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Surgical Management of Pleural Space Infection

Alessandro Maraschi and Andrea Billè

Abstract

Pleural space infections are a common clinical entity affecting a large number of patients. These are associated with considerable morbidity and mortality rate and they require significant healthcare resources. In this chapter, we discuss the disease characteristics with regards to the etiology (primary and secondary), clinical presentation, radiological findings, different stages of the condition and treatment options according to stage at presentation. Conservative management (medical treatment, pleural drainage, with or without intrapleural fibrinolytic) may be effective in management of simple pleural space infections, but surgical management may be required in loculated complex empyema to prevent acute sepsis, deterioration and trapped lung. Surgical treatment of complicated pleural infections either by VATS or thoracotomy will be discussed in order to understand when to perform debridement/decortication of the pleural cavity or less frequently a thoracostomy.

Keywords: Pleura, Empyema thoracic, Pneumoniae, Thoracoscopic debridement, Decortication

1. Introduction

Pleural infections are a frequent clinical entity which affect a large number of patients. The annual incidence in the UK and USA combined is up to 80,000 cases. The overall incidence worldwide is increasing both in the adult and pediatric population [1].

Infection of the pleural space remains a serious condition which continues to be associated with high morbidity and mortality rate. The outcome is poor and it is reported to have one-year mortality of 20%, which rises up to 30% in the elderly population. Approximately 20% of patients with pleural space infection will require surgical treatment due to a failure in the conservative management [2, 3].

Pleural infections consist in a continuum spectrum of evolving disease through 3 different stages, starting from an uncomplicated pleural effusion to a complicated effusion and eventually established empyema.

The diagnosis can be obtained with a detailed anamnesis, biochemical analysis and radiological test, such as ultrasound or computed tomography.

The treatment choice is based on patient condition and disease stage at presentation. The treatment can be either conservative or surgical.

2. Pleural space infection - etiopathogenesis

Pneumoniae is an infectious process resulting from invasion and proliferation of microorganisms which elude the host defenses within the lung parenchyma and cause the production of intra-alveolar exudates. Pneumonia may cause the development of parapneumonic effusion followed by an empyema. A parapneumonic effusion occurs in 35–40% of hospitalized cases of pneumoniae, empyema only develops in 20% of these.

The pleural space infection and the subsequent empyema can be classified as primary or secondary:

- Primary pleural infection/empyema is defined as a complication of intrinsic infection of the lung. Most commonly, an empyema develops as a complication of bacterial pneumoniae.
- Secondary pleural infection/empyema occurs as a complication of invasive procedure to the chest: lung surgery, thoracocentesis, chest drain insertion, penetrating chest trauma. Other causes are esophageal rupture, mediastinal infection, sub diaphragmatic or paravertebral abscess. Bronchopleural fistula can also lead to an empyema.

Patients with risk factors have an increased risk of developing a pleural infection. The most common risk factors are:

- Diabetes mellitus
- Immunosuppression (including corticosteroid use)
- Gastro-esophageal reflux
- Alcohol misuse
- Intravenous drug abuse
- Poor oral hygiene (correlates with anaerobic infection)
- History of aspiration (correlates with anaerobic infection)
- Pediatric and elderly population
- Impaired conscious level (risk of aspiration)

Other risk factors for the development of lung infection and therefore, to the development of pleural infection, are: underlying lung disease (COPD, emphysema, interstitial lung disease, deficiency/aberrant alveolar surfactant), tracheal intubation and antibiotic treatment.

Pediatric and elderly population patients affected by chronic diseases are more susceptible to developing lung infection.

Smokers are also included in the high-risk category due to the impact of the smoke on the airway defense mechanism in clearing secretions (thick secretions and impaired ciliary motility) and increased susceptibility.

Patients in the community and patients hospitalized present different risk factors. Impaired conscious levels and higher risk of aspiration is far more common in hospitalized patients, which explains the higher rate of gram-negative gut bacteria.

These present relatively later in the infection with pneumonitis involving the superior segment of a lower lobe or posterior segment or an upper lobe.

The evolution from the simple pleural effusion to the complicated empyema usually occurs following three well defined stages.

1. Exudative stage (uncomplicated or simple parapneumonic effusion)

This first stage of the disease is characterized by a simple pleural effusion with clear, free-floating fluid and usually too small to be sampled within the pleural cavity. The fluid is exudative, therefore, following the Light's Criteria:

- Ratio of pleural fluid to serum protein is greater than 0.5.
- Ratio of pleural fluid to serum LDH greater than 0.6.
- Pleural fluid LDH value is greater than two-thirds of the upper limit of the normal serum value.

The fluid is a neutrophil-rich effusion and is the result of an increased pulmonary permeability in response to the inflammation associated with the infection.

The balance between production and reabsorption of the pleural fluid is impaired due to the inflammatory process, which causes increased vascular permeability and neutrophil chemotaxis.

The fluid is sterile and the glucose and pH level are maintained within the physiological range. No microorganisms are seen in Gram stain culture.

This stage occurs between 2 and 5 days from the onset of the pneumonia.

2. Fibrinopurulent stage (complicated parapneumonic effusion)

This stage is characterized by the colonization of the microorganisms of the pleural fluid. The fibrin deposition causes loculation and pleural thickening, activation of the coagulation cascade and downregulation of fibrinolytic pathways. This process can create a uni-loculated or multi-loculated collection consistent in a separate pocket of infected viscous fluid within the pleural space. Bacterial invasion is often present, but Gram stain culture of the fluid may remain sterile due to the rapid bacterial clearance from the pleural space. The fluid is characterized by pH < 7.2, LDH > 1,000 U/L and a decreased glucose level (< 60 mg/dL). Bacterial infection increases the immune response, attracting more neutrophils which by killing the microorganisms increases the CO₂ and lactate levels in the effusion, producing a self-maintaining process.

This stage occurs approximately 5–10 days after the pneumonia onset.

3. Organizing stage (pleural empyema)

In the final stage the pleural fluid begins to organize. Thick and viscous pus created by fibroblast chemotaxis, accumulates within the pleural space and creates a thick fibrinous rind (fibrous peel) covering the lung surface encasing the organ and preventing the re-expansion (trapped lung). The trapped lung causes decreased ventilation leading to a perfusion-ventilation mismatch, which causes a restrictive syndrome. Microorganisms are normally present in the pus and the disease at this stage is non-reversible.

Findings in analysis of pleural fluid include a pH < 7.2, glucose < 50 mg/dL, LDH > 1,000 IU/L.

Even after eradication of the infection a functional impairment will persist. This stage occurs after 2–3 weeks from the onset of the disease.

3. Microbiology

Numerous microorganisms may be involved in pleural space infections. The incidence of these pathogens varies widely according to several factors including the source of infection (haematogenous diffusion, following invasive procedure in the chest cavity, such as, thoracic surgery procedures), community or hospital acquired infections, geographic location and age group.

Parapneumonic pleural infections secondary to community acquired pneumonia (CAP) tend to be caused by the same organisms responsible for the pneumonia. CAP is defined as a low respiratory tract infection (LRTI) in a patient who has not been hospitalized in the previous 14 days from the diagnosis. This can be classified as typical and atypical.

Although a causative organism is not always isolated, the most common pathogens responsible for typical CAP, accounting for 85% of cases are:

- *Streptococcus pneumoniae* (commonest)
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Pseudomonas aeruginosa*
- *Klebsiella pneumoniae*

Atypical CAP is most commonly caused by:

- *Legionella* species
- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Coxiella burnetii*
- *Chlamydia psittaci*
- *Francisella tularensis*

Hospital-acquired pneumoniae (HAP) is defined as a LRTI with the onset 48–72 hours after admission to hospital. In the context of hospital acquired infections (HAP) the most common species of bacteria isolated are:

- *Pseudomonas aeruginosa*
- *Escherichia coli*
- *Klebsiella pneumoniae*

- Staphylococcus aureus and methicillin-resistant S. aureus (MRSA)
- Streptococcus pneumoniae
- Haemophilus influenzae

Parapneumonic pleural infections that result from aspiration are often caused by several pathogens (polymicrobial) mainly including oral streptococci (*S. anginosus*, *S. intermedius*, *S. constellatus*) and anaerobes, which colonize the oropharynx.

Staphylococcus aureus methicillin-resistant is present in 25.8% of the CAP infections and 68.8% in HAP infections [4, 5].

The prevalence of the pathogens is also related to the selected patients. For instance, patients affected by diabetes mellitus have increased risk of empyema secondary to *Klebsiella pneumoniae* [6].

Mycobacterial infections are far less common than bacterial infections. Tuberculous pleural effusion must always be investigated in areas where tuberculosis is endemic and in patients who have risk factors for TB. Tuberculous pleural effusion is the second most common form of extrapulmonary tuberculosis (after lymphatic involvement). Tuberculous empyema needs to be differentiated from tuberculous pleurisy. In the former, the mycobacterium can be found by stain or culture in the effusion, while in the latter, a lymphocytic effusion is caused by the immunologic response to proteins released by the mycobacterium and TB organisms, which are scarce in the effusion.

This can occur as reactivation disease or primary tuberculosis whereas in children represents mostly a primary disease and in adults occur mainly due to a reactivation process [7, 8].

4. Presentation

As previously discussed most cases of parapneumonic effusion and empyema follow a previous case of pneumonia, with typical symptoms including productive cough, pleuritic chest pain, dyspnoea and fever.

The presentation may be insidious, with non-specific and delayed symptoms, especially when related to anaerobic infections. Some patients can present with loss of appetite and weight loss over a period of a few weeks to several months. Aerobic infections usually present with more acute onset.

The persistence of fever for more than 3 days following the initiation of adequate antibiotic treatment may indicate progression to pleural involvement and a necessity of more aggressive management.

Patients with empyema present with persistent fever and malaise for several days compared with those with pneumoniae alone or pneumoniae with simple parapneumonic effusion.

On physical examination decreased fremitus, dullness on percussion and decreased breath sounds related to the presence of pleural effusion are representative signs of pleural effusion. In case of overt empyema patients present with fever, tachypnoea and tachycardia, in combination with the above described findings of a pleural effusion.

Laboratory blood tests are nonspecific for parapneumonic pleural effusion and these usually are the common findings in an infection, such as, leukocytosis and elevated C-reactive protein.

The main markers for the diagnosis are pH, LDH and glucose in the pleural effusion, along with the symptoms and clinical presentation. The normal pleural fluid is

clear with pH ranges between 7.60 and 7.64. It contains a similar amount of glucose to that of plasma, LDH < 50% of plasmatic concentration, white blood cells <1,000/mm³ and scarce amount of protein (less than 2%, 1–2 g/dL).

However, since these are non-specific and require invasive test to be analyzed, numerous studies have investigated different biomarkers, inflammatory cytokines and enzymes to enhance and expedite the diagnostic process of empyema. These have not proven any diagnostic advancement compared to the traditional analysis [9–13].

A recent study by Wu et al. assesses the performance of four proteins (BPI, NGAL, AZU1 and calprotectin) in the diagnosis of complicated parapneumonic effusions. This study highlighted the superiority of BPI (bactericidal permeability-increasing protein) compared to LDH, glucose and pH in the diagnosis of complicated parapneumonic effusion [14].

5. Radiological findings of parapneumonic effusion and empyema

Chest radiography, ultrasonography (US) and computed tomography are paramount in the diagnosis and management of parapneumonic effusion and empyema, as well as, in their post-treatment and post-operative monitoring.

All patients diagnosed with pneumoniae should undergo new imaging considering the chest radiography as the first step in the diagnosis process to show presence of pleural effusion.

CT is generally performed when loculations are demonstrated or suspected at the US and also, when a surgical procedure is planned.

Magnetic Resonance Imaging (MRI) and positron emission tomographic scanning are not useful and they do not usually have a role in the diagnostic and management process of pleural effusions.

Occasionally, if esophageal perforation or intra-abdominal processes, such as, liver abscesses are suspected, contrast imaging may be required. Specifically, to identify an esophageal perforation: fluoroscopy with a low-osmolar water-soluble agent like barium for esophageal perforation; CT scan with water-soluble oral contrast administered 20 minutes before scanning to demonstrate extraluminal contrast leak and intravenous contrast to delineate the esophageal wall.

5.1 Chest radiography

Uncomplicated parapneumonic effusions are characterized by:

- Pulmonary consolidations or infiltrates
- Free pleural fluid which is characterized by:
- Blunt costophrenic angle. This indicates an amount of pleural fluid greater than 200 ml
- Dense linear shadow layering between the lung and the chest wall

Free-flowing fluid collects in the dependent areas of the chest cavity. To measure with good approximation the amount of fluid in the chest cavity with a radiography, the following details can be noted:

- In an upright standing patient in posteroanterior projection blunting of the costophrenic angle indicates an amount of fluid greater than 175 ml
- In a lateral chest radiograph blunting of the posterior costophrenic angle indicates amount of fluid greater than 75 ml
- Large effusions may obscure the diaphragm (> 500 ml) and demonstrate a meniscus sign

A pleural fluid depth ≥ 10 mm from the chest wall on the chest X-ray suggests sufficient fluid is present to perform diagnostic pleural aspiration.

Complicated parapneumonic effusions (**Figures 1-3**) are characterized by:

- Lung consolidations or infiltrates as in the previous stage
- Uni-loculated or multi-loculated pleural effusion. These can be identified by:
 - Pleural opacity in a non-dependent area
 - Linear densities in the pleura
 - No changes or minor changes in the imaging comparing erect and decubitus radiographs

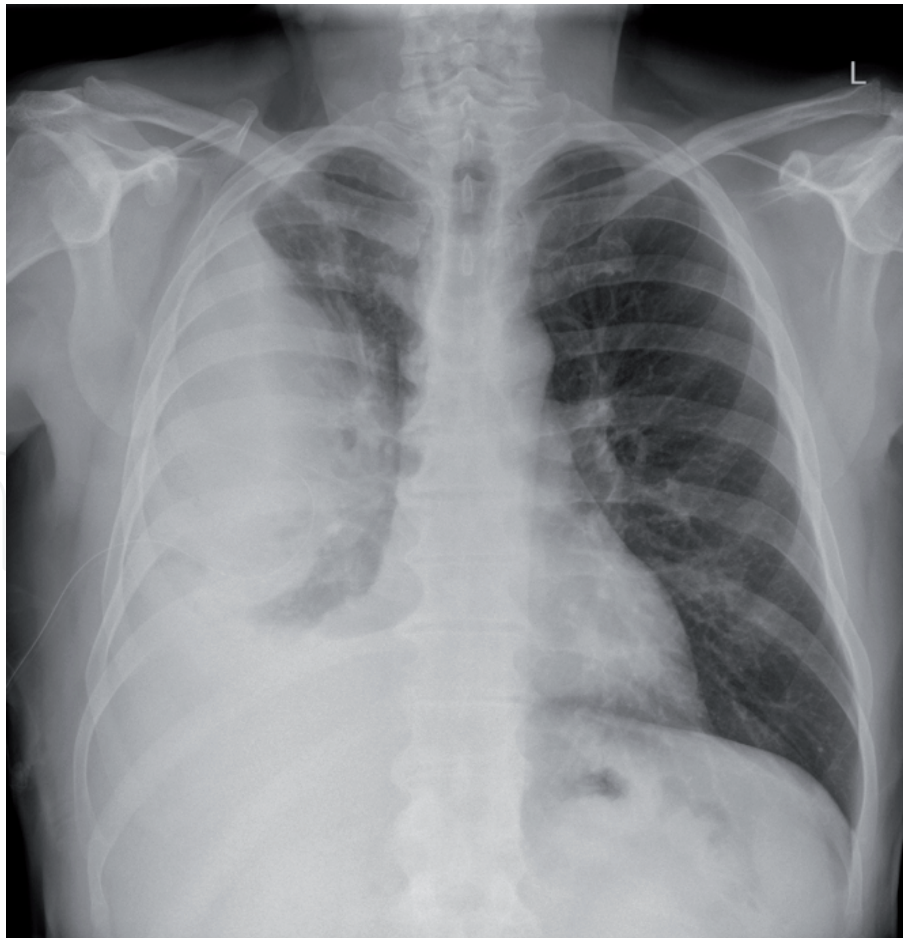


Figure 1.
Chest radiograph of a patient with complicated parapneumonic effusion, demonstrated by restricted expansion of the underlying lung in the right hemithorax. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust.

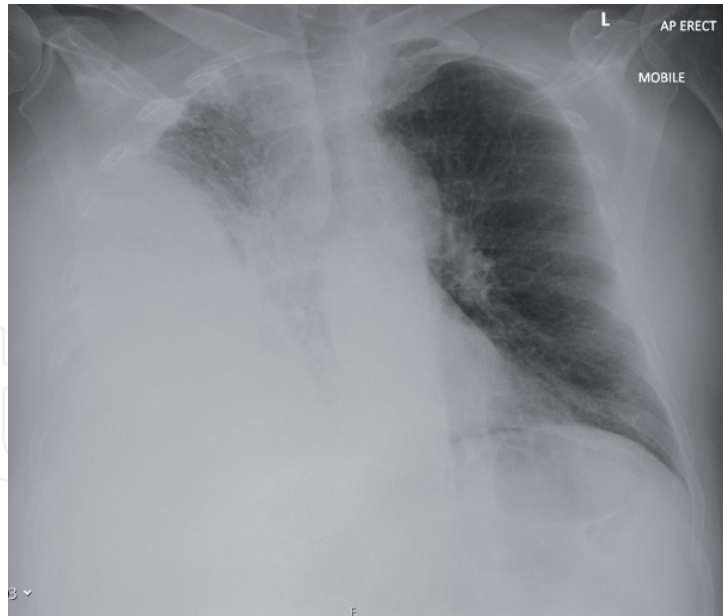


Figure 2.
Chest radiograph of a patient with empyema, demonstrated by lenticular opacity in the pleural cavity of the right hemithorax. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust.

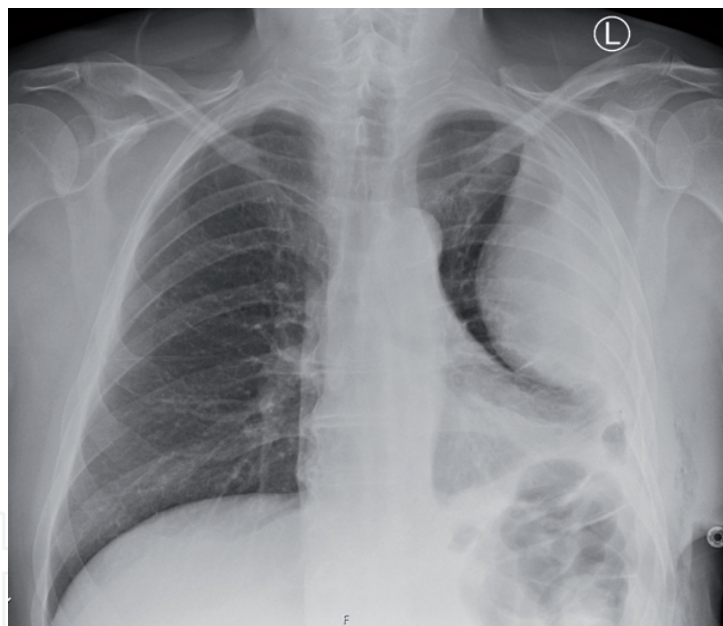


Figure 3.
Chest radiograph of a patient with empyema, demonstrated by lenticular opacity in the pleural cavity of the left hemithorax. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust.

Empyema is characterized by:

- Lenticular opacity in the pleural cavity, convex towards the lung
- Incomplete expansion of the lung

5.2 Ultrasound scan features of a parapneumonic effusion and empyema

US is reported to be superior to radiography and computed tomography to identify the presence of septations. It is also more sensitive than decubitus radiography in detection of the amount of fluid being capable of detecting a minimum of 5 ml of

fluid. Sonography has been reported having a sensitivity of 93% and a specificity of 96% in the diagnosis of pleural effusion [15].

Moreover, the US is particularly useful in critically ill patients allowing supine examinations when the patient cannot be mobilized [16].

It is also valuable in confirming the presence and size of pleural effusion and allows to determine the precise location of the fluid for needle-guided aspiration and drainage.

Tu and colleagues demonstrated the utility of the portable sonography in Emergency Departments and Intensive Care Units in critically ill patients. This allowed, based on the ultrasound features of the effusion, to indicate whether or not thoracentesis was necessary or could safely be deferred [17].

Four different patterns of imaging can be described in sonography evaluation, accordingly to the stage disease: [18].

- Homogeneous anechoic consistent with transudative effusion
- Complex non-septated effusion with internal echogenic foci consistent with fibrinopurulent phase
- Complex septated effusion with echogenic foci consistent with fibrinopurulent phase
- Homogeneously echogenic consistent with presence of blood or frank pus

5.3 Computed tomography features of a parapneumonic effusion and empyema

Chest CT is considered the gold standard to assess a complex pleural effusion. It is better performed with medium contrast in order to better identify the pleural membranes. This is the most sensitive method for detecting a small amount of fluid (limit of resolution 2 ml).

Computed tomography allows:

- Differential diagnosis between pleural empyema and parenchymal lung abscess
- Diagnosis of underlying etiology, such as, pneumoniae, endobronchial lesions or esophageal rupture
- Determine the extension of the infective process and allows to determine any spread into other structures including chest wall (empyema necessitans), mediastinum (determining a mediastinitis) or pericardium (pyopericardium)
- CT guided chest drain insertion, identify the pockets of fluid
- Pre-operative planning for surgery

Specific findings of an empyema include:

- A thick and contrast-enhanced pleural rind
- Pleural effusion which is loculated, septated, lenticular and with high density. Occasionally gas bubbles are seen within the effusion of pockets
- “Split pleura” sign due to pleural enhancement and fluid separating the parietal and visceral pleura surfaces

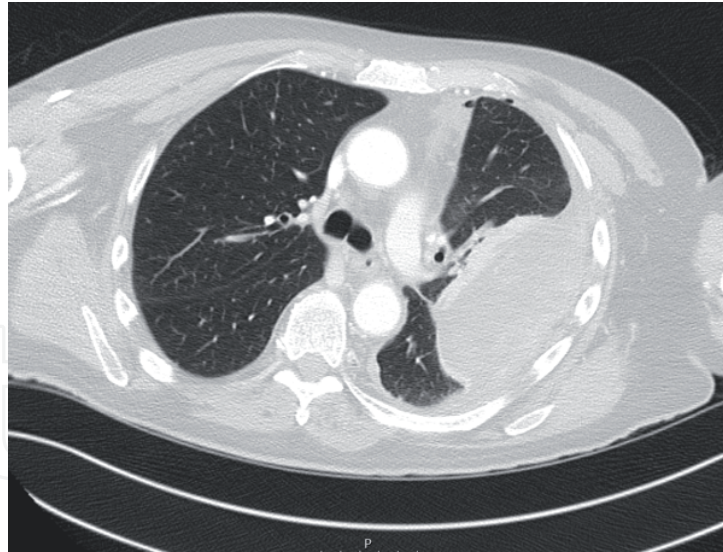


Figure 4.
Lung window computed tomography representative of a loculated left empyema. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust.

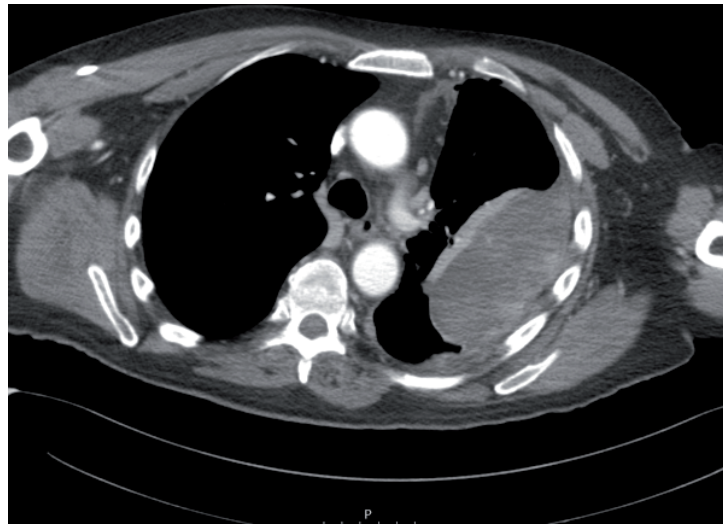


Figure 5.
Mediastinal window computed tomography representative of a loculated left empyema. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust

Although pleural thickening is found in both parapneumonic effusion and empyema, the pleural thickness is greater in purulent effusions, with the absence of pleural thickening suggesting an uncomplicated parapneumonic effusion (Figures 4 and 5).

6. Principles of management for parapneumonic effusion/empyema

Our Unit follows the guidelines of the British Thoracic Society, which are in accordance with the American College of Chest Physician guidelines.

The parapneumonic effusion and empyema are categorized according to radiological, biochemical and microbiological criteria. The staging of the disease based upon these criteria guides the management (Figure 6).

Patients can be divided in four categories which require different management:

Category 1: includes uncomplicated parapneumonic effusion with minimal free-flowing fluid (< 10 mm at the chest X-ray) and undetermined microbiology

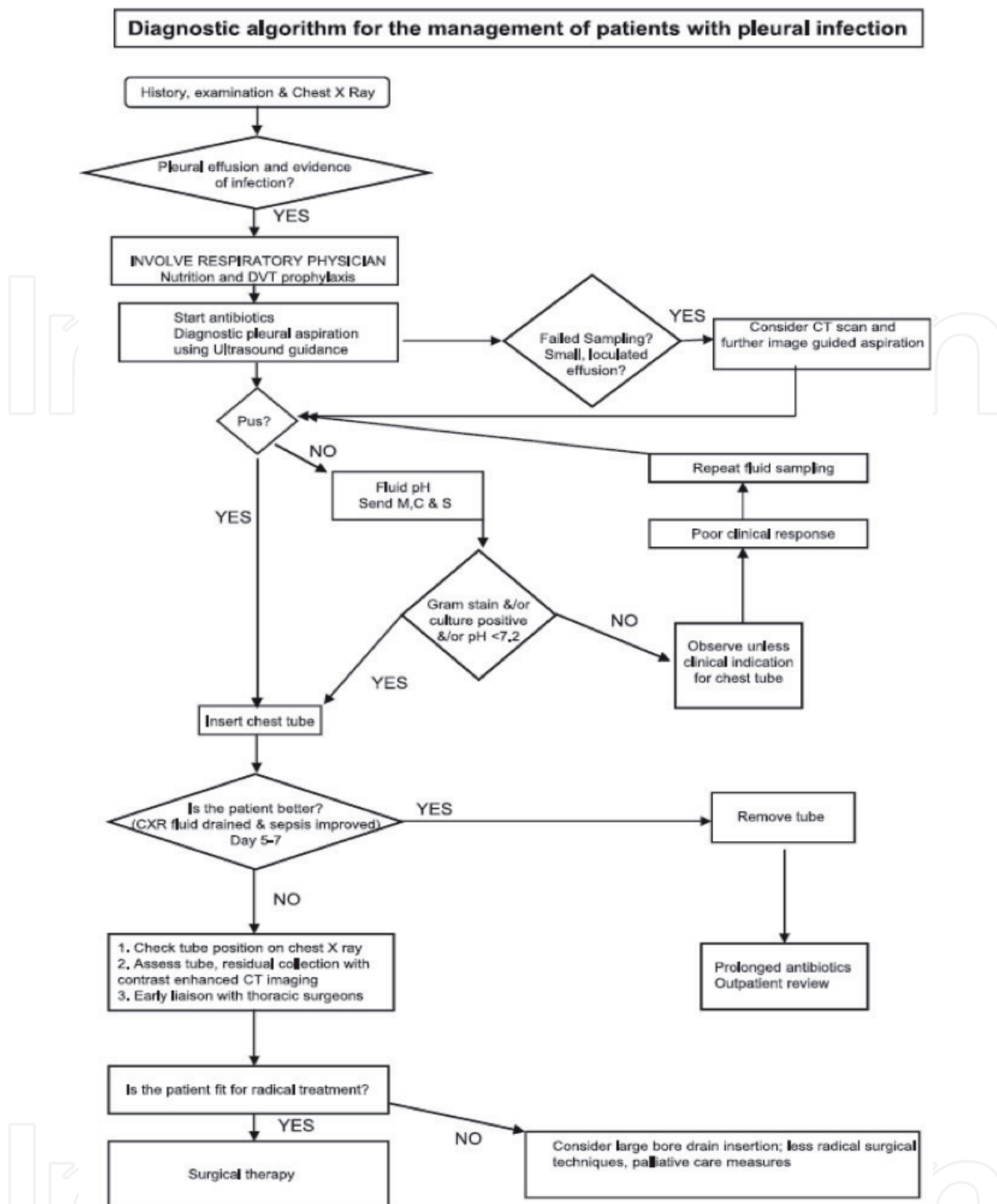


Figure 6. Management of pleural infection in adults: British Thoracic Society pleural disease guidelines 2010, © British Thoracic Society, 2010.

and biochemistry. Patients in this category can be treated with antibiotics only for the underlying pneumoniae.

Category 2: includes uncomplicated parapneumonic effusion with small to moderate free-flowing fluid (more than 10 mm of collection on the radiography). These patients have a negative culture and Gram stain. $\text{pH} \geq 7.2$ and glucose ≥ 3.4 mmol/L.

Patients in this category are treated with antibiotics regimens as the previous category with an addition of a thoracentesis (to determine the fluid quality) and a chest drain insertion if the effusion is large and the patient is symptomatic.

Category 3: includes complicated parapneumonic effusion with large or loculated collection and thickened parietal pleura. The cultures or Gram stains are positive. Acidotic effusion ($\text{pH} < 7.2$) and glucose level < 3.4 mmol/L.

These patients require, as the previous categories, antibiotic treatment, thoracentesis followed by chest drain insertion in symptomatic cases.

In presence of a pH < 7.2 a chest drain insertion is mandatory.

Multi-loculated effusions may require multiple chest drains and/or intrapleural thrombolysis.

Early surgical intervention with video-assisted thoracoscopic surgery (VATS) is recommended for evacuation of pleural fluid, debridement with the disruption of the loculations and decortication in presence of an immature pleural cortex. Early surgical intervention can minimize the impact of the lung restriction in long term effects, allowing a better and faster resolution of the infection and can also reduce the mortality.

Category 4: presence of frank pus which determines empyema. Also, radiological evidence of empyema on the CT scan.

These patients require antibiotic treatment of the underlying pneumoniae, chest tube insertion followed by surgical washout, debridement and decortication aiming for the re-expansion of the underlying lung.

7. Conservative management

When the patient presents in stage I, in most cases, uncomplicated parapneumonic effusions resolve with appropriate antibiotic therapy and drainage is not generally necessary.

It is important to strictly monitor the clinical and radiological evolution to decide if the patient does not respond to conservative treatment. Further pleural fluid sample should be taken to test possible resistance to antibiotics and further imaging considered.

For most community acquired complicated parapneumonic effusions and empyema an empiric intravenous antibiotic regimen that cover *S. pneumoniae* and the oropharynx pathogens including microaerophilic streptococci and anaerobic bacteria is instituted.

This consists in a third-generation cephalosporin associated with metronidazole or a combination beta-lactam/beta-lactamase inhibitor (amoxicillin-clavulanate, ampicillin-sulbactam).

In case of penicillin hypersensitivity who cannot have cephalosporin, options include carbapenem in single therapy, combination therapy with fluoroquinolone and metronidazole or a monobactam with metronidazole.

Clindamycin has been used for treatment of anaerobic lung infections, however, the increasing rates of resistance among anaerobes makes this antibiotic no longer routinely used for empiric treatment of anaerobic infections.

In case of hospital acquired parapneumonic effusions and empyema the empiric IV antibiotic regimen targets MRSA, gram-negative bacteria (including *Pseudomonas* spp) and anaerobic bacteria. Vancomycin with metronidazole associated with an antipseudomonal cephalosporin is appropriate. A combination of vancomycin and beta-lactam/beta-lactamase inhibitor is an alternative. However, since the combination of vancomycin and piperacillin-tazobactam is highly nephrotoxic, sometimes linezolid is used in place of vancomycin when piperacillin-tazobactam is used.

In case of penicillin allergy, an appropriate protocol can be vancomycin with metronidazole and an antipseudomonal fluoroquinolone or an antipseudomonal carbapenem.

While most uncomplicated effusions respond well to antibiotic treatment alone, there may be an indication for drainage in selected circumstances: in symptomatic and frail patients early drainage can be considered.

After the establishment of an appropriate antibiotic regimen, a good clinical response with improvement of signs and symptoms is expected. The antibiotic course is usually maintained for at least 7 days and in most of the times the coverage for the anaerobic species is not needed.

Radiographic improvement usually requires 2 to 4 days, especially with no chest drain inserted.

As a general principle, for self-resolving uncomplicated bacterial parapneumonic effusions, the antibiotic therapy can be protracted with good results and resolution, up to 1–2 weeks. Complicated parapneumonic effusions and empyema usually request longer treatment ranging from 3 weeks for a complicated effusion and 4–6 weeks for empyema.

The initial IV antibiotic regimen can be switched to an oral regimen with similar spectrum when the clinical response is clear, and more invasive procedures such as drainage are no longer needed. There is no demonstrated optimal duration of therapy. The duration of treatment is individualized and it is based upon the type of effusion, the adequacy of drainage, clinical and radiographic response to treatment. On top of that, the immune status and efficacy of immune response of the patient plays a primary role in the duration and efficacy of treatment.

7.1 Intrapleural fibrinolytics

In case of complicated parapneumonic effusions (stage 2) which demonstrate difficult resolution with the sole drainage and antibiotics, including circumstances when septations are proven at the imaging, intrapleural t-PA/DNase can be considered.

These are also a valid option in patients not fit for surgery.

These agents are not exempt from side effects, these include chest pain, fever, allergic reactions (more frequently with streptokinase) and pleural hemorrhage (the risk is increased in presence of renal failure, thrombocytopenia, anticoagulation).

Fibrinolytics are neutralized (usually within an hour) by plasminogen activator inhibitors that are increased during pleural infection.

The first Multicenter Intrapleural Sepsis Trial (MIST1), a double-blind prospective and randomized controlled trial of patients with pleural infection randomized in 2 groups

- Group 1 received streptokinase (250,000 IU b.d. for 3 days)
- Group 2 received a placebo

demonstrated no significant difference between the two groups for mortality percentage requiring surgery, radiological outcomes and lengthy hospital stay; therefore, reporting no benefit of the use of intrapleural streptokinase [19].

7% of patients in the treatment group reported serious adverse effects (chest pain, fever, allergy), compared to 3% in the placebo group.

The median length of stay in the streptokinase group was 13 days while in the control group was 12 days, reporting no significant difference.

Death and the need for surgical intervention data were analyzed separately and no difference was found between the groups at 3 or 12 months.

MIST2 analyzed 210 patients with pleural infection assigned randomly to four groups to receive: double placebo, intrapleural tissue plasminogen activator (t-PA) and DNase, t-PA and placebo, or DNase and placebo.

However, the MIST2 trial found that the intrapleural use of tissue plasminogen activator (t-PA) and DNase improved the drainage of infected fluid in patients affected by pleural infections [20].

This study reported that combination of TPA and DNase improves the drainage of empyema reducing the length of hospital stay (6.7 days less than the placebo groups) and the need for surgery (4% of surgical referrals at 3 months in the double treatment group, compared to 16% of surgical referrals at 3 months in the placebo arm).

8. Surgical treatment

Surgical treatment is often indicated in patients with stage III empyema with cortex encasing the lung or empyema that fails to resolve with antibiotics, chest drain insertion and if indicated t-PA/DNase (stage II) or in symptomatic patients despite control of infection and sepsis.

Failure of resolution of the pleural effusion and the sepsis within 5–7 days despite drainage (+/- t-PA/DNase) and antibiotics is indication for surgical treatment.

This involves minimally invasive approach or thoracotomy according to the stage of the disease. VATS is preferred as first approach. Thoracotomy and thoracostomy remain valid alternatives in patients with advanced staged empyema.

8.1 VATS/thoracotomy debridement and decortication

Thoracoscopy has been proven an effective procedure for the treatment of pleural infection and reporting high successful rate around 91% with few complications compared to thoracotomy.

In their study, Brutsche et al. [21] analyzed a retrospective series of 127 patients over a period of 4 years affected by empyema and treated with medical thoracoscopy.

Empyema was defined by frank pus on thoracocentesis or by pH < 7.2 with signs of infection. Chest radiography and CT scan were used to confirm the diagnosis.

Thoracoscopy was performed with a zero-degree scope through a 7 mm trocar.

Post-operative active suction of minus 20 cm H₂O was applied together with IV antibiotics for at least one week. They reported 9% of complications (surgical emphysema and prolonged air leak). No mortality was observed. 6% of cases required a thoracotomy and pleurectomy post thoracoscopy.

In a single centre, prospective study, Wait et al. [22] considered stage 2 empyema only. 20 patients were randomized to undergo either video-assisted thoracoscopic surgical decortication (11 patients) or chest tube drainage with streptokinase (9 patients). The VATS group reported higher treatment success (10/11, 91% vs. 4/9, 44%), lower chest tube duration (5.8 ± 1.1 vs. 9.8 ± 1.3 days), and decreased total hospital days (8.7 ± 0.9 vs. 12.8 ± 1.1 days). One death was reported in each group.

The authors concluded that VATS was the preferred primary approach for complex fibrinopurulent parapneumonic empyema.

In a recent Cochrane review, the authors [23] compared surgical with non-surgical treatment for pleural empyema.

The study included eight randomized controlled trials for a total of 391 participants comparing open thoracotomy versus drainage.

Six trials were focused on children and two on adults comparing tube thoracostomy drainage with or without intrapleural fibrinolytics, to either VATS or thoracotomy.

Of note, one trial, in children, showed a statistically significant reduction in mean hospital stay of 5.90 days (mean hospital stay of the control group was 15.4 days) and in complications for those treated with primary thoracotomy.

Seven studies were focused on the comparison between VATS versus thoracostomy drainage. No significant difference in mortality or complications between groups for both adults and children, with or without fibrinolysis, were reported. There was a significant reduction in mean length of hospital stay for patients who underwent VATS, 2.5 days less than the thoracostomy group.

A meta-analysis [24] based on 14 papers comparing VATS to traditional thoracotomy to perform decortication for the treatment of persistent pleural collections, in adults, demonstrated the superiority of VATS in terms of postoperative morbidity, complications and length of hospital stay, and gave equivalent resolution when compared with thoracotomy and decortication.

In 2005, Luh et al. [25] in a retrospective single centre study compared VATS decortication in the treatment of complicated parapneumonic effusion (stage 2) in 145 patients and loculated empyema (stage 3) in 89 patients, over a period of 8 years. Those with empyema had a conversion rate to thoracotomy and decortication of 21.3% compared with 3.5% with complicated effusion. The study reported also a significant reduction in postoperative length of stay on patients with complicated effusion (9.1 days) compared to patients with empyema (18.5 days). Reported perioperative morbidity; effusion group 6.2% vs. empyema group 11.2%. Perioperative mortality: effusion 2.1% and empyema 5.6%.

6.8% needed further surgery for empyema and 9 patients required open drainage or thoracoplasty, 7 patients needed re-decortication or repair of bronchopleural fistula.

Shahin et al. [26] in their single centre study over a period of 3 years reported a 3.5% conversion rate from VATS to thoracotomy to perform a decortication of 3.5% in patients with fibrinopurulent empyema (stage 2) and 19% in those with advanced organized empyema. Postoperative stay was shorter with VATS than thoracotomy (5 vs. 8 days) and no mortality was reported in both groups.

The authors conclude that we should consider VATS debridement and decortication as a first-choice treatment for primary empyema.

Another single centre study [27] analyzed a 10 years-experience comparing VATS decortication in 326 patients and 94 patients after thoracotomy and decortication. 11.4% of VATS cases were converted to thoracotomy. The VATS group reported reduced median post-operative hospital stays (7 vs. 10 days) and significantly reduced postoperative complications (atelectasis, prolonged air-leak, reintubation, ventilator dependence, need for tracheostomy, blood transfusion, sepsis,) and 30-day mortality. The mean operative time was VATS-thoracotomy 97 min – 155 min.

The study concluded that VATS approach is an effective and reasonable first-line option for most patients with complex pleural effusions and empyema.

Cardillo et al. [28] reported for VATS (185 patients) better results than thoracotomy decortication (123 patients) in terms of operative time, pain, postoperative air-leak, hospital stay and time to return to work. Conversion rate to open surgery was 11/185 (5.9%). Empyema recurred only in VATS group 3/185 (1.6%). The analysis of postoperative pain at six months follow-up showed no significant differences.

In conclusion, VATS and thoracotomy (open surgery) show similar postoperative outcomes, however, in terms of morbidity and hospital length of stay VATS is superior to open surgery. Therefore, when possible, VATS is preferred over the thoracotomy approach.

In advanced stage empyema open decortication should be considered: patients with stage III empyema or previous VATS procedures with still trapped lung or symptoms.

8.1.1 Our data

In our Institution regarding a single surgeon experience 103 patients were treated for empyema from August 2015 to May 2021: 33 were female and 70 males, with a median age of 58 years.

34 thoracotomies (33%) and 69 VATS were performed (28 decortications and 75 washout and debridement), Between VATS cases. The average operating time was 82 minutes. The average blood loss was 250 ml, ranging from 0 ml to 2500 ml. We reported 3 (4.3%) conversions for bleeding (one from parenchymal abscess and 2 from the lung surface).

The Median length of chest drain was 4 days and median length of hospital stay of 9 days (range 2 to 38 days): 8 and 9 days in the VATS and thoracotomy group respectively. Postoperative in-hospital mortality was 4.8% (n = 5): One COVID-related and one for progression of malignancy. One intraoperative mortality was due to bilateral PE.

9.7% of patients presented with postoperative complications: pneumoniae, bleeding (one required re-intervention), prolonged air leak, chylothorax and respiratory arrest due to mucus plug. Five patients were re-admitted within the first 30 days post discharge: 3 recurrent chest infections, one PE and one wound infection.

8.1.2 VATS washout and debridement technique

The main goal of the surgery is to achieve an adequate drainage of empyema and full re-expansion of the lung. This is easier if early intervention and adequate antibiotic treatment is undertaken.

Thoracoscopic debridement allows direct vision of the chest cavity facilitating the drainage. Usually the thoracoscope introduction is best performed after opening the pleura under direct vision.

Often, the best place to insert the first port is the intercostal space from which a needle exploration is positive for pleural fluid/pus. Alternatively, the creation of a pleural window by open dissection is requested, in presence of thickened pleural rinds. Subsequently, the port is inserted through the incision.

The risk of blind insertion of a thoracoscopic port in absence of confirmatory exploratory aspiration is to enter into the adherent lung parenchyma with a subsequent damage to the lung surface which will result in a postoperative air leak. Hence, blind port insertion should be avoided.

Following the first port insertion the pleural space is debrided, a second port can be inserted in order to achieve the complete debridement of the chest cavity. With the use of Yohan forceps, endoscopic ring-grasper or the swiping action of the scope itself, all the adhesions and loculations are separated and dissected in order to create space and have a clear vision of the chest cavity.

Repeated warm saline irrigations help loosen adhesions as well as improve vision by sucking and draining blood and purulent material.

A helpful maneuver to release adhesions is the use of endoscopic instruments to hold the membrane and twisting it from outside the port, which allows to peel the fibrinopurulent membrane effectively.

Most of the time, two ports are sufficient in case of early intervention, to clear the cavity. In presence of thick membranes, a third port may be required in order to achieve complete release of the trapped lung.

When satisfied with the debridement and subsequent lung re-expansion, port sites are closed and chest drain is inserted in the pleural cavity.

These procedures are often related to considerable bleeding related to the inflammatory state of the tissues. This generally stops following lung re-expansion. However, bleeding from intercostal vessels need to be controlled with coagulation

diathermy, endoclip or bipolar diathermy device. Arterial bleeding needs careful identification and control before intercostal drain insertion and ports closure.

It is generally preferred to start with a keyhole approach and then convert to an open thoracotomy if required by emergency or impossibility to complete the debridement/decortication.

Conversion to open thoracotomy is also appropriate in patients who do not tolerate single lung ventilation, uncontrollable bleeding or damaged structures not accessible by VATS.

Timing is crucial when surgery is discussed in the management on stage II or III empyema. Decortication is associated with prolonged hospital stay, bleeding, bacteremia and hypotension. The need of decortication may be less than expected if early treatment is started with antibiotics and VATS debridement of the pleural space. An open decortication should be probably deferred when infective process is resolved and natural remodeling of the pleural space is completed. An open decortication in presence of chest infection and not defined cortex can cause worse sepsis, prolonged air leak and poor lung re expansion.

Aquamantys © bipolar sealer uses radiofrequency energy and saline simultaneously to provide hemostasis and it is useful to control bleeding from the chest wall surface, as well as, from the lung parenchyma. It is provided with endoscopic handpiece and can be used in keyhole surgery, such as, VATS.

8.2 Thoracostomy

Rarely, when all the other interventions fail (antibiotics, tube thoracostomy, fibrinolytic therapy) and in patients not fit for major surgery with advanced stage empyema with thick cortex, an open thoracostomy should be considered, this can be obtained with a small rib resection and creation of thoracostomy. The empyema resolving process takes approximately 60–90 days.

The stoma needs multiple daily dressing changes, sometimes, a wound vacuum-assisted closure (VAC) device facilitate drainage of the empyema. However, this device can facilitate or worsen the creation of a bronchopleural fistula.

When compared with conventional management of open window thoracostomy, VAC therapy accelerates wound healing and improves re-expansion of residual lung.

Palmen et al. [29] retrospectively analyzed all 242 patients with empyema in a 19.5 years' experience. 19 patients had a recurrence of empyema, which required a thoracostomy. 11 patients were treated with VAC therapy in addition.

The non-VAC group consisted in 8 patients.

Thoracostomy-only group received saline-soaked gauzes application in the cavity, with daily dressing changes.

The total duration of open window thoracostomy and the duration of VAC therapy were 39 ± 17 and 31 ± 19 days, respectively.

All 11 patients were amenable for subsequent closure using pedicled muscular flaps.

In 2 patients, VAC therapy alone resulted in complete closure of the thoracostomy.

Four patients died from complications (1 bleeding, 3 recurrent infections) during follow-up. The average duration of OWT was $933 \pm 1,422$ days.

9. Conclusion

Parapneumonic effusion stage I can be managed conservatively with antibiotics treatment and chest drain insertion, in stage II VATS debridement and fibrinolytics

are recommended, in stage III VATS decortication should be considered the first treatment option considering better outcomes compared to thoracotomy. In case of septic patients or severely trapped lung open decortication should be considered. The preference is to delay the open decortication at a later phase if VATS failed to reduce the risk related to open decortication: bleeding, prolonged air leak and worsening sepsis.

Conflict of interest

The authors declare no conflict of interest.

Author details

Alessandro Maraschi* and Andrea Billè
Thoracic Surgery, Guy's and St. Thomas' NHS Foundation Trust,
London, United Kingdom

*Address all correspondence to: alessandro.maraschi@gmail.com

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References

- [1] Finley C, Clifton J, Fitzgerald JM, et al. Empyema: an increasing concern in Canada. *Can Respir J* 2008;15:85-89
- [2] Maskell NA, Batt S, Hedley EL, et al. The bacteriology of pleural infection by genetic and standard methods and its mortality significance. *Am. J. Respir. Crit. Care Med.* 2006;174:817-823
- [3] Asai N, Suematsu H, Hagihara M, et al. The etiology and bacteriology of healthcare-associated empyema are quite different from those of community-acquired empyema. *J. Infect. Chemother.* 2017;23:661-667
- [4] Park C-K, Oh H-J, Choi H-Y, et al. Microbiological Characteristics and Predictive Factors for Mortality in Pleural Infection: A Single-Center Cohort Study in Korea. Trottein F, editor. *PLOS ONE.* 2016;11:e0161280.
- [5] Maskell NA, Batt S, Hedley EL, et al. The Bacteriology of Pleural Infection by Genetic and Standard Methods and Its Mortality Significance. *American Journal of Respiratory and Critical Care Medicine.* 2006;174:817-823.
- [6] Chen KY, Hsueh PR, Liaw YS, Yang PC, Luh KT. A 10-year experience with bacteriology of acute thoracic empyema: emphasis on *Klebsiella pneumoniae* in patients with diabetes mellitus. *Chest.* 2000; 117(6):1685
- [7] Zhai K, Lu Y, Shi HZ. Tuberculous pleural effusion. *J Thorac Dis.* 2016;8(7):E486
- [8] Light RW. Update on tuberculous pleural effusion. *Respirology.* 2010;15(3):451
- [9] Alegre J, Jufresa J, Segura R, et al. Pleural-fluid myeloperoxidase in complicated and noncomplicated parapneumonic pleural effusions. *Eur. Respir. J.* 2002;19:320-325.
- [10] Alemán C, Alegre J, Segura RM, et al. Polymorphonuclear elastase in the early diagnosis of complicated pyogenic pleural effusions. *Respiration.* 2003;70:462-467.
- [11] Porcel JM, Vives M, Esquerda A. Tumor necrosis factor-alpha in pleural fluid: a marker of complicated parapneumonic effusions. *Chest.* 2004;125:160-164.
- [12] Iglesias D, Alegre J, Alemán C, et al. Metalloproteinases and tissue inhibitors of metalloproteinases in exudative pleural effusions. *Eur. Respir. J.* 2005;25:104-109.
- [13] Porcel JM, Vives M, Cao G, et al. Biomarkers of infection for the differential diagnosis of pleural effusions. *Eur. Respir. J.* 2009;34:1383-1389.
- [14] Wu K-A, Wu C-C, Chen C-D, et al. Proteome profiling reveals novel biomarkers to identify complicated parapneumonic effusions. *Scientific Reports.* 2017;7:4026.
- [15] Rocco M, Carbone I, Morelli A, Bertolotti L, Rossi S, Vitale M, Montini L, Passariello R, Pietropaoli P. Diagnostic accuracy of bedside ultrasonography in the ICU: feasibility of detecting pulmonary effusion and lung contusion in patients on respiratory support after severe blunt thoracic trauma. *Acta Anaesthesiol Scand.* 2008 Jul; 52(6):776-784
- [16] Kocijancic I, Vidmar K, Ivanovi Herceg Z, et al. Chest sonography versus lateral decubitus radiography in the diagnosis of small pleural effusions. *J Clin Ultrasound* 2003;31(2):69-74
- [17] Tu CY, Hsu WH, Hsia TC, et al. Pleural effusion in febrile medical ICU patients: chest ultrasound study. *Chest* 2004;126(4):1274-1280

- [18] Yang PC, Luh KT, Chang DB, et al. Value of sonography in determining the nature of pleural effusion: analysis of 320 cases. *Am J Roentgenol* 1992;159(1):29-33
- [19] Maskell NA, Davies CW, Nunn AJ, Hedley EL, Gleeson FV, Miller R, Gabe R, Rees GL, Peto TE, Woodhead MA, Lane DJ, Darbyshire JH, Davies RJ,; First Multicenter Intrapleural Sepsis Trial (MIST1) Group. U.K. Controlled trial of intrapleural streptokinase for pleural infection. *N England J Med* 2005; 352(9): 865-874
- [20] Rahman NM, Maskell NA, West A, et al. Intrapleural Use of Tissue Plasminogen Activator and DNase in Pleural Infection. *New England Journal of Medicine*. 2011;365:518-526
- [21] Brutsche MH, Tassi GF, Gyorik S, et al. Treatment of sonographically stratified multiloculated thoracic empyema by medical thoracoscopy. *Chest* 2005;128:3303e9.
- [22] Wait MA, Sharma S, Hohn J, Dal Nogare A. A randomized trial of empyema therapy. *Chest* 1997;111:1548-1551
- [23] Redden MD, Chin TY, van Driel ML. Surgical versus non-surgical management for pleural empyema. *Cochrane Database Syst Rev*. 2017; 3:CD010651. doi
- [24] Chambers A, Routledge T, Dunning J, Scarci M. Is video-assisted thoracoscopic surgical decortication superior to open surgery in the management of adults with primary empyema? *Interact Cardiovasc Thorac Surg*. 2010; 11(2): 171- 177. Doi
- [25] Luh SP, Chou MC, Wang LS, Chen JY, Tsai TP. Video-assisted thoracos- copic surgery in the treatment of complicated parapneumonic effusions or empyemas: outcome of 234 patients. *Chest* 2005;127:1427-1432
- [26] Shahin Y, Duffy J, Beggs D, Black E, Majewski A. Surgical management of primary empyema of the pleural cavity: 5 outcome of 81 patients. *Interact CardioVasc Thorac Surg* 2010;10:565-567
- [27] Tong BC, Hanna J, Toloza EM, Onaitis MW, D'Amico TA, Harpole DH, Burfeind WR. Outcomes of video-assisted thoracoscopic decortication. *Ann Thorac Surg* 2010;89:220-225
- [28] Cardillo G, Carleo F, Carbone L, Di Martino M, Salvadori L, Petrella L, Martelli M. Chronic postpneumonic pleural empyema: comparative merits of thoracoscopic versus open decortication. *Eur J Cardiothorac Surg* 2009;36:914-918
- [29] Palmén M, van Breugel HN, Geskes GG, van Belle A, Swennen JM, Drikkoningen AH, van der Hulst RR, Maessen JG. Open window thoracostomy treatment of empyema is accelerated by vacuum-assisted closure. *Ann Thorac Surg*. 2009 Oct;88(4):1131-1136. doi: 10.1016/j.athoracsur.2009.06.030. PMID: 19766795.