The impact of geriatric patients on outcomes in septic thoracic surgery outside academic institutions: an investigation of risk factors and postoperative courses

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THE IMPACT OF GERIATRIC PATIENTS ON OUTCOMES IN SEPTIC THORACIC SURGERY OUTSIDE ACADEMIC INSTITUTIONS: AN INVESTIGATION OF RISK FACTORS AND POSTOPERATIVE COURSES

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LIST OF ABBREVIATIONS

AATS – The American Association for Thoracic Surgery

ACCP – American College of Chest Physicians

IL-8 – Interleukin 8

TNF-α – Tumor necrosis factor α

VEGF – Vascular endothelial growth factor

GERD – Gastroesophageal reflux disease

CT – Computed tomography

LDH – Lactatdehydrogenase

MRSA – Methicillin-resistant Staphylococcus aureus

MIS – Minimal invasive surgery

PPEs – Pleural parapneumonic effusions

PE – Pleural effusion

IFT – Intrapleural fibrinolysis

VATS – Video-assisted thoracic surgery

VAC – Vacuum assisted closure

ICW – Initiative Chronische Wunden (Initiative of chronic wounds)

BPF – Bronchopleural fistula

US – Ultrasound

CXR – Conventional chest x-ray

BTS – British Thoracic Society

OWT – Open Window Thoracostomy

RCT – Randomized controlled trial

1. INTRODUCTION

1.1. Pleural empyema

1.1.1. Historical excursion

For over 2000 years, the guiding principle for treating pulmonary infections has been "Ubi pus, ibi evacua," in other words: one should drain the infectious fluid from the lung as quickly as possible (1). The history of treating thoracic diseases dates back a long way. From many accounts, scientists and physicians can infer how our human ancestors dealt with such diseases, examined them, and attempted to cure them long before the 21st century. To this day, ancient texts fascinate us because these diseases still pose a challenge. Reports of lung diseases extend far back. Hippocrates himself addressed the topic of pleural empyema. He was likely born around 460 on the island of Kos, Greece, and is considered the founder of the medical school of Kos (2). Through his writings, known as the Hippocratic Corpus, he demonstrated a significant shift from the prevailing religious and magical medicine that dominated the entire ancient world at the time, towards a more rational approach. He also delved into the clinical picture of empyema.

The word "empyema" derives from Greek. The prefix "en" means "in" or "within," and the root "pyema" translates to "pus" (2). In his writings, Hippocrates detailed the etiology, symptoms, diagnosis, prognosis of a patient with pleural empyema, as well as complications and treatment approaches. For example, he described the entry and cessation of foreign material into the lungs or parapneumonic diseases as triggering events for the development of empyema. Diagnostically, he described shaking the patient, during which a physician could produce a typical rattling sound comparable to the sound of shaking a half-full water bottle by placing the ear on the patient's thoracic wall. If this method failed, an alternative was to inspect the thorax and make a classic side-by-side comparison. The affected hemithorax would thus be warm and painful (2). Hippocrates also described the therapy. Interestingly, some of these approaches remain valid to this day. He named conservative therapy as the initial treatment, involving medications and physiotherapy. With the so-called paracentesis thoracis, Hippocrates described a procedure that remains relevant to this day. In his writings, he described the step-by-step surgical procedure for relieving empyema through a simple incision and drainage. Based on the colour and consistency of the draining pus, he could make predictions for healing and recovery. For example, he regarded the drainage of pure white pus with some blood as a good sign, whereas foul-smelling, muddy, or protein-coloured drainage was considered a sign of death (3).

1.1.2. Anatomical and physiological basics of the thorax

The thorax consists of the thoracic cavity, the chest wall, and the organs of the thorax. The upper boundary, which is open, is called the superior thoracic aperture. The lower thoracic aperture is closed by the diaphragm. The musculoskeletal wall of the thorax is flexible and consists of segmentally arranged vertebrae, ribs, muscles, and the sternum. There are three major cavities distinguished: the right pleural cavity, the left pleural cavity, and centrally the mediastinum, which contains the heart, esophagus, trachea, nerves, and blood vessels. It also separates the two pleural cavities from each other (4). Both pleural cavities are lined by a mesothelial membrane, the pleura, which consists of two layers:

- The parietal pleura, which lines the thoracic cavity
- The visceral pleura, which lies directly on the lung

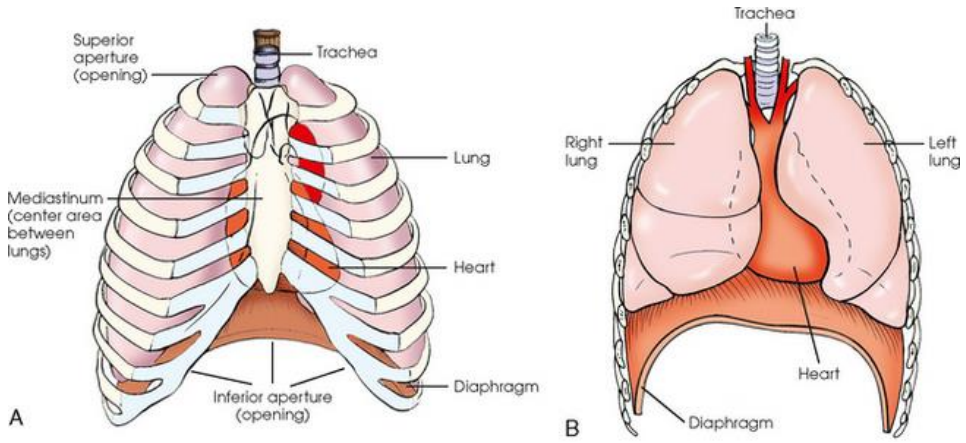

Figure 1. A, B: **A,** Thoracic cavity. **B,** Thoracic cavity with anterior ribs removed. (Cited March 4 2024) Link: https://radiologykey.com/thoracic-viscera/

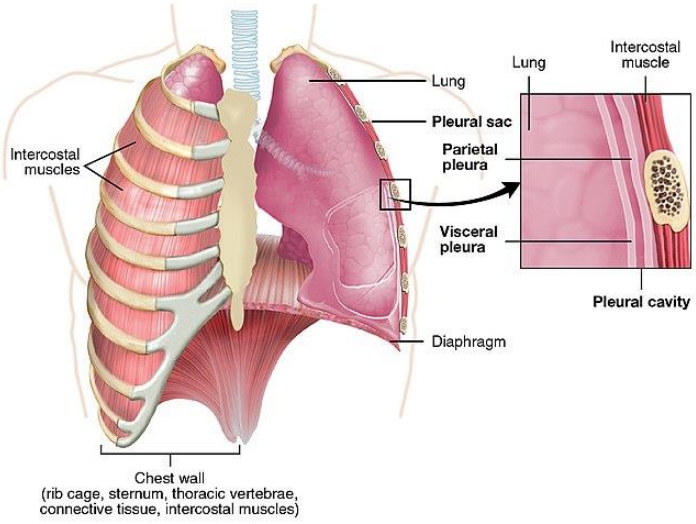

Figure 2. Anatomy of the lung with visible pleura. (Cited March 4 2024)
Link: https://de.wikipedia.org/wiki/Pleura

Between the two layers is a space called pleural cavity, which contains pleural fluid. This fluid is serous and allows the two layers to slide over each other. It also prevents the lung from sticking to the thorax (4). The amount of fluid in the pleural cavity is a few millilitres. If the quantity increases, excess fluid is transported away by the lymphatic system directly adjacent to the cavity. This also creates a negative pressure in the pleural cavity essential for the expansion of both lung lobes. The collapse pressure of the lung is approximately 4 mmHg. Since the negative pressure in the pleural cavity is around 7 mmHg, it is greater than the collapse pressure of the lung, thus preventing its collapse (5).

1.1.3. Etiology and risk factors for the development of pleural empyema

1.1.3.1. Etiology

Parapneumonic pleural effusion is a common complication of viral and bacterial pneumonia, occurring in approximately 57% of cases. Up to 10% of patients with parapneumonic pleural effusion will develop a treatable pleural empyema. Other causes for the development of empyema include penetrating chest trauma, thoracic surgery or esophageal rupture. In the following, pleural effusion, pneumonia, and hemothorax are explained in detail as the primary causes for the development of a pleural empyema (6,7,8).

1.1.3.1.1. Pleural empyema on basis of pleural effusion or pneumonia

In general, pleural effusions are classified into two categories: transudates and exudates. A transudative pleural effusion occurs as a result of an imbalance in the hydrostatic forces that affect the formation and absorption of pleural fluid, leading to an accumulation of fluid. In this scenario, capillary permeability to proteins remains unaltered. Conversely, an exudative pleural effusion develops when there are changes to the pleural surface and/or local capillary permeability (9). In general, in a state of physiological balance, pleural fluid originates from systemic pleural vessels, passes through permeable pleural membranes into the pleural space, and is drained by parietal pleural lymphatics located in the dependent portion of the cavity. In healthy adults, the pleural cavity typically contains a small volume (1-20 mL) of low-protein fluid, forming a thin lubricating film around 10 µm thick between the visceral and parietal pleural surfaces. Movement into the pleural space is driven by a pressure gradient, with intrapleural pressure being lower than interstitial pressure, and the pleural membranes offering minimal resistance to fluid or protein movement, primarily via bulk flow rather than diffusion or active transport.

The primary route for pleural fluid drainage is through parietal lymphatics. Accumulation of pleural fluid occurs when the rate of fluid formation surpasses absorption. Pleural lymphatics can enhance flow efficiently in response to increased pleural fluid filtration, acting as a negative feedback mechanism. The typical daily lymphatic flow is around 15 mL/day, corresponding to the usual amount of pleural fluid formed daily. However, the lymphatics have a capacity of about 300-700 mL/day. Therefore, unless lymphatic drainage is severely compromised, another factor must contribute to pleural fluid accumulation (10). Causes for these pleural effusions are very variable. On one hand, many drugs can cause pleural effusions. Some of these include for example: Amiodarone, Nitrofurantoin, Phenytoin and Methotrexate.

Common causes for transudative pleural effusions are for example: Left ventricular failure, liver cirrhosis, hypalbuminaemia, peritoneal dialysis. Or less commonly hypothyroidism, nephrotic syndrome, mitral stenosis, pulmonary embolism and many more.

The most common causes for exudative pleural effusions are malignancy or parapneumonic effusions, more rarely pulmonary infarction, rheumatoid arthritis, any kind of autoimmune diseases, pancreatitis, post-myocardial infarction syndrome and many more (9). The mechanism of development from a pleural effusion to pneumonia and eventually pleural empyema is as follows: The onset of bacterial infection triggers a localized inflammatory response, leading to heightened capillary microvascular permeability and a swift release of fluid

rich in inflammatory cells into the pleural space. Concurrent comorbidities, such as heart failure, exacerbate interstitial edema. Mediators involved in this process include IL-8 (interleukin 8), TNF-α (tumor necrosis factor α), and VEGF (vascular endothelial growth factor) (10).

On the other hand, empyema can develop on the basis of parapneumonic effusion. Parapneumonic effusion refers to any pleural effusion resulting from viral or bacterial pneumonia or lung abscess. From the patients admitted to the hospital, 20-40% have a parapneumonic effusion. In approximately 10% of these cases, empyema or complicated effusions can develop. (10). A "complicated" parapneumonic effusion is characterized by the need for invasive procedures like tube thoracostomy for resolution, often accompanied by positive pleural fluid cultures (10). Pleural empyema can develop as a complication of pneumonia when infectious material spreads from the lung parenchyma into the pleural space, leading to the accumulation of purulent fluid. This process typically occurs when bacteria invade the pleural cavity either through direct extension from the infected lung tissue or via lymphatic or hematogenous dissemination.

1. Direct Extension: Bacterial pneumonia can directly involve the visceral pleura, leading to the formation of a localized infection within the pleural space. This occurs when the inflammatory process extends through the alveolar wall into the adjacent pleura. The presence of bacteria and inflammatory mediators triggers an intense inflammatory response within the pleural space, resulting in exudation of fluid and fibrin deposition. (11)
2. Lymphatic Spread: In some cases, bacteria from the lung parenchyma can spread to the pleural space via lymphatic channels. The lymphatic vessels draining the lungs communicate with the pleural lymphatics, providing a route for bacterial dissemination. Once bacteria reach the pleural space, they can incite an inflammatory response, leading to the development of pleural effusion and potentially progressing to empyema if left untreated (12)
3. Hematogenous Dissemination: In rare cases, bacteria can disseminate hematogenous from the primary lung infection to the pleural space. Bacteraemia allows pathogens to reach the pleura via the bloodstream, where they can initiate an infectious process within the pleural cavity. This mechanism is less common but can occur particularly in cases of severe or complicated pneumonia (13).

1.1.3.1.2. Pleural empyema on the basis of hemothorax

Hemothorax is a condition mainly cause by trauma. A pleural empyema can develop from a hemothorax through a suppurative process involving the serous pleural layers (14). A hemothorax typically occurs when blood accumulates in the pleural cavity, due to mainly trauma or injury to the chest wall or lung parenchyma. Reasons for these events are often blunt or penetrating trauma, ruptured blood vessels, or complications of medical procedures such as thoracentesis or chest tube insertion. If bacteria are introduced into the pleural space or if blood becomes contaminated during the initial event, there is a risk of infection (15).

1.1.4. Classification of pleural empyema

Even though, empyema is defined generally as a collection of pus in the pleural cavity due to translocated bacteria in the pleural space (16, 17), there are many ways to classify it further. The most special classifications are the classification according to The American Association for Thoracic Surgery (AATS), Light-Classification and the Classification after the American College of Chest Physicians (ACCP).

1.1.4.1 AATS-Classification

First classification of pleural empyema was performed in 1962 by AATS. They classified the pleural empyema according to the natural course of the disease (18).

Table 1: Classification of the pleural empyema according to AATS

Stage I	Exudative phase
Stage II	Fibrinopurulent phase
Stage III	Fibroblastic / organizing phase

Empyema usually arises from the initial stage of parapneumonic exudative condition (Stage I). This stage is marked by exudation, which may or may not yield positive cultures. At the beginning, stage I is characterized by sterile exudation, low granulocyte count, low lactate dehydrogenase activity, physiological pH, and normal glucose concentration. As it processes it can manifest with a presence of free-floating leukocytic pleocytosis containing polymorphonuclear neutrophilic, eosinophilic, or lymphocytic cellular infiltrate. As the leukocyte count increases, there is a decline in pleural fluid pH and glucose levels, while the LDH level begins to elevate during this phase (19, 20).

This then progresses to a fibro-purulent stage (Stage II) with increased neutrophil count, high LDH concentration, decreased pH (7.21–7.29), and low glucose concentration (<40 mg/dL). Stage II is also marked by increasing fibrin deposition on the visceral and parietal pleura, sometimes compartmentalized (19, 20).

The final is the stage of fibrous organization (Stage III). In this stage, fibrin strands can transform into rigid connective tissue membranes due to the migration of fibroblasts. These membranes often cause encapsulated fluid compartments and frequently result in significant restrictive impairment of lung function. Especially the functional reserve capacity (FRC) decreases. Furthermore, contraction of the hemithorax can happen (19, 20).

1.1.4.1.1. Light-Classification of pleural effusion

The classification of Light was published in 1995 and is based on the quantity of the present fluid, Gram stains, cultures and biochemical characteristics of the pleural fluid. Furthermore it is based on the presence or absence of loculations and the gross characteristics of the pleural fluid (21). Light differentiates classes and shows therapy methods for each class. Class 1 to 3 describe parapneumonic effusions with a negative microbiological culture (21). They are structured in

- Nonsignificant parapneumonic effusion
- Typical (uncomplicated) parapneumonic effusion
- Complicated parapneumonic effusion (Borderline)

In contrast to that, class 4 to 7 describe a complex situation (22, 21). They are structured in

- Simple complicated parapneumonic effusion
- Complex complicated parapneumonic effusion
- Simple empyema
- Complex empyema

Light mentions in his work, that a nonsignificant parapneumonic effusion does not need any kind of drainage. Thoracic drainage is for complex effusions. Difference between complex effusion and empyema is the presence of pus in empyema (23).

Table 2: Light Classification for parapneumonic effusions and empyema (21).

Class	Additional name	Hallmarks
Class I	Nonsignificant	< 10 mm thick on decubitus x-ray
Class II	Typical parapneumonic	> 10 mm thick, Glucose > 40 mg/dL, pH > 7.20, Gram stain and culture negative
Class III	Borderline-complicated	7,00 < pH < 7.20 and/or LDH > 1000 and glucose >40 mg/dL, Gram stain and culture negative
Class IV	Simple complicated	pH < 7.00 and/or glucose < 40 mg/dL and/or Gram stain or culture positive, not loculated not frank pus
Class V	Complex complicated	pH < 7.00 and/or glucose < 40 mg/dL and/or Gram stain or culture positive, multiloculated
Class VI	Simple empyema	Frank pus present, single locule or free flowing
Class VII	Complex empyema	Frank pus present, multiple locules

1.1.4.1.2. Classification after the American College of Chest Physicians (ACCP)

In 2000, the ACCP published clinical practice guidelines. These guidelines include the medical and surgical approach to pleural effusions and empyema (8). Focus of these guidelines is the risk of a poor therapeutic outcome.

The ACCP defines three variables that are directly related to poor outcome: pleural space anatomy, pleural fluid bacteriology and pleural fluid chemistry (8, 24). These can then be categorized into category 1 – 4 for poor outcome: Category 1 (very low risk), category 2 (low risk), category 3 (moderate risk), and 4 (high risk) (25).

Table 3: Guidelines of the ACCP: Categorizing risk for poor outcome in empyema and parapneumonic effusion

Risk factors:	Pleural space anatomy		Pleural fluid bacteriology		Pleural fluid chemistry	Category
	Minimal, free-flowing effusion (<10 mm on lateral decubitus)	and	Culture and Gram-stain results unknown	and	pH unknown	1
	Small to moderate free-flowing effusion (>10 mm and <½ hemithorax)	and	Negative culture and Gram stain	and	pH ≥ 7.20	2
	Large, free-flowing effusion (≥½ hemithorax), loculated effusion, or effusion with thickened parietal pleura	or	Positive culture or Gram stain	or	pH < 7.20	3
	Large, free-flowing effusion (≥½ hemithorax), loculated effusion, or effusion with thickened parietal pleura	or	Pus	or	pH < 7.20	4

1.1.5. Epidemiology of pleural empyema

The incidence of pleural empyema varies depending on factors such as geographic region, population demographics, and healthcare access. The incidence has been increasing in recent years, possibly due to factors like antibiotic resistance and increased awareness, but also and very importantly due to an ageing population living longer with comorbidities and also the increased prescribing of agents that suppress the immune system. Additionally, it's associated with significant morbidity and mortality rates, particularly in severe cases (11,26, 27).

In general, it is estimated to occur in approximately 0.4 to 0.6 cases per 1,000 population per year (28). Trends of rising incidence have been demonstrated (29). It's more common in children and older adults ageing from 18-64 years, but the increases were highest in those aged >60 years. A marked male dominance was demonstrated being around 2.3:1 (70%), especially in people >60 years. Reasons for the male predominance are possibly due to differences in hygiene and preexisting comorbidities (30–32).

The occurrence of pleural empyema is in some cases associated with an underlying infectious process, most of the times being pneumonia. The infectious process is often preceded by pleural effusion. It is assumed that this was not adequately or promptly treated (7). The reasons for pleural effusions are multiple and divers: most commonly the underlying cause for the effusion is congestive heart failure, but also cancer, pulmonary embolism or pneumonia can be the cause. A more rare cause of pleural effusion are specific drugs as for example nitrofurantoin, amiodarone, methotrexate or clozapine (7).

1.1.5.1. Epidemiology in Germany and Upper Franconia

Since our hospital in Coburg belongs to the county of upper Franconia, we wanted to gain an overview of the patient population there. On December 31, 2022, the administrative region of Upper Franconia had 1,073,783 inhabitants, which corresponds to approximately 8% of the population of Bavaria (33). Of interest for this work was the information on how many people over the age of 75 are admitted annually to a REGIOMED clinic as inpatients. Statistical evaluation showed that from January 1, 2018, to December 31, 2023, a total of 128,259 patients over the age of 75 were admitted as inpatients to one of the REGIOMED clinics. Additionally, an overview of the number of patients diagnosed with pleural empyema during the same period was to be provided. Ultimately, it was found that between January 1, 2018, and December 31, 2023, a total of 490 patients with a diagnosis of pleural empyema were admitted. Of these, 168 were over 75 years old, which corresponds to approximately 34.3% of patients with diagnosis pleural empyema. Since the catchment area with 200.000 inhabitants of REGIOMED clinics

does not only include parts of Bavaria but also Thuringia, we can conclude that per year approximately 30/200.000 cases are treated in this area.

1.1.6. Risk factors for the development of pleural empyema

There are many risk factors that can contribute to the development of a pleural infection with pre-existing comorbidities being the most important ones. Patients with chronic respiratory and cardiovascular condition have the highest prevalence in developing pleural empyema (29). Other, independent risk factors for the development of pleural empyema include: Age under 60 years, poor oral hygiene, conditions predisposing to aspiration, intravenous drug abuse, diabetes, liver cirrhosis, and immunosuppressive diseases (8). One prospective study has identified six risk factors predicting the development of complicated parapneumonic effusion or empyema: albumin <30 g/l, sodium <130 mmol/l, platelet count >400 x 10(9)/l, C-reactive protein >100 mg/l and a history of alcohol abuse or intravenous drug use (34).

1.1.6.1 RAPID Score as risk factor evaluation

A new method to assess the risk of developing an empyema is the so-called RAPID score. The word RAPID is an acronym of Renal (urea), Age, fluid Purulence, Infection source (community vs. hospital acquired), Dietary (albumin) (35). RAPID score helps in assessing the severity of pleural empyema. To identify individuals at high risk of death and enhance therapeutic strategies, the RAPID score was developed. This score, one of the newer yet widely used clinical risk assessments, categorizes risk based on the aforementioned factors. Patients are then classified into low, medium, and high-risk categories. By doing so, healthcare providers can better plan the management of pleural empyema. Surgical intervention is a crucial aspect of treating pleural empyema, and the RAPID score aids in decision-making regarding the need for surgical procedures. Higher RAPID scores are associated with higher 90-day mortality rates, making it a valuable tool in assessing patient prognosis in pleural empyema cases (35,36).

1.1.7. Microbiology

There are many pathogens identified for the development of pleural empyema. First distinction is into Gram positive or Gram negative. Secondly it has to be differentiated between community and hospital acquired infections. A community acquired infection is defined as pneumonia that develops >48h after hospital stay (37). Depending on the underlying etiology, the causative bacterial agents are different. The most common cause of both, hospital and

community acquired infection are Gram positive aerobic bacteria. Also, in relation to surgery or trauma, *Staphylococcus aureus* seems to be the most important pathogen. (17, 38).

In the context of community-acquired empyema, gram-positive bacteria, particularly species within the *Streptococcus genus*, emerge as the primary causative agents (17). Namely *Streptococcus pneumoniae* and the *Streptococcus milleri (constellatus-intermedius-anginosus)* group (39) being the most prevalent. However, it's noteworthy that the presence of gram-negative bacteria in these cases often signals the presence of underlying comorbidities, such as alcohol abuse, gastroesophageal reflux disease (GERD), and diabetes, suggesting a more complex clinical scenario.

Conversely, hospital-acquired empyema presents completely different, with *Staphylococcus aureus* and *Pseudomonas species* being more prevalent. Of particular concern is the emergence of *methicillin-resistant S. aureus (MRSA)* strains, *Enterobacter species* and *Pseudomonas species* in healthcare settings, posing significant challenges to treatment due to their resistance profiles (17, 39). In literature, there are sources documenting the occurrence of pleural empyemas due to fungal infections. Primarily, there appears to be a correlation between prolonged hospitalization and immunosuppression in patients with pleural empyema due to fungal infections (40).

In general, pleural infection is mostly a polymicrobial infection, meaning not only one pathogen is responsible for the infection (41). Problematic in the diagnosis of pleural empyema is the high incidence of negative aspirates in standard culture. Therefore, blood culture bottles are used to increase the yield. To further increase the yield, pleural biopsy culture can be performed (42).

1.1.8. Symptoms

Various sources in the literature describe the symptoms of pleural empyema mostly as a nonspecific presentation. However, some complaints are commonly encountered: Cough, sputum production, fever, pleuritic-type chest pain (22, 17). Additionally, weight loss, loss of appetite, fatigue, and deterioration of general condition may also occur (43). Auscultatory findings in pleural empyema may include diminished breath sounds, dullness to percussion, and restricted chest wall movement. These manifestations can occur suddenly or over a period of several weeks. Distinguishing the symptoms from those of pneumonia is challenging, with no fundamental differences (43, 15). In the literature, it is described that lung diseases caused by aerobic bacteria clinically tend to present with sudden onset fever, chest pain, leucocytosis, and sputum production. Anaerobic infections appear to have a more insidious course. Loss of

appetite and weight loss are reported here. Infections with anaerobes are said to be common in patients with poor dental hygiene, in association with gastric content aspiration, and in alcohol dependence. In immunocompromised and elderly patients, the infection may be disproportionately mild compared to the severity of the infection. Similarly, the size of the effusion varies and does not provide insight into the precise cause of the disease (44).

1.2. Diagnosis

Essential for initiating appropriate therapy is a comprehensive diagnostic assessment. Unfortunately, the majority of parapneumonic effusions are not detected until later stages of infection due to their minimal expansion in the initial stages (43). Initially, a detailed medical history should be taken followed by a clinical examination. Subsequently, diagnosis is made through laboratory tests, imaging, and aspiration of the effusion. The initial indication can be seen in the differential white blood cell count, which typically shows leucocytosis (18). If suspicion of a pleural empyema is confirmed, a two-view chest X-ray should be performed (22, 18, 43). In the case of empyema, encapsulated effusion with air-fluid levels is visible. Another important diagnostic method is ultrasonography, which may reveal an inhomogeneous fluid collection in the pleural space, sometimes with partial organization, as well as septations (43, 18). Additionally, computed tomography (CT) is mentioned as a complementary diagnostic tool, providing information on the extent, characterization, and staging of the empyema. Even small effusion volumes can be detected by CT. CT imaging is especially important and useful for the differential diagnosis of malignant processes or abscesses (22, 43). Contrast-enhancing pleural thickening and the presence of air within the infiltrate strongly suggest pleural empyema, especially when contrast agent is applied (22). Following imaging procedures, effusion aspiration is usually performed. This should be done for any unclear pleural effusion that exceeds the dimensions of a typical simple pleural effusion. The microbiological, cytological, and biochemical analysis of the aspirate significantly influences subsequent therapeutic options (18). Parameters such as pH, glucose, LDH (Lactatdehydrogenase), and protein content are determined. For the appropriate selection of therapy, microbiological evidence is of utmost importance. Therefore, both aerobic and anaerobic blood cultures, as well as tuberculosis diagnostics, should always be conducted (43).

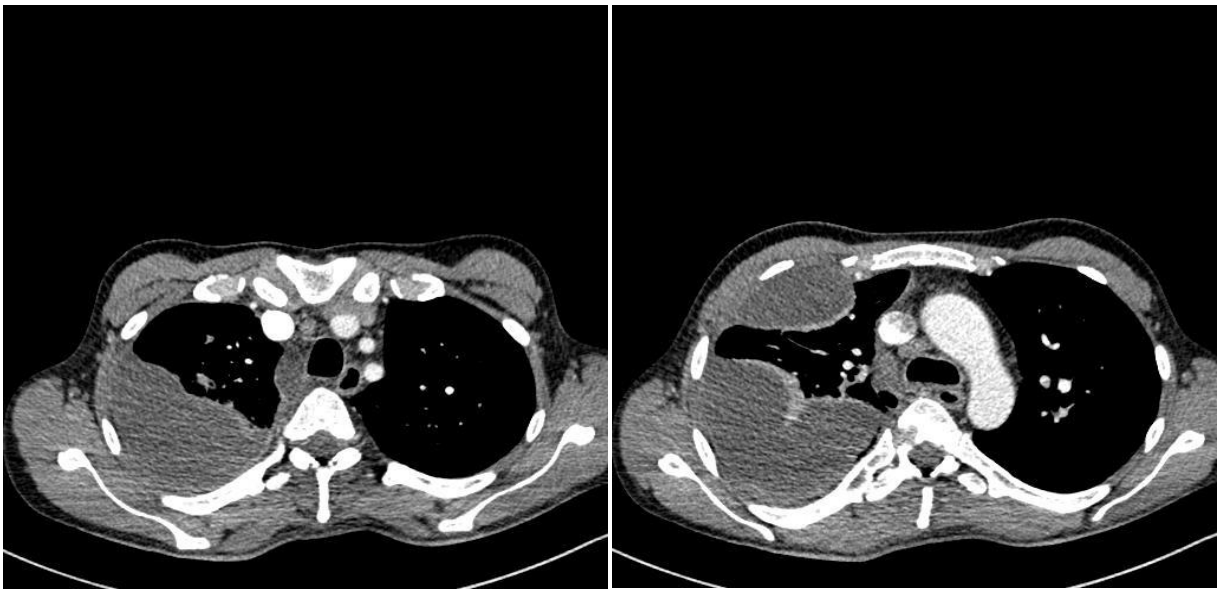

Figure 3 and 4. Thoracic CT scan: Atelectasis of the middle lobe, subsegmental atelectasis of the lower lobe due to fluid accumulation in the right pleural space.
Source: Sziklavari, Zsolt, PhD

1.2.1. Differential diagnosis

The differential diagnosis of pleural empyema encompasses a wide range of non-infectious and infectious etiologies. The most common non-infectious causes are malignancies (e.g. lung cancer or mesothelioma), connective tissue diseases (e.g. rheumatoid arthritis, systemic lupus erythematosus), pulmonary embolism, iatrogenic complications (e.g. postoperative empyema, chest-tube-related infections) (17). Macroscopically, a chylothorax can lead to wrong diagnosis of a pleural empyema. Therefore, triglyceride values must always be determined (43).

1.3. Therapy of pleural empyema

At first, different treatment options will be mentioned, before mentioning the treatment algorithm.

1.3.1. Conservative therapy

Conservative therapeutic strategies for pleural empyema include:

- Antibiotic therapy
- Ultrasound-guided puncture
- Chest tube alone
- Chest tube with fibrinolysis

- Chest tube with vacuum clothing with negative pressure (18).

1.3.1.1. Antibiotic therapy

The indication for antibiotic therapy is established from the moment of diagnosis of pleural empyema or complicated parapneumonic effusion. This also applies in cases where no microorganism can be detected microbiologically (22). It is recommended to administer antibiotics via intravenous access, with a minimum therapy duration of 14 days (43).

The AATS consensus guidelines for the management of empyema suggest the following for antibiotic therapy: The selection of empiric antimicrobial agents in the management of pleural empyema necessitates careful consideration of several key factors. Among these considerations are the risk of encountering resistant infections and the necessity for adequate coverage against anaerobic organisms. In cases where anaerobic infection is suspected or likely, empirical treatment with agents such as metronidazole or clindamycin is recommended to ensure comprehensive coverage. Moreover, the routine inclusion of empiric antibiotics targeting atypical organisms is generally deemed unnecessary in the management of pleural empyema. Instead, tailored antimicrobial therapy based on identified pathogens and their susceptibilities is done. In the context of hospital-acquired or postsurgical infections, a broader spectrum of antibiotic coverage is uses. This includes ensuring activity against methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa, which are commonly implicated in nosocomial infections. Aminoglycosides, although effective in many bacterial infections, are not recommended for the treatment of pleural empyema due to their inactivation within the empyema fluid environment. Furthermore, in cases of slowly progressing or chronic empyema, clinicians may withhold empiric therapy until culture results become available. This approach allows for more targeted and effective antibiotic therapy directed towards identified pathogens. In instances where there is a favourable response to initial therapy and adequate source control has been achieved, transitioning to oral antibiotic therapy may be considered to facilitate outpatient management and improve patient comfort (45).

1.3.1.2. Drainage therapy

Drainage therapy of pleural empyema is an essential part of the large therapy concept. Chest tube drainage is recognized as fundamental and essential for the management of acute empyema. Patients with empyema and a fluid collection require chest tube drainage to reach a reexpansion of the lung (43).

Uncomplicated parapneumonic effusions can be drained and treated through single or multiple punctures (43). As pleural parapneumonic effusions (PPEs) can rapidly progress to empyema within days, the decision regarding drainage therapy should lean towards installation of a thoracic drainage. Single puncture is a widespread technique, also in non-hospital clinical practice. Problematically, there is a known reluctance towards thoracic drainage placement these in non-surgical departments. This can lead to further delay of treatment and bad outcome of therapeutical success. Both small-bore (8 to 16 French) and large-bore ("surgical") drains (22 to 36 French) are utilized for drainage therapy. While single drainage placement is typical, some centres prefer combining apical and distal drains. Drainage procedures can be performed with or without imaging guidance (CT, ultrasound). Larger lumens are generally favoured, although controlled studies are lacking. However, numerous radiological publications suggest successful, sometimes superior, applicability of small-bore drains in PPE and pleural effusion (PE) cases. All drains should ideally be connected to continuous suction drainage (15 to 20 cm water column). Regular functional checks of the entire drainage system are crucial to ensure proper positioning and fast detection of any tube obstructions or kinks (17, 43).

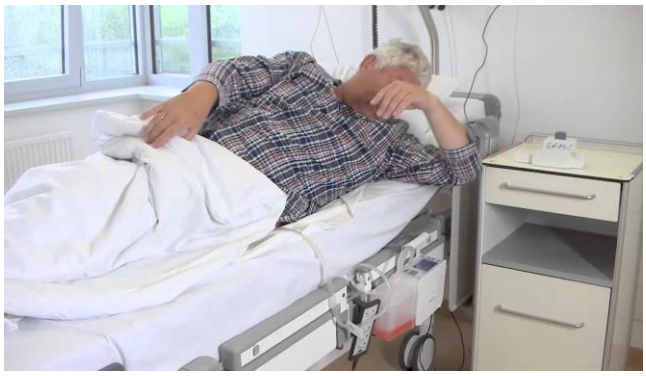

Figure 5. Geriatric patient with thoracic drainage. (Cited March 14 2024)
Link: https://www.youtube.com/watch?v=HH2dxSw0ZHQ

1.3.1.3. Intrapleural fibrinolytic therapy

Already in 1949, streptokinase pioneered intrapleural fibrinolysis (IFT), a therapeutic approach later reintegrated into the treatment protocols for PPE and PE over the past two decades. While streptokinase initially dominated IFT, recent years have seen a shift towards urokinase. The advantages of urokinase in IFT include improved tolerability and reduced risk of allergic reactions, albeit at a higher cost compared to streptokinase. Success rates of IFT are high, regarding literature (43). Practically, administering 100,000 IU of urokinase or 250,000 IU of streptokinase daily (46), diluted in 50 to 100 mL of isotonic NaCl solution, via a reclining drainage catheter, followed by clamping the drainage for two hours and then continuing with

continuous suction drainage, is carried out. The aim of IFT is to completely mobilize pleural fluid (47). If there is no immediate increase in drainage rate, it indicates IFT failure, prompting the exploration of alternative approaches. The duration of IFT should range between one and a maximum of ten days. If the treatment with IFT remains unsuccessful, an operative treatment should be considered (43).

1.3.2. Operative therapy

The aim of operative therapy is to evacuate pus, perform decortication, debridement and finally drainage.

The "Initiative Chronische Wunden" (ICW) defines debridement of chronic wounds as the removal of adherent, necrotic tissue, crusts, or foreign bodies from wounds (48). The aim is to remove pus and fibrinous septae within the pleural space and to clean the all the surfaces. This is done by rinsing the space with saline solution (49).

The first lung decortication was performed in 1895 by Delorme and is until now a well-known and often performed surgical procedure in the treatment of empyema. Primarily, it is indicated in cases of chronic empyema thoracis. It is performed by resecting the restrictive layer of the fibrous tissue overlying the lung, diaphragm and chest wall. This tissue typically develops in Stage III (fibrinous/organizing stage) according to ATS classification (Table 1), because of the fibroblastic ingrowth during that stage. Decortication is performed to reexpand the lungs, clearance of infection and prevention of fibrothorax and possible deformity that comes with it (50). Also, it is the preferred method over thoracoplasty which is another way to treat chronic empyema. Preference is because of less invasiveness (51).

In surgical therapy, a distinction must first be made into different operative techniques: open surgical therapy and minimal invasive surgery. The following operative techniques will be explained in more detail:

- VATS (Video-assisted thoracic surgery)
- Thoracoplasty
- Open window thoracostomy (OWT)
- VAC (Vacuum assisted closure)

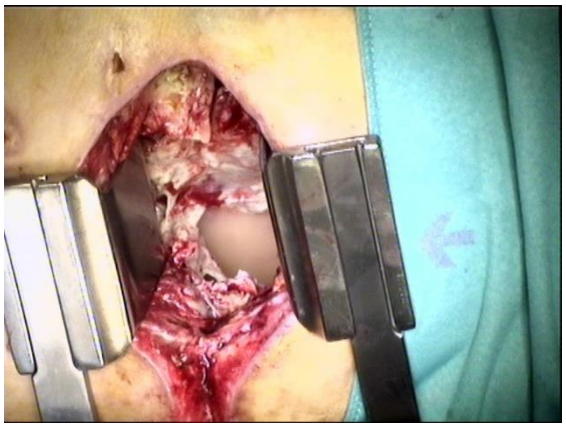

Figure 6. Intraoperative picture of pleural empyema.
Source: Intraoperative picture taken by Sziklavari, Zsolt, PhD

1.3.2.1. VATS

The typical VATS procedure entails making 3 to 4 incisions arranged in a triangular configuration to accommodate the insertion of scopes and instruments. Alternatively, a variation of VATS involving a single port has also been documented (52).

The technique is performed as follows: After confirming the proper positioning of the double-lumen tube (DLT) and cuff placement via fibreoptic bronchoscope, the patient is positioned laterally with the arm raised, and the operating table is adjusted for optimal surgical exposure. Three incisions are made for the anterior approach, forming a triangular configuration, with one incision serving as the utility port. The camera is inserted through this incision, and additional ports are created for instrumentation. The thoracoscope is used to assess the surgical field, and subsequent steps are determined based on the specific procedure. These are: Pus evacuation, debridement, decortication and drainage at the conclusion of surgery, connected to an underwater seal drain, depending on the surgical intervention (53, 52).

1.3.2.2. Open surgery

1.3.2.3. Thoracoplasty

The process known as thoracoplasty involves the surgical removal of certain sections of the chest wall, typically portions of the ribs, with the objective of either reducing the size of the chest cavity to address issues such as hollow spaces or to apply pressure to diseased lung tissue (54). Originally utilized primarily for treating severe forms of lung tuberculosis and resolving empyematous cavities, thoracoplasty has evolved over time. Contemporary approaches often incorporate adjunct procedures like thoracomyoplasty. Initially introduced in the late 19th

century as a remedy for advanced lung tuberculosis and as a final recourse for chronic pleural empyema, its necessity diminished with the advent of effective tuberculosis medications and advancements in empyema treatment. Despite its historical significance, the practice of thoracoplasty has significantly declined in recent decades, with instances of its application becoming increasingly rare and often executed incorrectly due to waning expertise and awareness of its precise indications and techniques (55). Common reasons for undergoing thoracoplasty include persistent or treatment-resistant abnormalities within the pleural cavity and infections of the lung or pleura that are resistant to multiple therapies (54). Examples encompass various conditions such as severe fibrotic changes in the remaining lung tissue following surgical resections, postoperative pleural empyema occurring after lung surgeries often in conjunction with limited remaining lung function, advanced destructive changes due to lung tuberculosis, ongoing presence of bronchopleural fistula (BPF) linked to empyema, and empyema that persists despite prior pneumonectomy attempts (55). Thoracoplasty follows two therapeutic goals:

- Infection cleansing and decontamination of wound
- Elimination of the cavity

Over time, many thoracoplasty methods have been developed by famous surgeons as for example Ferdinand Sauerbruch (55), with only two remnants that are mainly performed today:

- Thoracoplasty modified according to Lampl
- Video-assisted extrapleural thoracoplasty according to Giller

One of the key advantages of the technique according to Giller is the significantly reduced surgical trauma, with particular attention paid to minimizing disruption to the muscle structure. This approach, akin to other minimally invasive surgical methods, results in markedly reduced postoperative pain perception when compared to conventional techniques. Furthermore, another notable advantage is the lesser degree of deformation observed in the thoracic cage following the procedure (55).

1.3.2.4. Installation of OWT

Another treatment method for thoracic empyema is the installation of OWT. The thoracic window is the typical therapy for debilitated patients or patients after surgical pretherapy or drainage therapy who suffer from a persistent infection. Often, these patients suffer from postoperative empyema or bronchopleural fistulas (56). Open window thoracostomy is a drainage procedure for thoracic empyema that involves making a

thoracostomy on the suitable position to the empyema space. The skin incision is made along the costal bone just at the most expanded position of the empyema. After making the incision, the muscle is split to expose the thoracic wall, and a costal bone just under the incision is removed to create a window. The window is typically 8-10 cm long and up to 5 cm in diameter. The thickened empyema wall is then cut out according to the size of the window, and the skin edge and empyema wall are roughly sutured along the circular edge. In some cases, muscle flap transposition may be performed along with other procedures such as curettages on the empyema surface, closure of bronchopleural fistula, and thoracoplasty. This technique involves introducing a muscle flap into the cleaned-up space and suturing it on the empyema surface at several points (56).

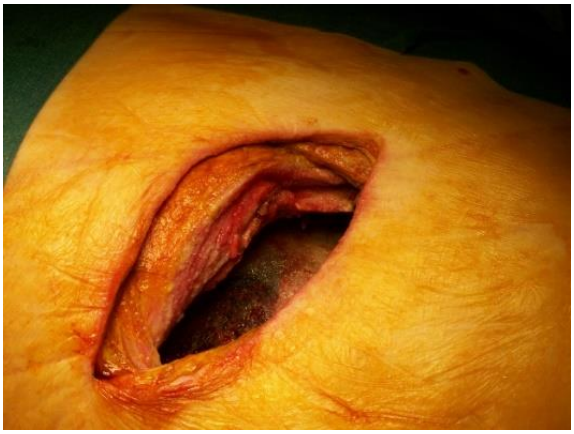

Figure 7. Intraoperative picture of open thoracotomy.
Source: Picture taken by Sziklavari, Zsolt, PhD

1.3.2.5. VAC-therapy

VAC is a treatment option for complicated pleural empyema and lung abscesses. It involves the use of negative pressure to promote wound cleaning and healing and the application of negative pressure to the pleural cavity using a vacuum sponge, which helps in the removal of infected fluid and promotes wound healing by formation of granulation tissue (57). VAC therapy has shown promising results as a safe and feasible treatment alternative for pleural empyema. It can be used as a primary treatment option for patients with stage II and III pleural empyema, especially in cases where conventional surgical approaches are not feasible. The therapy has been used in patients who have undergone thoracic surgery, with success rates in terms of infection resolution being high irrespective of previous treatment and cause of empyema (58). The procedure has been evaluated for both extrathoracic and intrathoracic/pleural applications. Initially, the intrathoracic VAC treatment was performed

through a thoracic window, but later a minimally invasive procedure called Mini-VAC was developed. This procedure minimizes damage to the osseous thorax. In cases of proven germ populations, an additional intrapleural rinsing with antiseptics called Mini-VAC-Instill can be beneficial. The advantages of the Mini-Vac/Mini-VAC-Instill method include immediate secretion suction, rapid germ eradication, improvement of lung expansion, and shorter treatment times (59).

1.3.3. Treatment algorithm

1.3.3.1. AATS algorithm for the optimal treatment of pleural empyema

Considering the AATS, an algorithm of treatment for pleural empyema, acute or chronic can be established:

1. Evaluation

Firstly, the patient has to be evaluated initially. Pleural ultrasound (US) should be routinely performed along with a conventional chest x-ray (CXR) for diagnostic purposes and image-guidance for pleural interventions. Computed tomography (CT) of the chest is recommended when pleural space infection is suspected. The choice of initial approach depends on the patient's condition, pleural space status, and underlying lung condition.

2. Conservative therapy

In cases of uncomplicated pleural effusion without signs of infection, conservative management with antibiotics and observation may be sufficient without the need for surgical intervention. Also, in cases of early empyema or uncomplicated pleural effusions, surgical intervention may not be necessary, and conservative measures like antibiotics and drainage may be effective. Finally, patients who are low risk for complications and have a well-controlled infection may not require immediate surgical intervention; conservative management can be considered in such cases.

3. Fibrinolytic therapy

Fibrinolytic therapy is potentially beneficial in the management of parapneumonic effusions and empyemas in adults, especially when there is evidence of loculated effusions or inadequate drainage. It may be indicated when initial treatments such as antibiotics and drainage are ineffective in resolving the pleural infection or empyema.

4. Surgical therapy

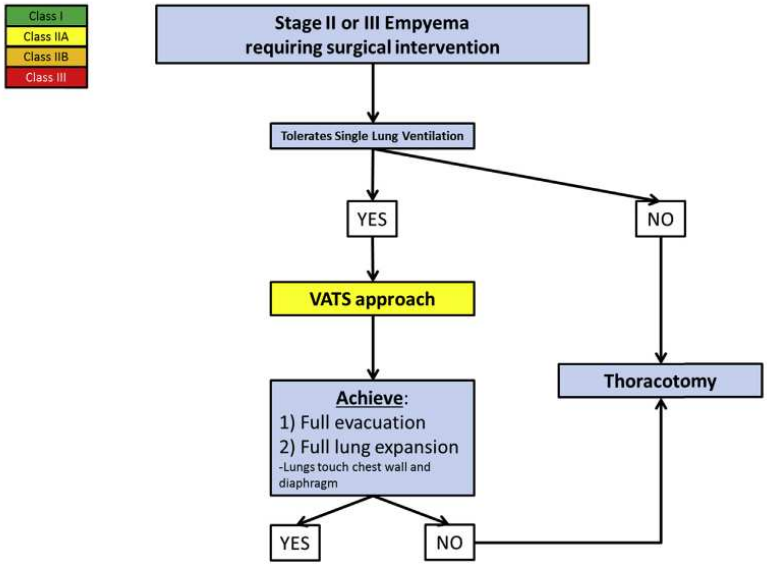

Figure 8. Treatment algorithm of AATS.
Link: https://www.jtcvs.org/article/S0022-5223%2817%2930152-6/pdf

Surgical therapy should be considered when conservative measures such as antibiotics and drainage fail to resolve the empyema or pleural infection effectively. In cases of complicated empyema with loculated effusions or significant septations, surgical intervention may be necessary for adequate drainage and resolution. If the patient continues to exhibit symptoms of infection, such as persistent fever, chest pain, or respiratory distress, despite appropriate medical management, surgical therapy should be considered. Patients with recurrent empyema or those at high risk for recurrence may benefit from surgical intervention to prevent future episodes and complications. Chronic empyema cases that do not respond to conservative measures may require surgical therapy for definitive management and resolution of the infection as pleural drainage procedures become ineffective at this stage. Generally, VATS is preferred over thoracotomy for acute empyema due to benefits like improved pain control, shorter hospital stay, and reduced complications. VATS is also cost-effective compared to open thoracotomy for managing empyema (60). Open thoracotomy is indicated for stage II and III empyema cases, where more extensive surgical intervention, such as decortication, is required for effective management. If a VATS approach is attempted but deemed inadequate or unsuccessful, open thoracotomy may be necessary for complete drainage and treatment. In cases where there is a BPF or visceral pleural rents leading to large air leaks, open thoracotomy may be preferred over VATS to address these specific. For patients with chronic or recurrent

empyema infections that require long-term drainage or management, open thoracotomy with the creation of a thoracostomy window may be indicated for definitive treatment.

1.3.3.2. Algorithm of the British Thoracic Society

The British Thoracic Society (BTS) has provided comprehensive guidelines for the management of pleural diseases, including recommendations for the treatment of pleural infections. The algorithm begins with the initial assessment of patients presenting with suspected pleural infections, including a thorough clinical history, physical examination, and diagnostic investigations such as chest imaging and pleural fluid analysis (27). Once the diagnosis of pleural infection is confirmed, the algorithm proceeds as follows:

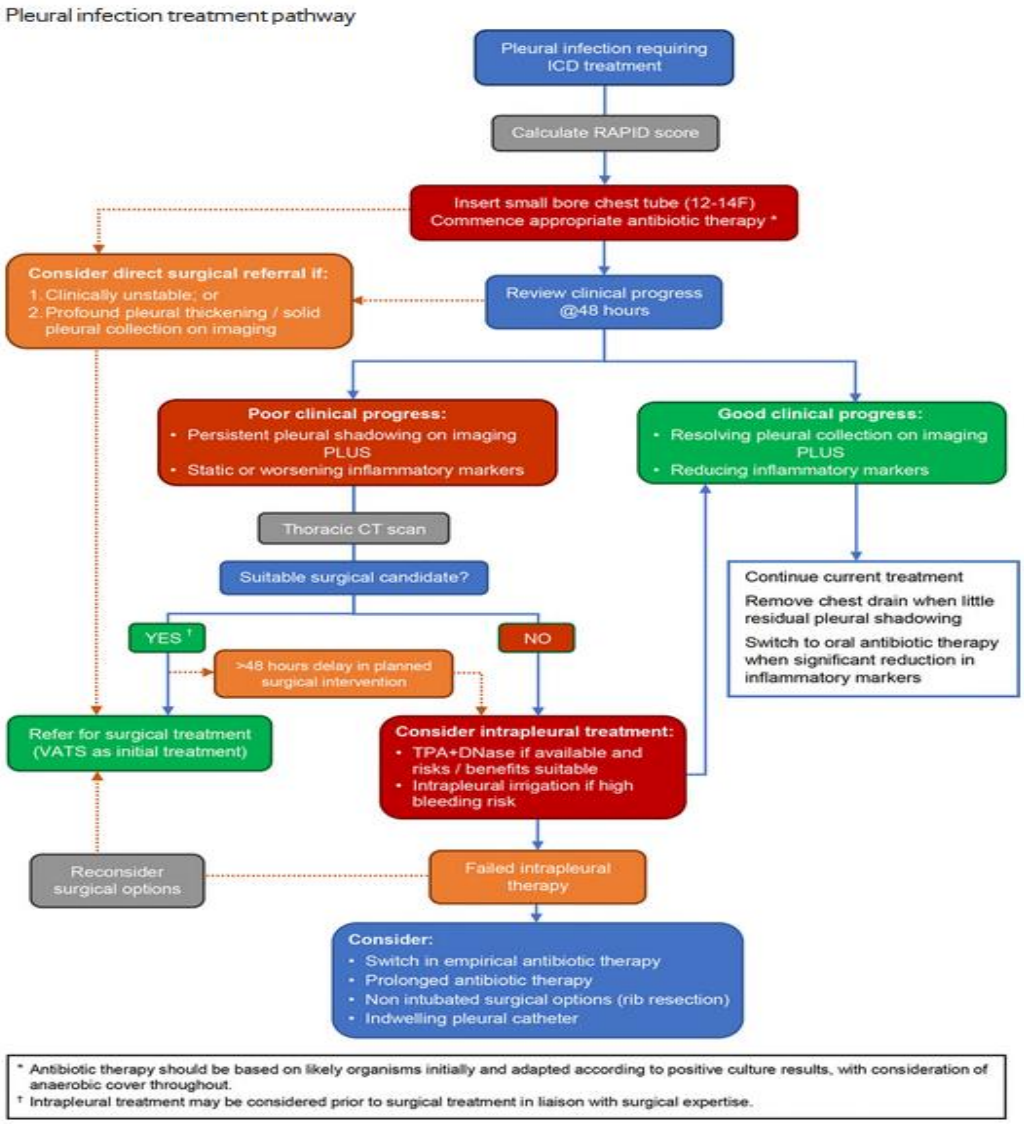

Figure 9. Treatment algorithm of BTS (Cited April 3rd 2024):
Link: https://thorax.bmj.com/content/thoraxjnl/78/11/1143.full.pdf

1. **Assessment of Severity:**

The severity of the pleural infection has to be determined, based on clinical and radiological findings, as well as the presence of systemic signs of infection such as fever, tachycardia, and leucocytosis. Additionally, pleural infections should be classified into uncomplicated, complicated, and loculated based on the extent of pleural involvement and the presence of complicating factors.

2. **Initial Management:**

Algorithm suggests the initiation of broad-spectrum empirical antibiotic therapy targeting common pathogens implicated in pleural infections, including Streptococcus pneumoniae, Staphylococcus aureus, and anaerobic bacteria. On top of that, the need for pleural fluid drainage should be considered, either by thoracentesis or chest tube insertion, based on the severity of symptoms, presence of loculations, and risk of progression to complicated disease. Provide supportive measures such as analgesia, oxygen therapy, and fluid resuscitation as indicated.

3. **Assessment of Response:**

Monitor clinical response to initial management, including resolution of symptoms, improvement in inflammatory markers, and radiological findings. Re-evaluation of the need for further interventions based on the patient's clinical course and response to treatment should be made.

4. **Further Interventions:**

Additional pleural interventions such as fibrinolytic therapy or surgical decortication in patients with complicated or loculated pleural infections who fail to respond adequately to initial management have to be considered. Consult with multidisciplinary teams, including respiratory physicians, infectious disease specialists, and thoracic surgeons, for decision-making regarding further interventions is important.

5. **Long-term Management:**

For long term management, the algorithm suggests to optimize antibiotic therapy based on culture and sensitivity results, with consideration of de-escalation or continuation of therapy to complete the course. Also, appropriate follow-up care, including monitoring for recurrence of pleural infection, resolution of any residual pleural collections, and rehabilitation as needed should be provided (27).

1.4. Complications of pleural empyema

The consequences of a pleural empyema can be serious. Not only can an empyema lead to sepsis, it can even result in septic shock and, in the worst-case scenario, death. Complications may also arise from the improper placement of a drainage tube. Even if the drainage does not evacuate all of the wound secretion, this can lead to serious complications such as pneumothorax, bronchopleural fistulas, and pleural fibrosis with subsequent trapped lung. One rare complication, empyema necessitans, refers to the extension and subsequent dissection into the subcutaneous tissue of the chest wall (8). Also, respiratory distress can be a common symptom of complications (17).

1.5. Hallmarks of the geriatric patient

Geriatric patients are primarily characterized not by their age on the calendar ("chronological age"), but by a distinct multifaceted array of issues within an aging body ("biological age"). As defined by both scientific societies (the German Society of Geriatrics, the German Society of Gerontology and Geriatrics) and the Federal Association of Geriatrics e. V., geriatric patients are identified by either 1. exhibiting typical geriatric multimorbidity and being of advanced age (typically 70 years or older); in this context, the presence of typical geriatric multimorbidity takes precedence over chronological age; or 2. being aged 80 and over due to the inherent heightened vulnerability associated with aging, such as the onset of complications and subsequent illnesses, the risk of chronic conditions, and the increased likelihood of losing autonomy leading to a decline in self-care capabilities (61).

The number of geriatric patients continues to increase. Increased age is often associated with high degree of frailty and multimorbidity and thus more susceptibility to infections and other severe conditions (62). With older age, the incidence of falls increases and thus the risk for fractures of bones following hospital stays and often surgery. Risk factors that contribute to falls include changes in postural control, changes in vision, presence of acute and chronic illnesses, changes in CNS and less strength. Also medication can increase the risk for falling (63). On top of that many geriatric patients are immunodeficient due to undernutrition (64). Age is an acknowledged risk factor for pneumonia and pleural empyema (65). The incidence of community acquired pneumonia increases with every decade of life. Pneumonia of the elderly is associated with higher lethality due to increased age, comorbidities and decreased functionality of the patients (37). Due to comorbidities, is frailty more likely that geriatric patients have a poorer clinical course resulting, in case of pleural empyema, in sepsis more easily. (65). Studies evaluated that highest morbidity is among patients with nursing-home acquired pneumonia that are bedridden (37).

2 OBJECTIVES

2.1. Aims

The aim of the presented study was to analyse clinical data of geriatric patients over 75 years of age with diagnosed pleural empyema hospitalized at the REGIOMED Clinics and to evaluate and compare outcomes of different types of therapy under the influence of bad prognostic factors. Furthermore, the importance of RAPID diagnostics in predicting the outcome in geriatric patients was analysed.

2.2. Hypothesis

1. Older people with diagnosis of pleural empyema can be treated invasively, because the outcomes are acceptable.
2. RAPID diagnostics can effectively predict certain clinical outcomes in patients over 75 years old.

3 MATERIALS AND METHODS

3.1 Patient Selection and Inclusion Criteria

Data retrieval was carried out by reviewing and analysing medical case records. Also, family doctors and hospitals that took part of the primary care were consulted in case of missing data.

For the retrospective study, patients who met the following criteria were included:

- Patients who were hospitalized between January 2017 and May 2023 in one of the REGIOMED hospitals: Coburg, Lichtenfels, Sonneberg, Hildburghausen, Neustadt bei Coburg
- Diagnosis of pleural empyema in stage I, II, or III was mandatory
- Treatment and information about the entire patient's stay had to be traceable and accessible

3.2 Data collection

At the onset of data collection, lists of patient names were generated for those diagnosed with pleural empyema (pyothorax) between January 2017 and May 2023 at REGIOMED hospitals in Coburg, Lichtenfels, Sonneberg, Hildburghausen, or Neustadt bei Coburg, and were subsequently treated. Data collection took place at the facilities of the Medical School REGIOMED in Coburg, at the Coburg Hospital, and at the IT training room at the Coburg site. The ORBIS program was used as the data source. The primary source of data was the final discharge letters from the Thoracic Surgery Department in Coburg, as many patients were either directly admitted there, consulted by Coburg, or transferred there for further treatment. In addition to the letters from the Thoracic Surgery Department in Coburg, letters from other departments in Coburg, such as Cardiology or Trauma Surgery, as well as letters from Lichtenfels, Sonneberg, Hildburghausen, or Neustadt bei Coburg, were used for data collection. The collected data were then entered into an Excel spreadsheet. Categorical variables were encoded as 0 = not applicable and 1 = applicable. Quantitative variables were either recorded or entered as numerical values into the table. If a value was missing or not found, the corresponding field was left blank. Patients were coded with an ID, and therefore names were not mentioned.

For calculation of RAPID score, Mdcalc was used. The scoring system for assessing risk is based on several parameters. For blood urea nitrogen (BUN) levels in serum: a level less than 14 mg/dL (5 mmol/L) scores 0 points, between 14 and 23 mg/dL (5-8 mmol/L) scores 1 point, and greater than 23 mg/dL (8 mmol/L) scores 2 points. Age is scored as follows: under 50 years scores 0 points, 50 to 70 years scores 1 point, and over 70 years scores 2 points. For

the presence of purulent pleural fluid, the scoring is 0 points for yes and 1 point for no. The source of infection is scored 0 points for community-acquired and 1 point for hospital-acquired. Serum albumin levels are scored as follows: levels greater than or equal to 2.7 g/dL (27 g/L) score 0 points, and levels less than 2.7 g/dL (27 g/L) score 1 point. The risk assessment based on the total points is categorized as follows: 0 points indicate low risk with a 1.5% mortality rate at 3 months, 1 point indicates low risk with a 1.5% mortality rate at 3 months, and 2 points also indicate low risk with a 1.5% mortality rate at 3 months. A score of 3 or 4 points indicates medium risk with a 17.8% mortality rate at 3 months. Scores of 5, 6, or 7 points indicate high risk with a 47.8% mortality rate at 3 months.

3.3 Material and Methods

Patients with diagnosis of pleural empyema were included in the study. The study included N = 344 patients (table 4). During the assessment, some patients were excluded due to missing data. 91/344 (26.5%) were women and 253/344 (73.5%) were men.

Initially, we explored and statistically analyzed five different treatment options. Due to overlapping treatments, which distorted the overall evaluation and resulted in a lack of clinical relevance, we reduced our treatment options to three parameters. Some patients had to be excluded due to missing data on the different treatment options, leaving us with a pool of 332 patients for the various types of therapies. The first of these three subgroups is the conservative treatment group, which includes antibiotic administration, puncture, drainage, and physiotherapy. In our Analysis 66/332 (19,9%) Patients were treated conservatively. The next subgroup is the minimally invasive surgical treatment group, treated operatively with VATS in our data analysis 225/332 (67,8%). The last group is the open surgically treated group which accounted for 41/332 (12,3%) patients.

Another parameter identified the cause of the pleural empyema, categorized into parapneumonic origin, superinfection, and other causes. Parapneumonic origins were seen in 205/344 patients (59.6%), superinfection in 98/344 (28.5%) patients, and other causes in 40/344 patients (11.6%). The "pathogen" parameter aimed to identify the pathogens involved. The most common pathogens were Staphylococcus aureus in 40 patients, Escherichia coli in 23 patients, and Streptococcus pneumoniae in also 23 patients. Other pathogens were identified in smaller numbers. In a significant portion of cases, however, no specific pathogen could be identified and documented.

The initial antibiotic therapy was examined to determine whether there was a change in antibiotic treatment during the clinical course. In total, we identified 12 different antibiotics. In

some patients, more than one antibiotic was given, ergo a switch occurred. This antibiotic switch was performed in 158/344 (45.9%) patients and not performed in 186 /344 patients (54.1%), indicating that the therapy was continued with the initial antibiotic treatment.

The evaluation led to a decision between three treatment options. On one hand, the conservative method (antibiotics/puncture/pleural drainage) in 66/332 (19.9%), additionally the therapy involving insertion of a chest drain. Furthermore, we distinguished between MIS (minimally invasive surgery) 225/332 (67.8%) and open surgical therapy in 41/332 (12.3%).

Another parameter was the timing of the initiation of therapy. Here, we differentiated between initial surgical therapy before or after 5 days of primary presentation. Regarding the initiation of therapy, 250/344 (72.6%) were treated within a time range of five days, whereas 92/344 (26.7%) were treated after 5 days. In 2/344 cases (0.06%), data was not correctly documented. In these cases it was not possible to conclude when treatment started.

We defined immunocompromised patients as those currently undergoing chemotherapy, taking steroids, or immunocompromised for other reasons. In total, 99/344 (28.8%) patients were classified as immunosuppressive, while 244/344 (70.9%) showed no signs of immune system weakness. One patient is missing due to missing data in this case.

Finally, we calculated the RAPID score in 342 patients. 19/342 (5%) had a RAPID score of 0. 37/342 (10.8%) of 1, 57/342 (16.7%) of 2 and 88/342 (25.7%) of 3. 67/342 (19.6%) had a RAPID score of 4, while 61/342 (17.8%) had a score of 5. Finally, 13/342 (3.8%) had a RAPID score of 6.

3.4 Statistical analysis

The data was analysed using statistical program and Microsoft Excel. Crosstabulation (Cross-tab) presents the frequencies and percentages of observations for each combination of categories between two variables. This method provides a clear overview of the data distribution across categories, allowing for an initial assessment of potential associations. The chi-square test is a statistical method used to determine if there is a significant association between two categorical variables. It compares the observed frequencies in the crosstab table to the expected frequencies if the two variables were independent. The null hypothesis for the chi-square test states that there is no association between the variables. A low p-value (typically < 0.05) leads to the rejection of the null hypothesis, indicating evidence of an association between the variables. Fisher's exact test is another statistical test used to determine the association between two categorical variables, particularly when the sample sizes are small. It calculates the exact probability of observing the data under the null hypothesis of independence. The Omnibus Test was used to evaluate whether there are any statistically significant

differences among multiple groups or variables. Levene's Test was used to compare the means of two or more groups, ensuring that the variance among these groups is similar to validate the results of subsequent analyses. Cox and Snell R Square provides an indication of how well a logistic regression model explains the variability of the outcome variable. It measures the proportion of the variance in the dependent variable that is predictable from the independent variables. Additionally, the Nagelkerke R Square Test was used because it offers an adjusted version of the Cox and Snell R^2, modifying it to achieve a maximum value of 1, making it more interpretable and comparable to the traditional R^2 used in linear regression. Finally, the -2-log likelihood was used in model comparison, hypothesis testing, and assessing model fit.

4 RESULTS

As shown in table 4 and 5 as well as figure 10 and 11, the median age of the individuals in the sample is 66.2 years, with ages ranging from 3 to 96 years, indicating a diverse age distribution. The standard deviation of 15.28 years points to significant variability in the ages of the participants. The age percentiles reveal that most individuals are between 59 and 78 years old. The gender distribution is skewed towards males, who represent nearly three-quarters of the sample (73.5%), while females make up just over a quarter (26.5%).

When focusing on the population >75 years old being in fact 110/344 (32%) individuals in this age group, the average age is 81.4 years, with a relatively narrow spread indicated by a standard deviation of 4.07 years. The ages range from 76 to 96 years, with the majority falling between 78 and 84 years, as shown by the 25th and 75th percentiles. In terms of gender distribution, males constitute a larger proportion at 66.4%, with females making up the remaining 33.6%.

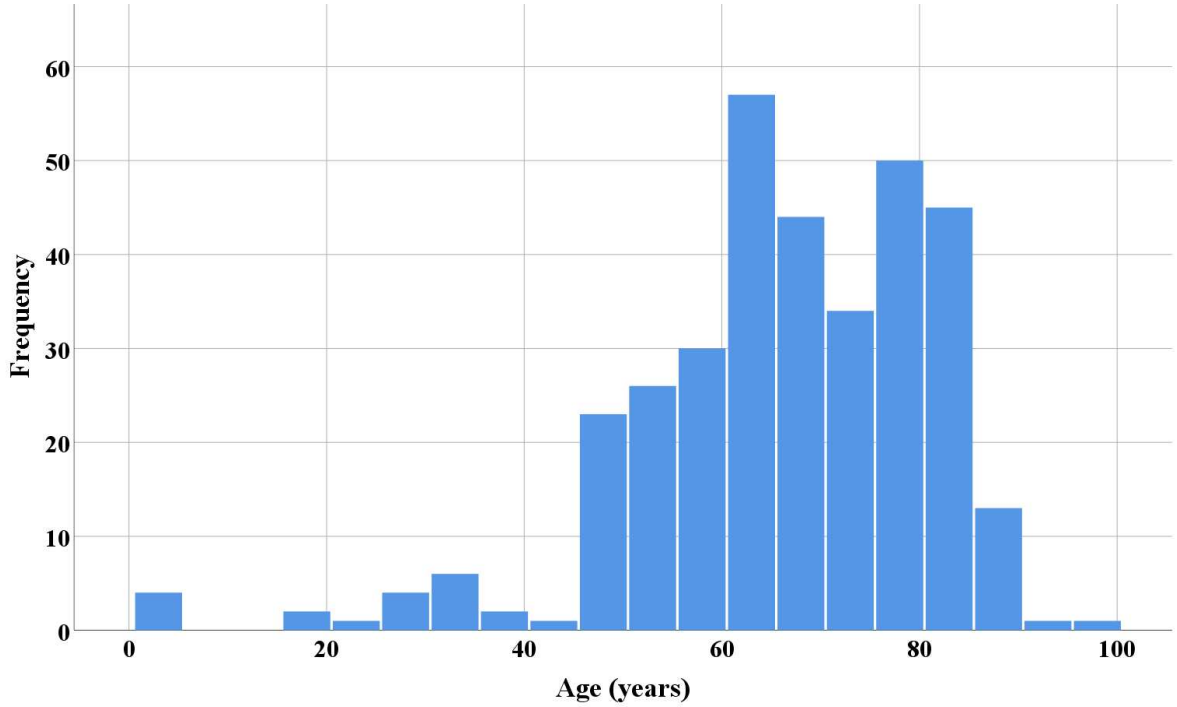

Figure 10. Age and gender, descriptive statistics, total

Table 4: Age, gender, descriptive statistics, total

Age (years)	Valid N	344
	Mean	66.2
	Standard Deviation	15.28
	Minimum	3

	Percentile 25		59.0
	Median		67.0
	Percentile 75		78.0
	Maximum		96
Gender	male	N (%)	253 (73.5%)
	female	N (%)	91 (26.5%)
	Total	N (%)	344 (100.0%)

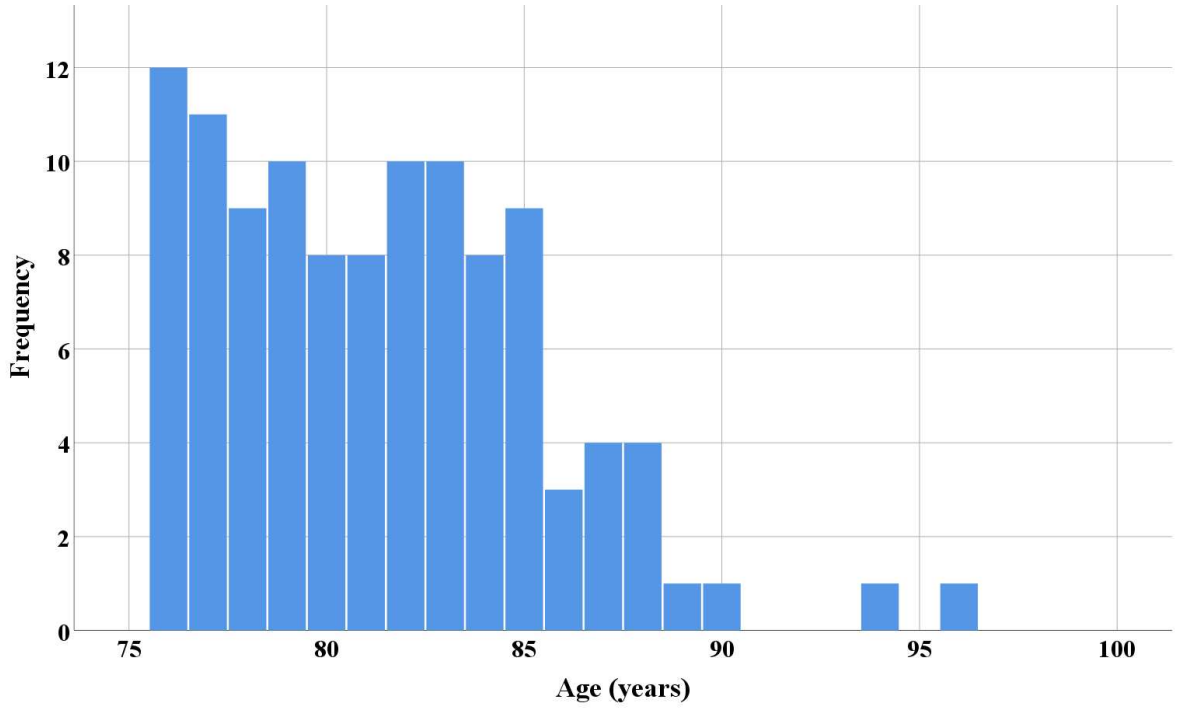

Figure 11. Age, total

Table 5: Age and gender, descriptive statistics, >75 years

Age	Valid N	110
	Mean	81.4
	Standard Deviation	4.07
	Minimum	76
	Percentile 25	78.0
	Median	81.0

	Percentile 75		84.0
	Maximum		96
Gender	male	N (%)	73 (66.4%)
	female	N (%)	37 (33.6%)
	Total	N (%)	110 (100.0%)

4.1 Treatment outcomes in patients > 75 years

4.1.1. Hospital mortality

When focusing on the whole population, out of 110 patients, due to missing data, only 106 patients were analysed. 20/106 (18.9%) out of all patients died in hospital, while 86/106 (81.1%) survived. An overview of patients who received minimal invasive surgical treatment compared to hospital mortality is provided in table 6.

Since minimal invasive surgery is the treatment of choice in stage II and stage III pleural empyema, the mortality rate associated with this type of treatment was assessed secondly. Out of 71/106 (66.9%) patients over 75 years of age underwent minimal invasive surgery. Out of these 71 patients, 5 died. So, the overall in hospital mortality in patients >75 years of age who underwent minimal invasive surgery was 7%. On the other hand, 66 patients survived after the intervention, in percent 92.9%.

Table 6: Type of the therapy, minimal invasive surgery vs. in hospital mortality >75 years

			In hospital mortality		
			no	yes	Total
Minimally invasive	No	Count	20	15	35
		% within Minimally invasive	57.1%	42.9%	100.0%
		% within In hospital mortality	23.3%	75.0%	33.0%
		% of Total	18.9%	14.2%	33.0%
	Yes	Count	66	5	71
		% within Minimally invasive	93.0%	7.0%	100.0%

		% within In hospital mortality	76.7%	25.0%	67.0%
		% of Total	62.3%	4.7%	67.0%
Total		Count	86	20	106
		% within Minimally invasive	81.1%	18.9%	100.0%
		% within In hospital mortality	100.0%	100.0%	100.0%
		% of Total	81.1%	18.9%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	19.644[a]	1	0.000		
Fisher's Exact Test				0.000	0.000
N of Valid Cases	106				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 6.60.

b. Computed only for a 2x2 table

An overview of hospital mortality in people >75 years associated with factors correlating with this hospital mortality is provided in table 7. These factors are gender, cause, no change of antibiotics, initial therapy, multimorbidity and immunosuppression. The provided data outlines the outcomes of logistic regression analysis concerning in-hospital mortality among patients aged over 75 years. The logistic regression model yielded a non-significant result, with a p-value of 0.173. It explained approximately 14.8% of the variability in in-hospital mortality among patients in this age group, as indicated by the Nagelkerke R Square value. The omnibus test of model coefficients revealed that the overall set of predictor variables, including gender, cause of empyema, antibiotic therapy change, initial therapy, multimorbidity, and immunosuppression, did not significantly correlate with in-hospital mortality among patients over 75 years old. Specifically, the model examined the associations of various variables with in-hospital mortality among patients over 75 years old, such as gender and cause of empyema along with antibiotic therapy change, initial therapy, multimorbidity, and immunosuppression. Detailed logistic regression coefficients, standard errors, Wald statistics, degrees of freedom, and p-values for each predictor variable are provided.

Table 7. Variables correlating with in hospital mortality >75 years

Omnibus Tests of Model Coefficients				
		Chi-square	df	Sig.
Step 1	Step	10.281	7	0.173
	Block	10.281	7	0.173
	Model	10.281	7	0.173

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	94.355[a]	0.094	0.148

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than 0.001.

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	Gender (female)	-0.980	0.653	2.253	1	0.133	0.375	0.104	1.349
	Cause			5.127	2	0.077			
	Cause (superinfection)	0.403	0.601	0.448	1	0.503	1.496	0.460	4.861
	Cause (other causes)	1.678	0.741	5.126	1	0.024	5.353	1.253	22.877
	Change of antibiotic (no)	-0.515	0.536	0.923	1	0.337	0.597	0.209	1.709
	Initial therapy (yes)	-0.678	0.658	1.062	1	0.303	0.508	0.140	1.843
	Multimorbidity (yes)	1.403	1.137	1.521	1	0.217	4.066	0.438	37.770
	Immunsuppression (yes)	-0.016	0.589	0.001	1	0.979	0.984	0.310	3.122
	Constant	-2.360	1.134	4.334	1	0.037	0.094		

a. Variable(s) entered on step 1: Gender, Cause, Change of antibiotic_no, Initial therapy, Multimorbidity, Immunsuppression.

4.1.2 Hospital stay

Another parameter in our statistics was the length of hospital stay. Shown in table 8, we distinguished between patients who stayed in the hospital for more than 14 days, which in our case was 237/344 (68.9%) patients, and those who stayed for less than 14 days, totalling 104/344 (30.2%) patients. 60/344 (17.4%) patients were readmitted to the hospital within a year due to a recurrence or a secondary illness, while 282/344 (82%) did not require readmission within the year. After one year, 260/344 (75.6%) patients were still alive, while 80/344 (23.3%) patients died. Median postoperative stay, measured in days, was 14.14 days.

The logistic regression model concerning the hospital stay in patients aged over 75 years was not statistically significant, with a p-value of 0.101. This indicates that the model as a whole did not significantly predict hospital stays among patients over 75 years old. However, the model explained approximately 15.5% of the variability in hospital stays, as indicated by the Nagelkerke R Square value. The omnibus test of model coefficients indicates that the overall set of predictor variables did not significantly correlate with hospital stays among patients over 75 years old. Some specific variable effects as gender, cause of hospital stay, antibiotic therapy change, other variables such as multimorbidity and immunosuppression did not demonstrate significant associations with hospital stays among patients over 75 years old. Only initial therapy emerged as a significant predictor of hospital stays. Patients receiving initial therapy had substantially higher odds of hospital stays lasting over 14 days, with an odds ratio of 3.706 (95% CI: 1.120-12.256, p = 0.032).

Table 8: Variables correlating with hospital stay >75 years

Omnibus Tests of Model Coefficients				
		Chi-square	df	Sig.
Step 1	Step	11.987	7	0.101
	Block	11.987	7	0.101
	Model	11.987	7	0.101

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	114.732[a]	0.109	0.155

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than 0.001.

Variables in the Equation									
								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Gender (female)	-0.144	0.524	0.075	1	0.784	0.866	0.310	2.418
	Cause			0.559	2	0.756			
	Cause (superinfection)	0.041	0.525	0.006	1	0.938	1.042	0.372	2.918
	Cause (other causes)	-0.516	0.735	0.494	1	0.482	0.597	0.141	2.518

	Antibiosewechsel (no)	0.852	0.478	3.175	1	0.075	2.344	0.918	5.985
	Initial therapy (yes)	1.310	0.610	4.607	1	0.032	3.706	1.120	12.256
	Multimorbidity (yes)	0.710	0.676	1.104	1	0.293	2.035	0.541	7.657
	Immunsuppression (yes)	-0.881	0.506	3.033	1	0.082	0.414	0.154	1.117
	Constant	-0.065	0.688	0.009	1	0.924	0.937		
a. Variable(s) entered on step 1: Gender, Cause, Change of antibiotic_no, Initial therapy, Multimorbidity, Immunsuppression.									

4.1.3 Hospital readmission due to recurrence or following disease

Hospital readmission due to recurrence was associated with factors like gender, cause, no change of antibiotics, initial therapy, multimorbidity, and immunosuppression, as seen in table 9. The model was not statistically significant (p=0.133) but explained 16.4% of variability in readmissions (Nagelkerke R Square). Gender did not significantly influence readmission rates (p=0.421), while the cause did (p=0.046), with superinfection causing pleural empyema increasing readmission odds (odds ratio: 3.715). Antibiotic therapy change, initial therapy, and multimorbidity were not significant, but immunosuppression increased readmission odds (odds ratio: 3.214, p=0.044).

Table 9: Variables correlating with hospital readmission >75 years

Omnibus Tests of Model Coefficients				
		Chi-square	df	Sig.
Step 1	Step	11.124	7	0.133
	Block	11.124	7	0.133
	Model	11.124	7	0.133

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	88.171[a]	0.101	0.164
a. Estimation terminated at iteration number 5 because parameter estimates changed by less than 0.001.			

Variables in the Equation							
	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)

								Lower	Upper
Step 1[a]	Gender(female)	-0.521	0.648	0.646	1	0.421	0.594	0.167	2.116
	Cause			6.140	2	0.046			
	Cause(superinfection)	1.312	0.581	5.107	1	0.024	3.715	1.190	11.595
	Cause(orher causes)	-0.538	1.149	0.220	1	0.639	0.584	0.061	5.547
	Antibiosewechsel (no)	0.357	0.561	0.404	1	0.525	1.429	0.475	4.293
	Initiale Therapie(yes)	-0.019	0.615	0.001	1	0.975	0.981	0.294	3.272
	Multimorbidität(yes)	-0.434	0.776	0.312	1	0.576	0.648	0.142	2.967
	Immunsuppression(yes)	1.167	0.579	4.064	1	0.044	3.214	1.033	9.999
	Constant	-2.027	0.859	5.563	1	0.018	0.132		

a. Variable(s) entered on step 1: Gender, Cause, Change of antibiotic_no, Initiale Therapie, Multimorbidity, Immunsuppression.

4.1.4 Survival after one year

Finally, the survival after one year was analyzed, as shown in table 10. The logistic regression model was not statistically significant, with a p-value of 0.187. This indicates that the model as a whole did not significantly predict survival after one year among this demographic. However, the model explained approximately 12.8% of the variability in survival, as indicated by the Nagelkerke R Square value. The omnibus test of model coefficients suggests that the overall set of predictor variables did not significantly correlate with survival after one year among patients over 75 years old. Again, specific variable effects included gender, cause of survival, antibiotic therapy change and initial therapy, multimorbidity and immunosuppression. All these variables were not statistically significant.

Table 10: Variables correlating with survival after one year >75 years

Omnibus Tests of Model Coefficients				
		Chi-square	df	Sig.
Step 1	Step	10.035	7	0.187
	Block	10.035	7	0.187
	Model	10.035	7	0.187

Model Summary									
Step	-2 Log likelihood		Cox & Snell R Square		Nagelkerke R Square				
1	124.666[a]		0.094		0.128				
a. Estimation terminated at iteration number 5 because parameter estimates changed by less than 0.001.									
Variables in the Equation									
		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	Gender(female)	-0.027	0.483	0.003	1	0.956	0.973	0.378	2.509
	Cause			2.256	2	0.324			
	Cause (superinfection)	0.325	0.496	0.429	1	0.513	1.384	0.523	3.663
	Cause (other causes)	-0.809	0.696	1.350	1	0.245	0.445	0.114	1.743
	Change of antibiotic (no)	0.431	0.438	0.969	1	0.325	1.539	0.652	3.632
	Initial therapy (yes)	0.663	0.514	1.662	1	0.197	1.941	0.708	5.316
	Multimorbidity (yes)	-2.012	1.096	3.369	1	0.066	0.134	0.016	1.146
	Immunsuppression (yes)	-0.284	0.483	0.345	1	0.557	0.753	0.292	1.941
	Constant	2.096	1.093	3.675	1	0.055	8.131		
a. Variable(s) entered on step 1: Gender, Cause, Change of antibiotic_no, Initial therapiy, Multimorbidity, Immunsuppression.									

4.2 Effectiveness of RAPID diagnostics in preventing additional therapy in patients >75 years of age

Finally, RAPID score was used to determine hospital mortality in people >75 years of age. The data shown in table 11 provided comparison of people who died in hospital setting to those who did not. The number of 109 patients consists of those from whom we knew the hospital mortality status and for whom the RAPID score could be calculated. In table number 15, firstly a summary-statistics for RAPID scores for two groups of patients was made: those who survived (no) and those who did not survive (yes) in the hospital was provided. Out of all, 87 patients survived, with an average RAPID score of 4.05. Standard deviation in this sample was 1.077, while standard error of the mean was 0.116. Patients who died in hospital were 22 in number, with an average RAPID score of 4.82. Standard deviation was 1.006, standard error

of the mean in this case 0.215. Afterwards, independent sample test was performed. It included results from an independent samples t-test, comparing the means of RAPID scores between the two groups (survived vs. not survived). Levene's Test for equality of variances showed a p-value of 0.471, which is greater than 0.05. This indicates that the assumption of equal variances is not violated, the variances of the two groups are assumed to be equal. T-test for equality of means assessed whether there is a significant difference in the mean RAPID scores between the two groups. The p-value (Sig. 2-tailed) is 0.003, which is less than 0.05, indicating that there is a statistically significant difference in the mean RAPID scores between the two groups. The mean RAPID score for those who did not survive is significantly higher by 0.772 points compared to those who survived. To summarize the data: Patients who died in the hospital had a higher mean RAPID score (4.82) compared to those who survived (4.05). The independent samples t-test indicates that this difference is statistically significant (p = 0.003), suggesting that a higher RAPID score is associated with increased in-hospital mortality. The 95% confidence interval for the difference in means (-1.275 to -0.269) does not include zero, further supporting the significance of the difference. There was no significant difference in RAPID scores between patients with shorter (<14 days) and longer (>14 days) hospital stays (p=0.854) as seen in table 12. Similarly, the RAPID score was not significantly different between those who were readmitted due to recurrence or a following disease and those who were not (p=0.320) as shown in table 13. As shown in table 14, there was no significant difference in RAPID scores between patients who survived one year after hospitalization and those who did not (p=0.069), although the difference approached significance.

Table 11: RAPID Score and in hospital mortality >75 years

Group Statistics					
	In hospital mortality	N	Mean	Std. Deviation	Std. Error Mean
RAPID-Score	no	87	4.05	1.077	0.116
	yes	22	4.82	1.006	0.215
Independent Samples Test					
	Levene's Test for Equality of Variances	t-test for Equality of Means			

		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
RAPID-Score	Equal variances assumed	0.524	0.471	-3.042	107	0.003	-0.772	0.254	-1.275	-0.269
	Equal variances not assumed			-3.169	34.230	0.003	-0.772	0.244	-1.267	-0.277

Table 12: RAPID Score and hospital stay >75 years

Group Statistics					
	In hospital stay	N	Mean	Std. Deviation	Std. Error Mean
RAPID-Score	< 14 days	31	4.23	1.055	0.190
	> 14 days	77	4.18	1.144	0.130

Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
RAPID-Score	Equal variances assumed	0.041	0.840	0.185	106	0.854	0.044	0.238	-0.428	0.516
	Equal variances not assumed			0.191	59.806	0.849	0.044	0.230	-0.416	0.504

Table 13: RAPID Score and hospital readmission >75 years

Group Statistics										
	Hospital readmission due to recurrence or following disease		N	Mean	Std. Deviation	Std. Error Mean				
RAPID-Score	no		91	4.14	1.141	0.120				
	yes		19	4.42	0.902	0.207				
Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
RAPID-Score	Equal variances assumed	1.632	0.204	-0.998	108	0.320	-0.278	0.279	-0.830	0.274
	Equal variances not assumed			-1.164	31.347	0.253	-0.278	0.239	-0.765	0.209

Table 14: RAPID Score and survival after one year >75 years

Group Statistics					
	Survival after one year	N	Mean	Std. Deviation	Std. Error Mean
RAPID-Score	no	39	4.44	1.142	0.183
	yes	68	4.03	1.079	0.131
Independent Samples Test					
	Levene's Test for Equality of Variances	t-test for Equality of Means			

		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
RAPID-Score	Equal variances assumed	0.159	0.691	1.836	105	0.069	0.406	0.221	-0.032	0.845
	Equal variances not assumed			1.808	75.583	0.075	0.406	0.225	-0.041	0.854

5 DISCUSSION

Pleural empyema is a critical condition. Older individuals are often severely affected, primarily due to frequently existing serious comorbidities, which often lead to a more severe clinical course (65). This fact is important due to the rapid increase of advanced-aged sufferers in the western world (66). Since age is advanced, the immune system often compromised and comorbidities often severe, one might wonder if treatment of ill geriatric patient is useful.

In our study, out of 344 patients in total, a number of 110/344 (32%) patients were aged over 75 years. Conclusively, out of these patients, 4 were excluded due to missing data. 20/106 (18.9%) out of all patients died in hospital, while 86/106 (81.1%) survived. We compared these results to the studies of Schweigert et al. (65) and Luciani et al. (67).

In contrast these studies by Schweigert et al. and Luciani et al., our mortality rate was significantly higher. This is likely due to our population being considerably larger. Schweigert et al. included 37/222 patients (16%) geriatric patients (65), while Luciani et al. included a total of 29 patients, almost 50% of whom were under 70 years old. 14/29 (48.2%) were geriatric patients (67). Compared to these studies, we included 106 geriatric patients in our study. We included patients being 75 years and older, while Schweigert et al. included patients being 80 years and older and Luciani et al. patients being 70 years and older al (65, 67).

Conclusively, it is difficult to compare mortality rates of different studies when the samples differ largely in size, and the definition of geriatric patients in terms of age are not the same.

Since minimal invasive surgery was treatment that was used the most in our geriatric population, we wanted to gain an overview of the mortality rate in this subgroup. Regarding the geriatric subgroup, 71/106 (66.9%) of these were treated surgically via VATS intervention, with 66/106 (92.9%) survivors. These results demonstrate the appropriateness and benefits of surgical intervention in elderly patients, with a low mortality rate. Again, the study by Schweigert et al. from may 2012 provided similar results with VATS having good survival rates in geriatric patients who are 80 years or older with coexisting morbidities. They analyzed the surgical outcome in N=222 patients with pleural empyema, 37/222 (16%) being 80 years or older. Since 92% of the old population survived, they concluded that advanced age is no contraindication for early surgical therapy (65). Also, Luciani et al. provided a study especially about the treatment of stage II pleural empyema with uniportal VATS. They included N=29 patients, with 14/29 (48.2%) being older than 70 years. No mortality was found. Ergo, they also concluded the safety and effectiveness in risk reduction and progression of empyema to higher stages in elderly patients (67). These results contribute the first major and significant part to the

hypothesis that older patients with pleural empyema can be treated because the outcomes are acceptable.

The study aimed to identify factors affecting in-hospital mortality, length of stay, readmission, and one-year survival in patients over 75 years of age. Logistic regression assessed variables like gender, admission cause, antibiotic changes, initial therapy, multimorbidity, and immunosuppression to provide insights into elderly healthcare outcomes and their influence on patient prognosis.

At first, we explored the influence of these factors on the hospital mortality. Female gender was associated with lower odds of in-hospital mortality (Exp(B) = 0.375), but this was not statistically significant ($p = 0.133$), same applied for antibiotic change. Patients with no change in antibiotic therapy had lower odds of mortality (Exp(B) = 0.597), though this was not statistically significant ($p = 0.337$). Also, initial therapy start was associated with lower mortality odds (Exp(B) = 0.508), but not significant ($p = 0.303$). On top of that, multimorbidity (Exp(B) = 4.066), increased the odds of mortality, but again, no significant correlation was made. Superinfection did not influence the hospital mortality, while other causes of mortality, on the other hand, can influence the hospital mortality, suggesting that underlying causes play a critical role in patient outcomes. Interestingly, our study found that patients with weaker immune systems, such as those with chronic illnesses or advanced age, still achieved favourable outcomes. In our study, immunosuppression had no impact on mortality ($p = 0.979$). This challenges the traditional view that a robust immune system is essential for recovery in cases of pleural empyema. Also, a study from Sziklavari et al. challenges the point of view of our study. Here, negative prognostic factors for morbidity included confirmed pathogens, sepsis, older age, multiple comorbidities, malignancy, immunosuppression, and changes in antibiotics. Their study included 359 patients with diagnosis of pleural empyema. The median age in this study was 59 years ± 14 years of age.

Although both studies compare outcomes in patients with pleural empyema, a clear distinction must be made. While Dr. Sziklavari's team studied patients of all ages, we focused specifically on the geriatric population over 75 years old. Unlike their study, as previously described, we did not find a significant correlation between gender, changes in antibiotics, initial treatment onset, and multimorbidity (68). This can likely be attributed to the age of our cohort, as geriatric patients are often inherently multimorbid, and the use of multiple medications is not uncommon, whereas this is usually not the case in a younger patient group. In contrast to our findings, immunosuppression had an impact on mortality in the patient group in the colleagues' study. Again, this can be explained by the different ages of the patients.

Geriatric patients often have physiological immunosuppression due to their advanced age. The immune system experiences immunosenescence, which reduces its functionality. This includes decreased production, proliferation, and response of T-lymphocytes to antigens, reduced phagocytic activity and impaired function of macrophages and conclusively increased susceptibility to infections, decreased vaccine efficacy, and impaired tumor defense. These changes lead to inflammaging, a chronic low-grade inflammation associated with aging (69). Again, it is difficult to compare geriatric to non-geriatric patients.

Like the study of Sziklavari et al. we concluded that the cause of infection, in example malignant disease influences mortality.

Due to the model´s lack of statistical significance suggests that while these factors may influence mortality, other unmeasured variables could play a more substantial and influencing role. Our study showed that neither age, nor antibiotic change, nor start of therapy, nor immunosuppression had a significant impact on the in-hospital mortality of people over 75 years of age. We suggested that some types of morbidity can thus influence the in-hospital mortality in older patients. Other studies also support this thesis. An example is a study from April 2023 by Salahuddin et al. A total of 202 patients with active malignancy and empyema were included in the study. The overall mortality rate at three months was 32.7%. Multivariable analysis revealed that female gender and elevated urea levels were significantly associated with an increased risk of death from empyema at three months. Patients with active malignancy and empyema had a high likelihood of mortality. Compared to our study, in this study, key risk factors in this study for death from empyema include female gender and higher urea levels (70).

In analyzing poor prognostic factors for a negative outcome in elderly individuals, the length of hospital stay also plays a crucial role. According to the Federal Statistical Office of Germany, in 2022, the average hospital stay was 7.2 days, unchanged since 2018. However, the length of stay varied across different departments. Internal Medicine and General Surgery, which handle the majority of cases, had average stays of 5.2 and 5.3 days, respectively. Departments with significantly longer stays included Geriatrics at 15.3 days and psychiatric departments with stays ranging from 24.1 to 43.9 days (71). Since the geriatric hospital stay belongs to the significant longer stays, we were interested in finding factors that influence these longer hospital stays in older patients. In our study, gender, cause, antibiotic therapy change, multimorbidity, and immunosuppression did not significantly predict hospital stay duration. Interestingly, initial therapy, beginning after or before 5 days of diagnosis, had a significant influence on the duration of hospital stays. It emerged as a significant predictor ($p = 0.032$), with patients receiving late initial therapy having substantially higher odds of extended hospital

stays (Exp(B) = 3.706). This could be explained by eradication or control of earlier stages of disease and prevention of progression of disease. An early surgical therapy can thus influence the outcome in old patients for the good and prevent longer hospital stays.

This hypothesis is supported by a study from 2023 by Bedawi et al. Here, 97 patients were included. This study was the first multicenter randomized controlled trial (RCT) comparing early intrapleural enzyme therapy and early surgery for pleural infection. The objectives were to establish the feasibility of randomizing patients in a surgery-versus-nonsurgery trial and to identify relevant patient-centered outcomes for a future RCT. They concluded, like our study did, the potential benefits of early surgery in shortening hospital stays (72). Although this study did not specifically focus on the geriatric population, its results are nevertheless groundbreaking.

Also, Semenkovich et al. underline the importance of early initial surgical therapy. In their study, that included a cohort of 4095 patients that underwent a procedure for empyema including chest tube, VATS (video-assisted thoracoscopic surgery), or open drainage and decortication. The majority received definitive operative management (chest tube: 38.2%, VATS: 32.1%, open: 29.8%; $p < 0.001$). They also concluded that higher readmission and reintervention rates were observed in patients managed with chest tubes, suggesting some of these patients may benefit from earlier definitive surgical intervention This, in turn, aligns with our hypothesis that early initial surgical therapy shortens the duration of hospitalization (73).

The next factor that influences bad outcome in the elderly is the hospital readmission due to recurrence or following disease. Our statistics revealed that gender, change of antibiotic therapy, initial therapy and multimorbidity did not influence the probability of hospital readmission. Especially multimorbidity is an important factor, since older patients suffer often from many comorbidities. Since our study showed that it did in fact not influence the risk for a hospital readmission in the elderly and thus contribution of bad outcome, this could potentially ease any decision in whether to treat a patient or not. On the other hand, the cause of readmission significantly impacted the odds of readmission ($p = 0.046$). Specifically, superinfection significantly increased the likelihood of readmission (Exp(B) = 3.715, $p = 0.024$). This shows the importance in preventing these secondary infections by either better hospital hygiene and, of course, by vaccination. This hypothesis is supported by a study from 2023 by Häder et al. that in clinical practice, prioritizing prevention strategies like vaccination and managing comorbidities is essential to reduce lung infection risks in the elderly. Early detection and treatment of infections are also critical. A comprehensive approach, including targeted vaccination, effective comorbidity management, and promoting respiratory health through

exercise and smoking cessation, can significantly decrease morbidity and mortality from lung infections in this vulnerable population (74).

The next parameter, that was interesting in our study was the one-year survival rate in patients >75 years of age and what influences is, to get an overview of the long-term outcomes. In our study, other variables as already mentioned in the sections before (gender, cause, antibiotic therapy change, initial therapy and immunosuppression) did not significantly predict one-year survival. It can be concluded that if these factors are present, they do not necessarily impact one-year survival. Interestingly, even individuals with weaker immune systems have achieved good results, supporting the statement that people with conditions like pleural empyema can be treated effectively, as the outcomes are favorable. While not statistically significant, multimorbidity showed a trend towards reducing the odds of one-year survival (Exp(B) = 0.134, p = 0.066). This underlines the need for comprehensive management strategies that address multiple comorbid conditions to improve long-term outcomes. For instance, a study by Ahmed et al. (2020) demonstrated that no specific comorbidities were found to be significant predictors of inpatient death. It appears that the total number of comorbidities, rather than their individual types, is the most predictive factor for death in cases of hospitalizations due to empyema. Patients with multiple comorbidities often present complex medical scenarios, necessitating numerous medications and carrying an elevated risk of adverse health outcomes that extend beyond the effects of individual diseases. Healthcare providers should acknowledge the critical importance of early intervention with antibiotics and drainage of pleural fluid, especially in medically complex patients who face heightened risks of poor outcomes. Their findings revealed an inpatient mortality rate of 3.5%, consistent with a recent systematic review indicating a lower-than-anticipated median in-hospital/30-day mortality rate of 4% (75).

The second hypothesis was RAPID diagnostics that can effectively predict certain clinical outcomes in patients over 75 years of age. Our study revealed, that RAPID diagnostics hat an impact only on in-hospital mortality, while length of hospital stay, readmission due to following disease or survival after one year could not really be predicted by using RAPID score. This hypothesis is partially supported by a study from 2014 by Rahman et al., who also proved that RAPID score was increased in patients who experienced in-hospital mortality later on. Interestingly and in contrast to us, they claimed that RAPID score could also influence hospitalization duration (76). Limitation of their study is that they focused on all age groups, while we looked only on patients >75 years of age. Also, Carneiro et al. demonstrated in their study that there exists a strong correlation between the RAPID score and 3-month mortality in

patients undergoing lung decortication for pleural empyema (77). Since high RAPID score is associated with high in-hospital mortality, one can conclude that low RAPID score carries a lower risk for in hospital death. The fact that a low RAPID score is associated with low mortality should not be overlooked. The earlier the intervention to prevent a poor outcome of an empyema, the lower the likelihood of dying in the hospital. Accordingly, the RAPID score should be used to distinguish patients with a good chance of recovery from those who are severely ill. The reason for this is that healthier patients, due to their lower RAPID scores, are more likely to survive an intervention than those with higher scores. Therefore, the RAPID score can form the basis for choosing treatment in older patients who appear inoperable but whose score and values indicate otherwise.

This study has potential limitations. Despite utilizing additional sources such as operation reports, transfer reports, laboratory results and other findings, capturing some parameters proved to be incomplete, while other were counted double in the beginning due to transfer between the REGIOMED hospitals. Some patients were transferred to hospitals outside the REGIOMED hospitals and were not able to be reconstructed. Furthermore, searches for relevant information in the topic of geriatric septic surgery of pleural empyema have yielded limited information since official research on this topic is scarce. Another limitation is the follow-up for one year. A long- term follow-up would lead to possibly other results and possibly other survival data. A limiting factor is the coding of the diagnosis of empyema. Often, a pyothorax was coded in the system, even though the patient had a different condition. Therefore, these cases could not be evaluated. For future projects of any kind, the coding in the respective hospital's system should be clear and precise.

6 CONCLUSION

With this study regarding the impact of geriatric patients on thoracic septic surgery, we demonstrated that advanced age is no contraindication to surgical therapy due to good survival rates and only some factors that influence bad outcome in this population. Although, it was demonstrated that older patients can be operated and the outcomes are acceptable, one must not forget about the time of initiation of treatment. The significance of initial therapy suggests that the nature and immediacy of treatment play crucial roles in determining hospital stay lengths. This finding highlights the need for effective early interventions to manage and possibly reduce extended hospitalizations in elderly patients.

Also, immunosuppression plays an important role in the outcome of the elderly. Since older people have per se a weaker immune system, being confronted with further immunosuppression might bring extra challenges in the treatment of an old patient. Conclusively, to prevent bad outcome in the treatment of pleural empyema, one must treat and think of other diseases that could potentially harm or influence the treatment of the patient. The implications of these findings are multifaceted. Clinically, they suggest that age and immune status should not be seen as insurmountable barriers to successful treatment outcomes. Instead, a focus on timely, appropriate interventions can lead to positive results even in high-risk populations. This is particularly relevant in the context of an aging population, where the incidence of pleural empyema is likely to rise. The findings suggest that a holistic approach, addressing various health aspects, including comorbid conditions and immunosuppression, is vital for improving the health outcomes of elderly patients. On the other hand, since most of the variables were not statistically significant, the results of our study suggest that there are not so many factors that influence bad outcome in patients >75 years of age with diagnosis of pleural empyema. Consequently, old patients can be treated because the outcomes and, on top of that, factors that influence these outcomes, are acceptable.

Finally, we demonstrated that RAPID Score can be an important method in predicting the outcome in geriatric patients and also strengthen the hypothesis that older patients with pleural empyema can be operated because the outcomes are acceptable, partially due to good initiation of treatment by using the RAPID Score. Overall, with this study, we were able to demonstrate that even elderly patients with sometimes severe conditions are worth treating, including surgically.

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8 SUMMARY

Title: The impact of geriatric patients on outcome in septic thoracic surgery outside academic institutions: An investigation of risk factors and postoperative courses.

Objectives: The aim of the presented study was to analyze clinical data of patients aged over 75 years with diagnosis of pleural empyema hospitalized at the Regiomed Clinics and to evaluate and compare outcomes of different treatment methods with regards factors that influence bad prognostic outcome and the importance of using RAPID Score system.

Materials and methods: Patients who were hospitalized between January 2017 and May 2023 in one of the REGIOMED hospitals: Coburg, Lichtenfels, Sonneberg, Hildburghausen, Neustadt bei Coburg with diagnosis of pleural empyema in stage I, II, or III were included in this retrospective study. Focus was on patients aged over 75 years of age. Patient outcome in regards of in hospital mortality after minimal invasive surgery, bad prognostic factors (in hospital mortality, length of hospital stay, readmission due to recurrence or following disease, survival after one year) was analyzed. Finally, effectiveness of RAPID diagnostic in preventing additional therapy was discussed.

Results: Pleural empyema is a serious condition, especially in older patients who often have severe comorbidities, leading to a more severe clinical course. Our study analyzed 344 patients, with 110 over the age of 75, focusing on 108 of these due to complete data. Surgical treatment via VATS showed an 89.5% survival rate in elderly patients, demonstrating the benefits of surgical intervention in this age group. Factors like gender, antibiotic changes, initial therapy, multimorbidity, and immunosuppression were analyzed for their impact on in-hospital mortality, hospital stay duration, readmission rates, and one-year survival. While none of these factors significantly predicted in-hospital mortality, late initial therapy significantly increased hospital stay duration, and superinfection significantly increased readmission rates. Multimorbidity showed a trend toward reducing one-year survival odds. Finally, the RAPID score effectively predicted in-hospital mortality but not other outcomes. This suggests that while a low RAPID score indicates a lower risk of in-hospital death, it should be used to identify patients who might benefit from early interventions to improve recovery chances.

Conclusion: This study demonstrates that advanced age is not a contraindication to surgical therapy for pleural empyema, given the good survival rates and the limited factors influencing poor outcomes in this population. Timely initiation of treatment is crucial in determining hospital stay lengths, highlighting the need for effective early interventions. Immunosuppression plays a significant role in outcomes, and addressing comorbid conditions is essential for improving health outcomes in elderly patients. The study found that while most variables were not statistically significant, advanced age and immune status should not be seen

as barriers to successful treatment. The RAPID Score proved to be a useful predictor of outcomes, supporting the notion that elderly patients with pleural empyema can benefit from surgical treatment. Overall, the findings suggest that even elderly patients with severe conditions are worth treating, including surgically, with appropriate interventions.

9 CROATIAN SUMMARY

Naslov: Utjecaj gerijatrijskih pacijenata na ishod kod septične torakalne kirurgije izvan akademskih ustanova: Istraživanje čimbenika rizika i postoperativnih tijekova.

Cilj: Cilj predstavljene studije bio je analizirati kliničke podatke pacijenata starijih od 75 godina s dijagnozom pleuralnog empiema hospitaliziranih u Regiomed klinikama te procijeniti i usporediti ishode različitih metoda liječenja s obzirom na čimbenike koji utječu na loš prognostički ishod, i važnost korištenja RAPID Score sustava.

Materijali i metode: Pacijenti koji su bili hospitalizirani između siječnja 2017. i svibnja 2023. u jednoj od REGIOMED bolnica: Coburg, Lichtenfels, Sonneberg, Hildburghausen, Neustadt bei Coburg s dijagnozom pleuralnog empiema u fazi I, II ili III uključeni su u ovu retrospektivnu studiju. Fokus je bio na pacijentima starijima od 75 godina. Analiziran je ishod pacijenata s obzirom na smrtnost u bolnici nakon minimalno invazivne operacije, loše prognostičke čimbenike (smrtnost u bolnici, duljina boravka u bolnici, ponovni prijem zbog recidiva ili slijedeće bolesti, preživljenje nakon jedne godine). Konačno, raspravljana je učinkovitost RAPID dijagnostike u sprječavanju dodatne terapije.

Rezultati: Pleuralni empiem je ozbiljno stanje, posebno kod starijih pacijenata koji često imaju teške komorbiditete, što dovodi do ozbiljnijeg kliničkog tijeka. Naša studija analizirala je 344 pacijenta, od kojih je 110 bilo starije od 75 godina, s fokusom na 108 njih zbog potpunih podataka. Kirurško liječenje putem VATS-a pokazalo je stopu preživljavanja od 89,5% kod starijih pacijenata, što ukazuje na prednosti kirurške intervencije u ovoj dobnoj skupini. Čimbenici poput spola, promjene antibiotika, početne terapije, multimorbiditeta i imunosupresije analizirani su radi utjecaja na smrtnost u bolnici, trajanje boravka u bolnici, stope ponovnog prijema i jednogodišnje preživljenje. Iako nijedan od ovih čimbenika nije značajno predvidio smrtnost u bolnici, kasna početna terapija značajno je povećala trajanje boravka u bolnici, a superinfekcija je značajno povećala stope ponovnog prijema. Multimorbiditet je pokazao trend smanjenja izgleda za jednogodišnje preživljenje. Konačno, RAPID skor učinkovito je predvidio smrtnost u bolnici, ali ne i druge ishode. To sugerira da, iako nizak RAPID skor ukazuje na manji rizik od smrti u bolnici, treba ga koristiti za identifikaciju pacijenata koji bi mogli imati koristi od ranih intervencija za poboljšanje šansi za oporavak.

Zaključak: Ova studija pokazuje da starija dob nije kontraindikacija za kiruršku terapiju pleuralnog empiema, s obzirom na dobre stope preživljavanja i ograničene faktore koji utječu na loše ishode u ovoj populaciji. Pravovremeni početak liječenja je ključan za određivanje duljine boravka u bolnici, što naglašava potrebu za učinkovitim ranim intervencijama. Imunosupresija igra značajnu ulogu u ishodima, a rješavanje komorbiditeta je bitno za

poboljšanje zdravstvenih ishoda kod starijih pacijenata. Studija je pokazala da, iako većina varijabli nije bila statistički značajna, starija dob i imuni status ne bi trebali biti prepreke za uspješno liječenje. RAPID zbir se pokazao korisnim prediktorom ishoda, podržavajući ideju da stariji pacijenti s pleuralnim empiemom mogu imati koristi od kirurškog liječenja. Sveukupno, nalazi sugeriraju da čak i starije pacijente s teškim stanjima vrijedi liječiti, uključujući kirurški, uz odgovarajuće intervencije.