients, the insertion of an additional chest tube or a second medical thoracoscopy was required. Finally, 94% of patients were cured by nonsurgical means. Six percent of patients required surgical pleurectomy, mostly through thoracotomy.

Conclusion: Multiloculated empyema as stratified by ultrasonography can safely and successfully be treated by medical thoracoscopy. (CHEST 2005; 128:3303–3309)

Key words: fibrinolysis; medical thoracoscopy; outcome; pleural disease; pleural empyema

Abbreviation: VATS = video-assisted thoracic surgery

Pleural empyema has a significant morbidity and an overall mortality of 2 to 30%.^{1–3} It is defined as a collection of pus in the pleural space and is usually classified as simple empyema without pleural loculations (category 6 according to Light⁴) and complex empyema (category 7), *ie*, multiloculated empyema.

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Drainage of pleural pus has always been regarded as the key to its successful management.⁵ A recent Cochrane review⁶ concluded that empyema requires some form of intervention such as chest tube drainage, thoracoscopy, video-assisted thoracic surgery (VATS), or thoracotomy associated or not with pleural fibrinolysis. However, it is still a matter of debate what the best approach to multiloculated empyema is, and when and how to intervene,⁷ although it is generally recommended to do an early intervention.^{8–11}

In recent years, several reports^{12,13} documented the superiority of intrapleural fibrinolysis over simple chest tube drainage. In contrast, in a large randomized saline solution-controlled trial¹⁴ in 427 patients, intrapleural streptokinase failed to improve mortality, the rate of surgery, or the length of the hospital stay among patients with pleural infection. In this trial,¹⁴ 124 of 427 patients (29%) had to be referred

for VATS or thoracotomy due to treatment failure of chest tube drainage with or without intrapleural fibrinolysis. When intrapleural fibrinolysis fails, there is the need for mechanical adhesiolysis, which can be done by VATS or thoracotomy with pleurectomy. There are many retrospective studies,^{15–21} usually including small numbers of patients, but only one small randomized controlled trial²² showing that VATS is more effective than fibrinolytics alone. However, VATS is an invasive technique requiring general anesthesia and double-lumen tube intubation.

Another way of performing mechanical adhesiolysis is via video-assisted thoracoscopy in local anesthesia and analgesia, also called *medical thoracoscopy*. It is a less invasive technique used throughout Europe since 1910^{23,24} to diagnose and treat pleural diseases including thoracic empyema.^{16,25,26} The role of medical thoracoscopy for the treatment of pleural empyema is not established as yet. The treatment choice for pleural empyema is more often guided by available resources and the philosophy of individual physicians, rather than scientific data, and varies considerably between different hospitals, regions, and countries. A more rational and evidence-based treatment strategy is needed urgently.

Could pleural ultrasonography help to stratify patients? It is an easy, accessible, inexpensive, and helpful tool to identify and quantify pleural septation early.^{27–29} With pleural ultrasonography, the pleural shadowing seen on chest radiography or contrast-enhanced thoracic CT can be further characterized. Liquid loculations can be distinguished from solid parts and septae. Also, an important feature is the evaluation of diaphragmatic motility. Immobilization of the diaphragm can be seen in heavily septated empyemas or fibrothorax. In respect to the characterization of an empyema, pleural ultrasonography clearly outperforms CT. A treatment strategy taking advantage of pleural ultrasonography could be conceived as follows: in the absence of clear septation on ultrasonography, simple chest tube drainage with fibrinolysis could become the standard treatment, whereas patients with clear septation would require a form of thoracoscopy or thoracotomy as a first-line treatment. Ultrasonography would, thus, allow stratifying treatment modalities on hospital admission, and not several hospital days later after unsuccessful first-line treatment with chest tube drainage.

The aim of the current study was to analyze the efficacy and safety of medical thoracoscopy in patients with multiloculated pleural empyema early stratified by chest ultrasonography. Furthermore, in order to appreciate the importance of the respective

treatment modalities, the incidence of pleural empyema and its treatment modalities were assessed.

MATERIALS AND METHODS

Study Design and Patients

We performed a retrospective case chart review in three departments of pulmonology (Basel, Switzerland; Brescia, Italy; and Montana, Switzerland). From 1989 to 2003, all files of patient referred for multiloculated pleural empyema and treated by medical thoracoscopy were reviewed. Empyema was defined as frank pus on thoracentesis with or without positive smear and bacteriologic culture findings, or pH < 7.2 with signs of infection. The diagnosis had to be confirmed by chest radiography, and most of the patients also underwent contrast-enhanced thoracic CT. All patients underwent chest ultrasonography to localize pleural fluid collection, to assess the echogenicity of the empyema and diaphragmatic motility. Multiloculated empyema was defined as ultrasonographic presence of multiple empyema loculations with presence of intrapleural septae (category 6 vs 7 according to Light⁴; Fig 1). Approximately one third of patients had unsuccessful chest tube drainage prior to medical thoracoscopy, proving the relevance of multiloculation and documenting the need for further intervention. Exclusion criteria were an empyema without multiple loculations on ultrasonography, or radiologic findings compatible with a general fibrothorax. The latter was considered to require surgical intervention. The patients initially received empiric antibiotic treatment according to current practice guidelines⁷ with adaptation depending on the results of the microbiological workup.

Empyema Prevalence Study

In order to estimate the relevance of medical thoracoscopy for the treatment of pleural empyema, the incidence of pneumonia and thoracic empyema between 2000 and 2003 was assessed based on a diagnosis coding system.

Thoracoscopy

Thoracoscopy was standardized as established by the European Study on Medical Video-Assisted Thoracoscopy group.³⁰ Thoracoscopy was carried out in the lateral decubitus position under local anesthesia with 1% lidocaine and analgesia using midazolam and pethidine or morphine. A 7-mm trocar was inserted under ultrasonographic guidance in the appropriate intercostal space. A 0° optical telescope was inserted and connected to a videotape camera and monitor. The pleura was carefully inspected through the thoracoscope (R. Wolf GmbH; Knittlingen, Germany) using supplemental air insufflation when necessary. With the closed biopsy forceps, step by step, fibrinous septae (Fig 1) were perforated, and fluid and fibrinopurulent material were aspirated and removed from the pleural cavity. At the end of the procedure, a drain (24 to 28F) was inserted and connected to underwater seal suction with a negative pressure suction of 20 cm H₂O for at least 2 days, until no further liquid was drained and then removed after the control chest radiograph. All patients received IV antibiotics for at least 1 week after the procedure. Treatment success was defined as survival without the need for further chest tube insertions or surgical interventions.

Pleural Fibrinolysis After Medical Thoracoscopy

In some patients, 250,000 U of streptokinase or 100,000 U of urokinase diluted in 100 mL of normal saline solution was

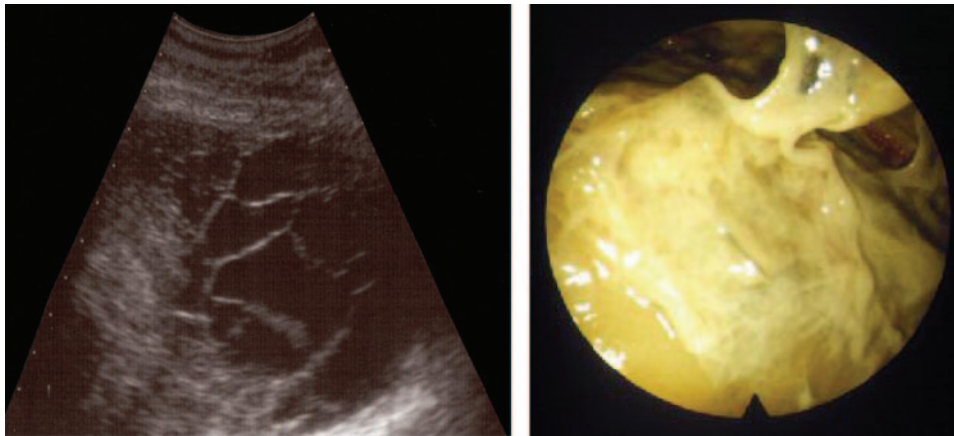


FIGURE 1. Ultrasonographic image of a multiloculated pleural empyema (*left panel*) and extensive fibrin deposition with septation and pockets of pus as seen during a medical thoracoscopy (*right panel*) in a patient with multiloculated pleural empyema (category 7 according to Light⁴). Such septae prevent a successful evacuation of pus by simple chest tube drainage.

administered into the pleural space once daily during 3 to 5 days. After rinsing with 100 mL of normal saline solution, the drain was clamped for 2 to 4 h.^{9,31,32}

Statistical Analysis

Results are expressed as median (range) or mean \pm SD as appropriate. Data were analyzed using statistical software (SPSS, version 11.5; SPSS; Chicago, IL). Comparisons are done using Mann-Whitney *U* tests for nonparametric variables and χ^2 tests for differences between proportions. Backward conditional logistic regression analysis was done to identify independent predictors of outcome after medical thoracoscopy. Age and intrapleural fibrinolysis were taken as independent variables. A conventional significance level of 5% was taken.

RESULTS

A total of 127 patients with multiloculated pleural empyema were included in the study, of whom 73% (93 of 127 patients) were male. Mean age was 58 ± 18 years (range 9 to 93 years). The etiology of multiloculated pleural empyema is given in Table 1. In 60 of 127 patients (47%), a microbiological diag-

nosis could be made (Table 2). The patients received antibiotic treatment prior to medical thoracoscopy for a median of 8 days (range, 0 to 73 days; $n = 42$). In 91% of cases, the duration of antibiotic treatment before intervention was ≤ 15 days.

All patients underwent medical thoracoscopy. Complications as a consequence of medical thoracoscopy occurred in 12 of 127 patients (9%), of whom 3 patients had subcutaneous emphysema and 9 patients had an air leak of 3 to 7 days. No in-hospital mortality was observed. Sixty-two of 127 patients (49%) received adjuvant postinterventional intrapleural fibrinolysis for 3 to 5 days.

Medical thoracoscopy was primarily successful without further intervention in 115 of 127 patients (91%; Fig 2). In four patients, the insertion of a further chest tube ($n = 2$) or a second medical thoracoscopy ($n = 2$) was required. Thus, finally, 119 of 127 patients (94%) were healed by nonsurgical means. Eight of 127 patients (6%) required

Table 1—Etiology of Multiloculated Pleural Empyema ($n = 127$)

Etiology	% (No.)
Parapneumonic	81 (103)
Chest neoplasia	9 (11)
After surgery	4 (5)
Esophagopleural fistula	2 (3)
Aspiration pneumonia	2 (2)
Chest trauma	2 (2)
Tuberculosis	1 (1)
Total	100 (127)

Table 2—Microbiological Diagnosis of Multiloculated Pleural Empyema

Germ	All Empyema, % (No.)	Identified Germs, %
Gram-positive germs, all	21 (27)	45
Streptococcus spp	16 (20)	33
Staphylococcus spp	6 (7)	12
Gram-negative germs	8 (10)	17
Mixed germs	10 (13)	22
Anaerobic germs	6 (6)	13
Fungi	1 (1)	2
Tuberculosis	1 (1)	2
No germs identified	53 (63)	
Total	100 (127)	

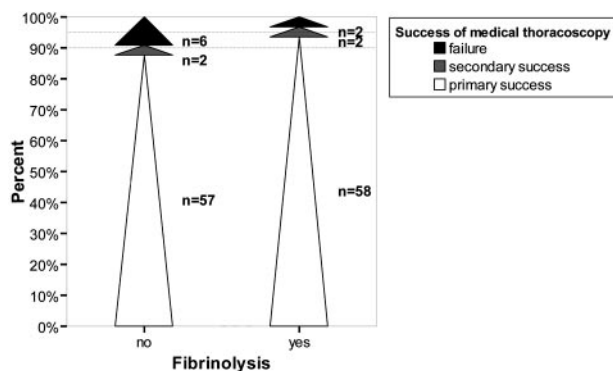


FIGURE 2. Outcome after medical thoracoscopy for empyema with and without postinterventional application of intrapleural fibrinolysis in 127 cases. Seven percent of patients not treated with intrapleural fibrinolysis vs 4% of patients who received either streptokinase or urokinase required further invasive procedures ($p = 0.16$).

surgical pleurectomy, mostly through thoracotomy. There was only a weak trend for a better outcome in patients treated with adjuvant intrapleural fibrinolysis ($p = 0.15$). In the multivariate analysis, neither intrapleural fibrinolysis, duration of disease before intervention, nor age were independent predictors of outcome after medical thoracoscopy. When comparing the microbiological etiology in patients with primary success after medical thoracoscopy ($n = 115$) and primary treatment failure ($n = 12$), the distribution of identified germs was comparable in both groups (Fig 3). How-

ever, in all but 1 patient with primary treatment failure vs 49 of 115 patients with primary success, a microbiological etiology could be identified ($\chi^2 = 10.5$, $p \leq 0.01$).

Chest tube drainage after medical thoracoscopy was maintained for a median of 7 days (range, 2 to 23 days). Time of drainage was ≤ 7 days and ≤ 14 days in 58% and 93% of cases, respectively. Antibiotic treatment was administered for a median of 10 days (range 7 to 23 days; 360 days for one patient with pleural tuberculosis) days after medical thoracoscopy.

In our prevalence study between 2000 and 2003, 3,564 patients were hospitalized for pneumonia, of whom 216 patients (6%) acquired pleural empyema (Fig 4). Of these, 32 patients (15%) with multiloculated empyema were treated with medical thoracoscopy and 23 patients (11%) were treated with surgical VATS or thoracotomy with pleurectomy; 161 of 216 patients (75%) were treated with simple chest tube drainage with or without intrapleural fibrinolysis.

DISCUSSION

Our study shows that multiloculated pleural empyema stratified by chest ultrasonography can safely and successfully be treated with medical thoracoscopy. In our 127 patients, no deaths and no chronic morbidity related to empyema were observed.

Like most of the published studies on pleural

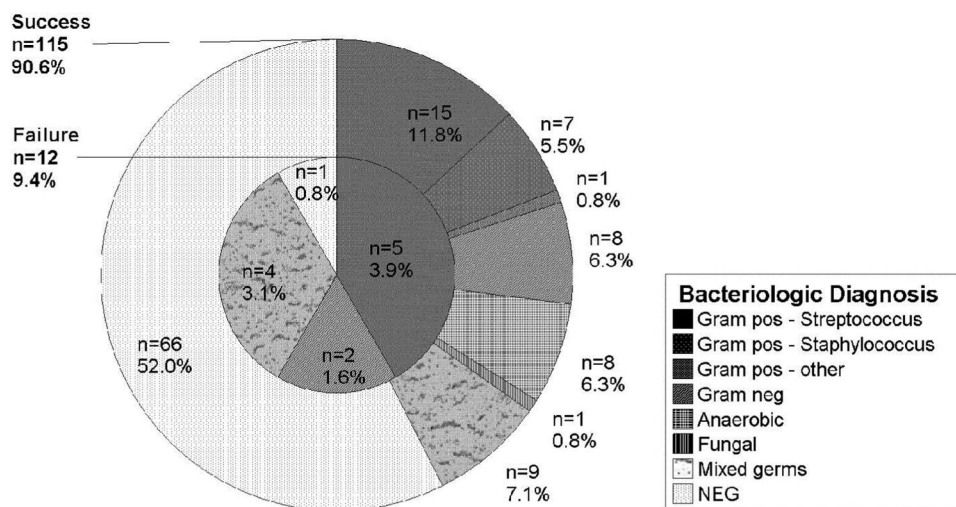


FIGURE 3. Comparison of the microbiological etiology in patients with primary success after medical thoracoscopy ($n = 115$) and primary treatment failure ($n = 12$). The distribution of identified germs was comparable in both groups. However, in 11 of 12 patients with primary treatment failure vs 49 of 115 patients with primary success, a microbiological etiology could be identified ($\chi^2 = 10.5$, $p \leq 0.01$). As higher germ loads lead to easier positive (pos) culture results, this could indicate that patients with treatment failures tend to have a higher germ load from the very beginning. Staph = staphylococcus, neg/NEG = negative.

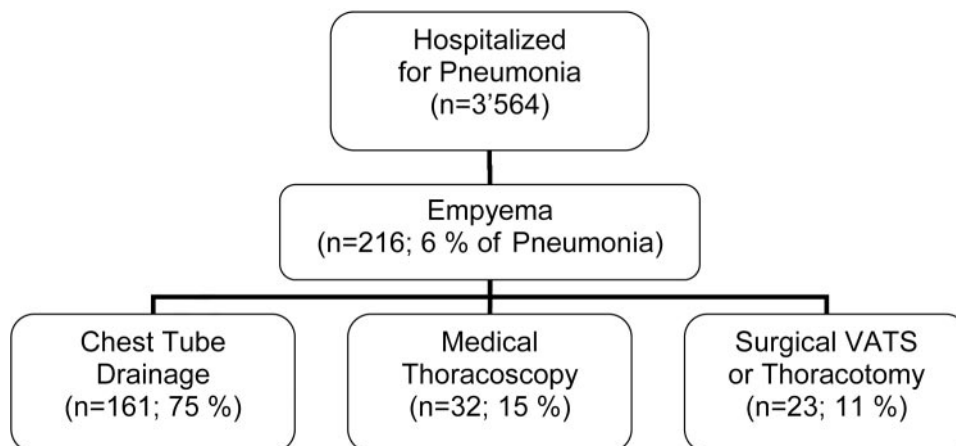


FIGURE 4. The prevalence of empyema was 6% of patients hospitalized for pneumonia. Most empyema cases were successfully treated by simple drainage. In case of multiloculated disease, either medical thoracoscopy or surgical VATS/thoracotomy with pleurectomy were performed.

empyema derived from a case series,³ patient selection and treatment biases cannot be excluded in this retrospective study. Over the study period, advances in the medical treatment of empyema were made including the development of new antibiotics. There is some temporal and methodologic heterogeneity in the therapeutic tools at disposal to treat pleural empyema in our series. However, we are confident that, although retrospective, our assessment of treatment efficacy and mortality is reliable because all original hospital charts were reviewed. We recognize that the retrospective data collection does not give a complete image of intervention-related complications, as minor complications are less likely to be recorded in case charts.³²

In Europe, medical thoracoscopy is a routine technique already used in the first half of the 20th century to treat tuberculosis by repeated adhesiolysis without complications even in patients in poor health.^{30,33} As already shown,^{16,26} medical thoracoscopy can safely be done in an endoscopic suite under spontaneous respiration in conscious analgesedation, making this procedure cheap and efficient. The technique has some limitations if full inspection of the pleural cavity or pleurectomy is necessary. In contrast to surgical VATS, medical thoracoscopy is often performed via a single port and the lung is not fully collapsed during the intervention. The procedure allows the disruption of septa very efficiently, and in most of our cases no relevant debridement was performed. The latter can be rather time-consuming when done via medical thoracoscopy. Due to the fact that there are still depots of fibrin, postinterventional

fibrinolytics after adhesiolysis might be useful. A medical thoracoscopy takes approximately 30 to 60 min.

Chest ultrasonography is a simple procedure and can be performed at the bedside. It is particularly useful to demonstrate early fibrin membranes and septations in the pleural cavity^{27,29} and to predict outcome of empyema.²⁸ In the current study, chest ultrasonography was used to show pleural loculations at an early time point and to choose the right time and modality of treatment. In the absence of clear septation on ultrasonography, simple chest tube drainage with or without fibrinolysis could be adequate, whereas patients with clear septation seem to require mechanical adhesiolysis via either form of thoracoscopy or thoracotomy as a first-line treatment. In case of massive septations, relevant pleural thickening and diaphragmatic immobilization extensive debridement via thoracotomy should be envisaged. Ultrasonography would, thus, allow stratifying treatment modalities on hospital admission, and not several hospital days later after unsuccessful first-line treatment with chest tube drainage. We are not aware of another large series systematically applying pleural ultrasonography in order to stratify patients to optimize treatment modality in case of pleural empyema. The results of our study support the usefulness of this stratification approach combined with medical thoracoscopy to early treat acute empyema in a cost-effective way, which obviates the need for general anesthesia and double-lumen tube intubation.³⁴

In contrast to smaller studies^{6,9,13,32} that concluded that intrapleural fibrinolysis may be bene-

ficial, the large UK trial¹⁴ using intrapleural streptokinase in 427 patients with empyema renewed the debate on the usefulness of intrapleural fibrinolysis. In the UK trial,¹⁴ no specific stratification was done and the failure rate was rather high. Overall, 124 of 427 patients (29%) patients had a treatment failure and required a secondary surgical intervention. Compared to this failure rate after chest tube drainage with or without intrapleural fibrinolysis of 29%, the failure rate observed after medical thoracoscopy in our study was only 9%. In addition, in approximately one third of our patients undergoing radical thoracoscopy, chest tube drainage together with intrapleural fibrinolysis failed prior to intervention. In these patients, a further intervention such as surgery, medical thoracoscopy, or minithoracoscopy³⁴ became necessary. In our case series, intrapleural fibrinolysis was used as an adjuvant therapy as soon as evidence for its efficacy was published. Adjuvant intrapleural fibrinolysis could potentially further improve the success rate of medical thoracoscopy. However, neither in the univariate nor multivariate analyses did the improvement of outcome after adjuvant intrapleural fibrinolysis reach statistical significance. Thus, no definite recommendations can be derived to date.

Thoracic empyema is not a common condition. Multicenter trials are needed to recruit the required number of patients and to improve the therapeutic approach by studying different outcomes such as duration or type of chest tube drainage, length of hospital stay, type of intervention, and timing and combination of procedures. As highlighted by a recent review,⁶ there are imminent difficulties in planning randomized trials due to inherent differences in the availability of infrastructure and preferences of teams receiving referrals.

In summary, our large series of patients with multiloculated thoracic empyema stratified by ultrasonography and treated early by medical thoracoscopy shows that this approach is safe, minimally invasive, and efficient in these patients with a disease having relevant mortality. However, prospective multicenter trials on this topic are required to make firm conclusions.

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