Comparison of surgical treatment for pleural empyema patients - open surgery versus minimally invasive surgery

Bruhn, Lea

UNIVERSITY OF SPLIT

SCHOOL OF MEDICINE

Lea Bruhn

COMPARISON OF SURGICAL TREATMENT FOR PLEURAL EMPYEMA PATIENTS - OPEN SURGERY VERSUS MINIMALLY INVASIVE SURGERY

Diploma thesis

Academic year:

2023./2024.

Mentor:

Prof. Johannes Brachmann, MD, PhD

Split, July 2024.

Table of Contents

ACKNOWLEDGEMENT

I would like to express my gratitude to my friend Annika, with whom I have spent countless hours in front of the computer, almost making it enjoyable. A big thank you to our supervisor, Dr. med. Zsolt Sziklavari, PhD, who has always been there to assist us and provided solutions whenever needed. Thank you for your time and for patiently responding to numerous emails. A huge thank you to Mr. Janos Fekete for his help in statistics and for always being available to answer all our questions. I am also thankful to Professor Brachmann, who has always been approachable and has made significant efforts to support each student individually.

At the end, I would like to express my gratitude to everyone I had the privilege of meeting and appreciating during my journey through medical school. It was the best six years. Thank you to my closest friends and my boyfriend for the wonderful moments we had. Of course I would like to thank my family and grandma for the greatest support.

LIST OF ABBREVIATIONS

AATS ..... engl. *American Association for thoracic surgery*
BTS Guidelines ..... engl. *British thoracic society guidelines*
CT ..... engl. *Computer Tomography*
DNAse ..... engl. *Desoxyribonuclease*
LDH ..... engl. *Lactatdehydrogenase*
MRI ..... engl. *Magnetic Resonance Imaging*
MRSA ..... engl. *Methicillin resistant Staphylococcus Aureus*
PET ..... engl. *Positron emission tomography*
TPA ..... engl. *Tissue Plasminogen Activator*
VATS ..... engl. *Video Assisted Thoracoscopic Surgery*

1 INTRODUCTION

The name of Pleural Empyema has a Greek origin and is simply defined as “Pus in the chest”. The term "empyema" is denoting the macroscopic identification of purulent pleural fluid in the pleural space (1). Despite medicine is continuously improving and more prevention against infections and antibiotics are used, pleural empyema is still a widespread disease and the most common complication of pneumonia. Pneumonia is the most common precursor but it is not the only one. Parapneumonic, posttraumatic or postsurgical are all underlying conditions that can lead to an empyema (2,3). The stages are separated due to morphology and they are time dependent. The first phase is called exudative phase, the second is the fibrino - purulent phase and the last is organization and pleural peel formation (3).

1.1 Epidemiology

In the United States, pneumonia leads to the hospitalization of approximately one million patients annually. Among these patients, approximately 20% to 40% develop a parapneumonic effusion, and 5% to 10% of these cases evolve to empyema, equating to roughly 32,000 cases annually. A concerning aspect is that approximately 15% of these patients succumb to the condition, while 30% necessitate to drain the pleural space by surgical intervention (2,4).

The interesting shift in the incidence of pleural empyema is well describes in the American Association guidelines. The AATS (engl. *American Association for Thoracic Surgery*) outlines that the incidence of empyema exhibited a notable decline in the first half of the 20th century. In the era prior to the availability of antibiotics, pleural empyema exhibited a heightened prevalence and constituted a complication in 5% of cases. With the introduction of antibiotics in the 1940s, there was a noticeable decline in the incidence of empyema to 2% of pneumonia cases. Unfortunately, this favorable trend reversed in the 1990s, witnessing a resurgence in the incidence of empyema across the United States (2, 4). There are different ways to explain this incidence but one important is that the observed alterations could potentially stem from heightened awareness regarding clinical diagnosis and the expanding array of diagnostic modalities at physician’s disposal, facilitating more precise identification of pleural cavity infections. Additionally, this trend may be influenced by the progressive aging of the population with each passing year (5).

1.2 Pleural Empyema

1.2.1 Anatomy

The anatomy of the pleural cavity illustrates the potential area between the visceral and parietal pleurae surrounding the lungs. This involves a serous membrane that folds inwards, forming a dual-layered membrane structure. Referred to as the pleural cavity, it holds a small quantity of pleural fluid typically only a few milliliters. The outer layer of the pleura is termed the *parietal pleura* and is directly adjacent to the chest wall. More specific it is subdivided into *pleura costalis* that envelops the ribcage, vertebral column, and the posterior aspect of the sternum, while the *pleura diaphragmatica* extends over the superior aspect of the diaphragm, and the *pleura mediastinalis* encompasses the mediastinum (6,7). Due to its sensory innervation the *pleura parietalis* is intensively responsive to pain. The blood supply is given via the intercostal arteries (6).The inner layer is called *visceral pleura* its envelopes the lungs and is fused with the lung surfaces, extending also into the interlobar fissures. In contrast the *visceral pleura* is not pain sensitive since there is no sensory innervation. The bronchial circulation supplies the visceral pleura with blood (6, 7). Both sheets the *pleura visceralis* and *pleura parietalis* merge at the lung hilum and at the pulmonary ligament (7).

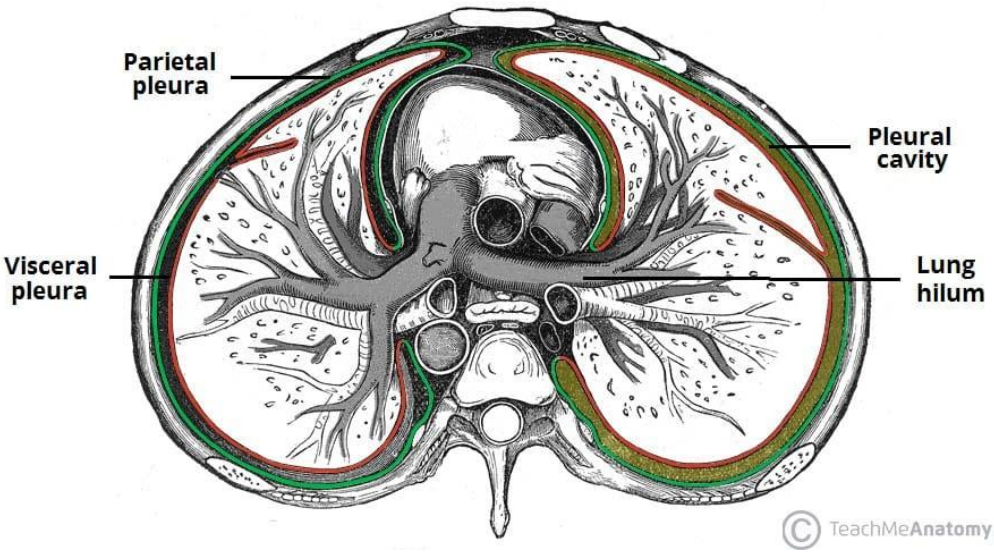


Figure 1. Anatomy of pleural space and thorax.
Source: https://teachmeanatomy.info/thorax/organs/pleurae/

1.2.2 Etiology

In roughly 20% of pneumonia cases, a parapneumonic effusion may develop, potentially leading to empyema. Seventy percent of cases of pleural empyema are associated with parapneumonic effusion. The remaining 30% can be attributed to factors such as esophageal ruptures, cervical infections, surgical interventions, or trauma. (1, 8). Primary empyema, which is not linked to prior pneumonia or intervention, accounts for a small percentage of cases.

The classification is divided into community-acquired and hospital-acquired, with the bacteriology varying depending on the origin of the infection, with consideration given to patient comorbidities. Streptococcus species represents a prevalent Gram-positive bacterium commonly associated with community-acquired empyema, while gram-negative bacteria may prevail in patients with comorbidities. Frequent comorbidities include conditions such as gastroesophageal reflux disease, diabetes and alcohol abuse, . In hospital-acquired empyema, pathogens commonly identified include Staphylococcus aureus (including methicillin-resistant S. aureus (MRSA)) and Pseudomonas. Fungal empyema, although rare, is associated with a high mortality rate. Candida species are the predominant fungi identified in cases of fungal empyema(8).

1.2.3 Pathophysiology

Pleural cavity infections progress through three distinct stages. The initial stage, known as the exudative stage, is characterized by pleural inflammation and the accumulation of neutrophils, resulting in increased vascular endothelial damage and permeability. Consequently, fluid enters the pleural cavity, leading to pleural effusion. During this stage, glucose levels in the effusion remain normal, and there is no biochemical evidence of microbial invasion (5, 9).

The second stage, termed the fibrin exudation and pus formation stage, involves the stimulation of neutrophil migration and fibrocyte chemotaxis by various proinflammatory factors. During this stage the endothelial damage and permeability worsen. Degradation products of bacteria can be found in the effusion, as the pathogens penetrate into the pleural space. Increased lactic acid levels, decreased pH and glucose levels, and elevated levels of lactic dehydrogenase occur due to bacterial metabolism and neutrophil phagocytosis. Additionally, the coagulation cascade and fibrinolytic system are activated, resulting in fibrin deposition on the visceral and parietal pleura, reduced fibrinolysis, and the development of pleural adhesions and encapsulated effusions (5,9).

The final stage, known as the organization stage, is characterized by increased fibrocyte infiltration. This leads to the formation of fibrous deposits on the surfaces of the pleural layers

as well as a fibrous membrane between the visceral and parietal pleura. The thickened fibrous tissue encases the lung, impairing its expansion.

The infection can be classified into uncomplicated parapneumonic effusion, complicated effusion, or empyema, based on levels of lactate dehydrogenase, glucose, and pH. Antibiotic therapy is suitable for uncomplicated infections corresponding to the exudative stage. However, complicated infections and empyema necessitate drainage or surgical intervention. Therefore, tailored clinical decisions are imperative at different stages of the infection (5,8,9).

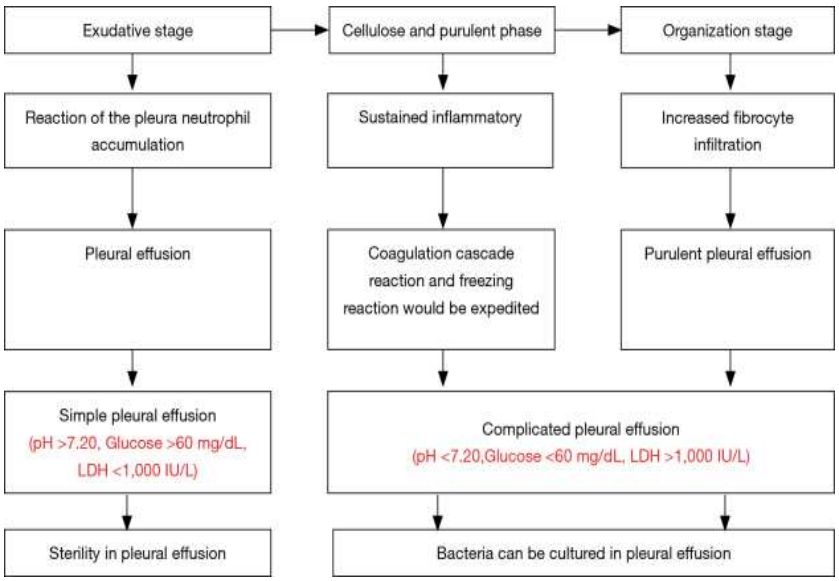


Figure 2. Pathophysiology of pleural empyema. Accessible via web on Journal of thoracic disease.

Source:https://cdn.amegroups.cn/static/magazine_modules/imgRender/dist/index.html?imgSource=https://cdn.amegroups.cn/journals/pbpc/files/journals/2/articles/16875/public/16875-PB4-R1.png

1.2.4 Clinical Presentation

Pleural empyema Patients have not very specific and clear to identify symptoms. The clinic is very similar to pneumonia and presents most commonly with thoracic pain, cough, fever, sputum and dyspnea (8). Usually, the duration of symptoms is prolonged in contrast to pneumonia (8, 10).

Thoracic pain is a pleuritic pain that manifests as sudden, intense, sharp, stabbing, or burning discomfort in the chest that worsens with both inhalation and exhalation (11). As

previously discussed in the anatomy section pain receptors are absent in the visceral pleura, whereas the parietal pleura is endowed with somatic nerves that perceive pain arising from trauma or inflammation. Inflammatory agents released within the pleural space activate local pain receptors (11).

Dyspnea can have several contributing factors. These include mechanical elements such as reduced chest wall compliance, altered biomechanics due to contralateral mediastinal shift, decreased volume in the ipsilateral lung, activation of compensatory reflexes triggered by chest wall receptors, and downward displacement of the diaphragm (12). A warning sign could be that patients who have received targeted antibiotic therapy for pneumonia and have not experienced improvement should be further evaluated for pleural effusions and empyema (2).

Furthermore, certain features can be identified during the physical examination. One might observe a dullness upon percussion in the affected region, egophony, heightened palpable fremitus, and fine crackles. In summary, it must be noted that there is no clear and distinct symptomatology or physical examination findings. The symptoms overlap significantly with those of pneumonia and other thoracic conditions (8).

A scoring system called the RAPID score has been developed to evaluate patient mortality using various parameters. These parameters provide a comprehensive picture of the patient and include kidney function (Renal), age, presence or absence of pus, whether the infection is hospital-acquired or community-acquired, and albumin levels (diet). Thus, the acronym "RAPID" is formed. High numbers of Rapid Scores are associated with higher mortality rates (13). The scoring system 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 old scores 0 points, 50 to 70 years old scores 1 point, and over 70 years old 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 at 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.

International guidelines for example the British Guidelines (engl. BTS Guidelines) recommend the use of the RAPID Score for risk assessment in adults in order to provide valuable insights for discussions with patients regarding potential infection outcomes (1).

1.2.5 Diagnostic

Since there are no clear clinical signs to identify a diagnosis, various diagnostic and imaging techniques are available to confirm the diagnosis of pleural empyema. According to the recommendations of the AATS, an X-rays should be performed, but additionally, a pleural ultrasound is also recommended to further investigate the pleural space infection. These routine examinations are suitable for diagnostic purposes and also facilitate image-guided pleural procedures (Class I; Level of Evidence B). Additionally, obtaining a chest computed tomography (CT) scan is advised when pleural space infection is suspected (Class IIa; Level of Evidence B)(2). The following section provides explanation of various imaging modalities and techniques used to diagnose pleura empyema.

Chest X-ray: The chest X-ray is typically the initial diagnostic tool used in the evaluation of pleural empyema; however, it is not 100% sensitive. Nonetheless, it offers the advantage of being uncomplicated, cost-effective, readily available, and generally present in every hospital setting. To detect fluid on an X-ray, approximately 75 ml of fluid must be present in the lateral view and 175 ml in the anterior view (8). Fluids may be obscured and remain undetected due to overshadowing and costodiaphragmatic angles. Smaller, loculated effusions may manifest as lenticular-shaped opacities adjacent to the pleura on posteroanterior views hard to differentiate from underlying parenchymal consolidation (2, 8).

Ultrasound: Ultrasound serves as a complementary method to X-ray. It can be performed at the patient's bedside and, when executed by a skilled operator, offers greater sensitivity than X-ray. Ultrasound enables differentiation between lung parenchyma and fluid, allowing for estimation of fluid volume (8). Additionally, it aids in diagnosing the characteristics of pleural fluid, which assist in staging. For instance, homogeneous and echogenic textures suggest empyema or hemorrhagic effusion, whereas complex septated textures indicate exudate. Anechoic fluids typically indicate transudate (2). These rapid assessments allow for preliminary patient categorization. Furthermore, ultrasound is valuable for therapeutic purposes, such as guiding chest tube placement for thoracentesis (2, 8).

CT Scan: When suspicion of pleural empyema arises, a CT scan is indicated. The CT is conducted with intravenous contrast medium to enhance visualization of the pleura (8). Pleural abnormalities are particularly well depicted on the CT scan, allowing for evaluation of

potential causes of the empyema. For instance, bronchogenic carcinoma, endobronchial foreign bodies, or esophageal rupture may be identified and subsequently treated. The following hallmarks are utilized as diagnostic indicators on CT: thickening of the pleura, pleural enhancement, septations, the split pleura sign, which occurs when both the visceral and parietal pleura thicken, and the air bubble sign in the absence of previous investigations. Similar to ultrasound, CT scanning can also offer therapeutic benefits by guiding chest tube placement for thoracentesis (2,8).

Positron emission tomography (PET) and **magnetic resonance imaging** (MRI): These are additional imaging modalities considered for diagnosing pleural-space infections (14). PET is not deemed beneficial due to its inability to accurately differentiate between inflammatory and malignant pleural effusions. On the other hand, MRI shows promise as a potential alternative to CT. It aids in distinguishing between transudates and exudates and enables assessment of soft tissue extension, such as involvement of the chest wall or spine (2).

In addition to imaging techniques, another crucial diagnostic tool is the analysis of pleural fluid following thoracentesis. Thoracentesis is indicated when >2cm of fluid is estimated on a CT scan and >1cm on an X-ray. Ultrasound guidance is recommended for performing diagnostic thoracentesis to minimize the risk of pneumothorax (15). If the pleural fluid appears purulent, pH measurements should be conducted. The presence of purulence or a positive Gram's stain or culture from the pleural fluid confirms the diagnosis of empyema, warranting appropriate therapy. Additionally, other parameters such as pleural glucose and LDH levels can be analyzed (2). Furthermore, it is recommended to obtain a culture from the pleural fluid. Unfortunately, cultures previously taken, such as those from catheters or tubing, are often inaccurate and cannot be used for diagnosis (2)

1.2.6 Classification

Pleural empyema is classified into three stages. The first stage is called the exudative stage. Patients present with fluid accumulation in the pleural space, which arises from a parapneumonic effusion. Due to increased capillary permeability and elevated pulmonary interstitial fluid, fluid can enter the pleural space.

The second stage is called the fibrino-purulent stage. In this more advanced stage, the effusion is increasingly infected and loculated. Positive blood cultures can be expected, along with a lower pH value and elevated LDH levels.

In the third stage, known as the chronic stage, thick pleural rinds form. These peels prevent the lung from expanding (16).

1.2.7 Treatment

The therapeutic management of pleural empyema encompasses various approaches and must be tailored to the individual patient in a stage-appropriate manner. The classification described above provides a guideline for the respective therapy option. Typically, it involves a combination of medical and surgical interventions. The following section will elucidate the available therapeutic options in detail.

Antibiotics: The utility of antibiotic therapy should be individualized to encompass multiple patient-related factors, including the geographic location, site of infection occurrence, and the patient's host status for drug selection. Initiation of antibiotic therapy should be guided by whether the infection is community-acquired or hospital-acquired (8). In cases of community-acquired infection, Gram-positive aerobic pathogens are often encountered, whereas in hospital-acquired settings, Gram-negative pathogens and resistant Gram-positive organisms such as MRSA are more common. Additionally, anaerobic involvement may occur in both settings (1). In cases of community-acquired empyema, effective coverage can be achieved by employing a cephalosporin of the third or fourth generation alongside metronidazole or ampicillin with a beta-lactamase inhibitor. For hospital-acquired empyema, as well as empyema due to trauma or surgery, it is necessary to include vancomycin, cefepime, and metronidazole or piperacillin-tazobactam to ensure coverage against Pseudomonas and MRSA (1,5,8). After bacterial culturing the more precise antibiotic therapy should then be customized to the bacteria source and bacterial culture. Nevertheless, in more than 40% of these instances, culturing pathogenic bacteria proves unsuccessful. Therefore, there is a need to explore further advancements in culture techniques or the utilization of nucleic acid amplification technology to boost the rate of positive microbiological diagnoses (5). The duration of antibiotic treatment for pleural infections lasts between 2 and 6 weeks, depending on how the patient responds clinically. Shorter courses may lead to a relapse. However, there haven't been any well-powered studies on shorter antibiotic durations specifically for pleural infections (1).

Thoracocentesis and Chest Tube: The prevailing method of drainage is the tube thoracostomy. Studies have found that larger tubes do not make a difference in terms of prognosis and mortality rates. Additionally, patients experience greater pain with larger tubes. Therefore, tubes smaller than 14F should be chosen (1). The correct placement of the chest tube holds more significance than its size, as misplacement often leads to treatment failure. A plain film or chest CT should confirm within the initial 24 hours a proper positioning. Typically,

chest tubes remain in position until drainage decreases to less than 50 ml within 24 hours or until there is evidence of lung re-expansion on chest radiography (17).

Intrapleural cavity injection: Fibrin deposition and the formation of septations occur during the progression of pleural infection, thus an often used method is the injection of intrapleural medication (1). There are different forms of medication that are controversially discussed. Evidence concerning the administration of one single fibrinolytic agent such as streptokinase, tissue plasminogen activator (TPA), and urokinase has been disappointing and are not recommended anymore (10,17). One recommended method is the combined injection of tissue plasminogen activator and DNAse, since it reduces the length of hospital stay, but causes no change in mortality rate (1).

Surgery: The primary objective of the surgical intervention is to restore lung expansion. This should be achieved by removing surgically the pus from the pleural space, this is usually the case if drainage via tube thoracostomy fails or there is a formation of a multiloculated empyema. Concurrently, the removal of purulent exudate and intrathoracic fibrin is essential to facilitate optimal lung expansion and to minimize the risk of subsequent reinfection within alternative thoracic compartments (8,17). The surgical procedure is to evacuate the septated areas and pus, which is a process known as debridement. In cases of fibrous thickening, it is necessary to decorticate the pleura. This decortication frees the lung, which is surrounded by the pleural rind and unable to expand (8,17). Lung decortication can be performed during open thoracotomy or VATS. The thick pleural peel, called the rind, needs to be carefully dissected away from the lung parenchyma, encompassing the fissures. After removing this peel, the lungs are inflated to identify any air leaks. Any significant air leaks must be closed by suturing(18).

There are two main types of surgical approaches. One is the so called VATS (Video assisted thoracoscopic surgery) which is a minimal invasive procedure. The other one is an open thoracotomy. In the following section these two methods are explained.

VATS: Usually VATS is performed under general anesthesia, after administration the thoracoscope is introduced, and the lung on the same side is deflated to enhance the visualization of intrathoracic structures. After inspection of the pleura and the thoracic cavity another access is induced to achieve another intercostal entry (19). Three 1cm incisions are utilized as ports. The central port is used for the camera whereas the other two are mainly for the biopsy and retraction instruments. The camera the so called thoracoscope is used to inspect the pleural space. Depending on the intrapleural findings, the surgeon can take appropriate action. As previously stated, there is the option to evacuate the pus and drain the infected fluid.

The clearly visible fibrous septae can be removed and broken down. Additionally, as mentioned above, decortication can be performed to break up possible pleural peels.

In cases where conversion to open surgery is necessary, the three incisions can be joined together to create an open thoracic window. Following the procedure a chest tube is inserted (19). The use of VATS minimizes trauma to the thorax but one of the main advantages of VATS surgery is not only smaller incisions but also the avoidance of rib spreading. This helps to preserve the underlying intercostal neurovascular structures and reduces pressure buildup (1, 2). Further advantages and comparisons with open thoracotomy will be discussed in the following sections. Despite all these advantages, there are also some contraindications in certain cases or patient groups. VATS may not be suitable for patients who are unable to withstand one-lung ventilation. Furthermore, obese patients or patients with narrow rib spaces make the thoracic approach difficult(2,19).

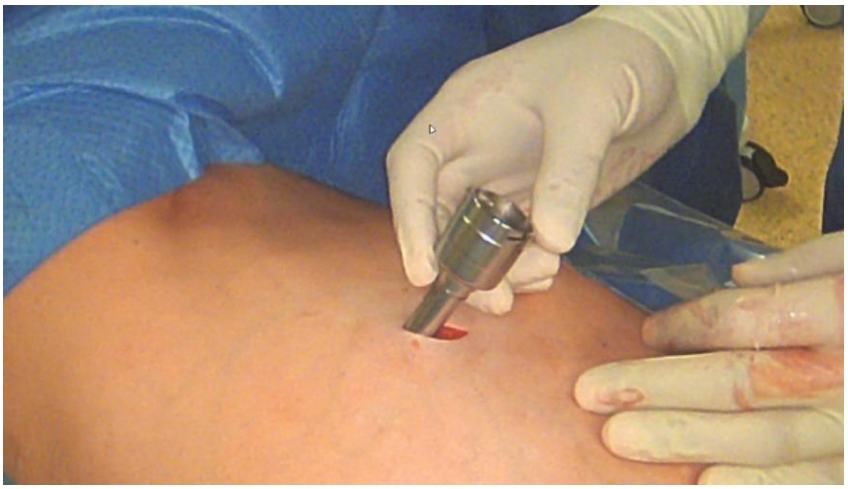


Figure 2. Insertion of the instruments.
Source: Dr. Zsolt Sziklavari.

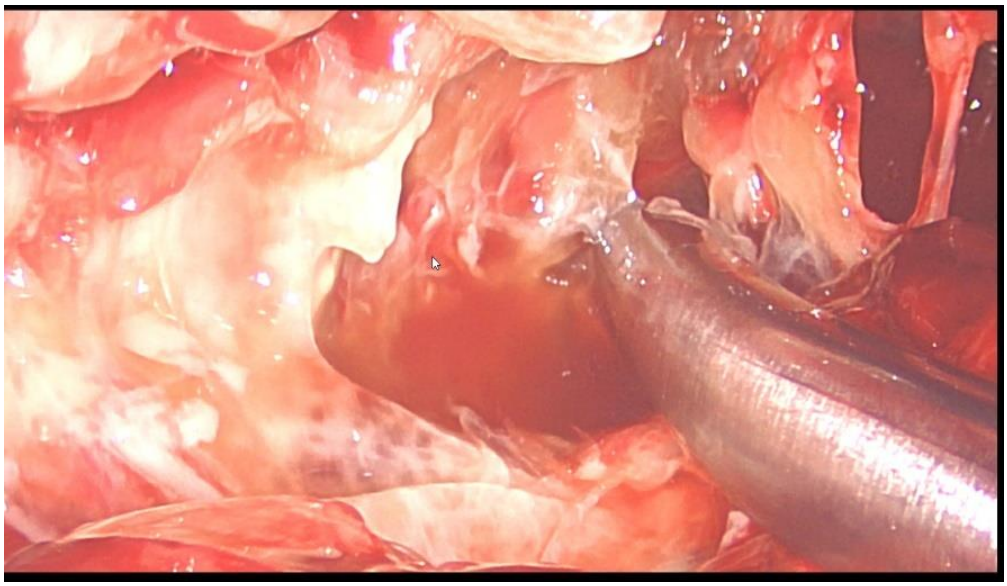


Figure 3. Intrapleural view of Pleuraempyema.
Source Dr. Zsolz Sziklavari

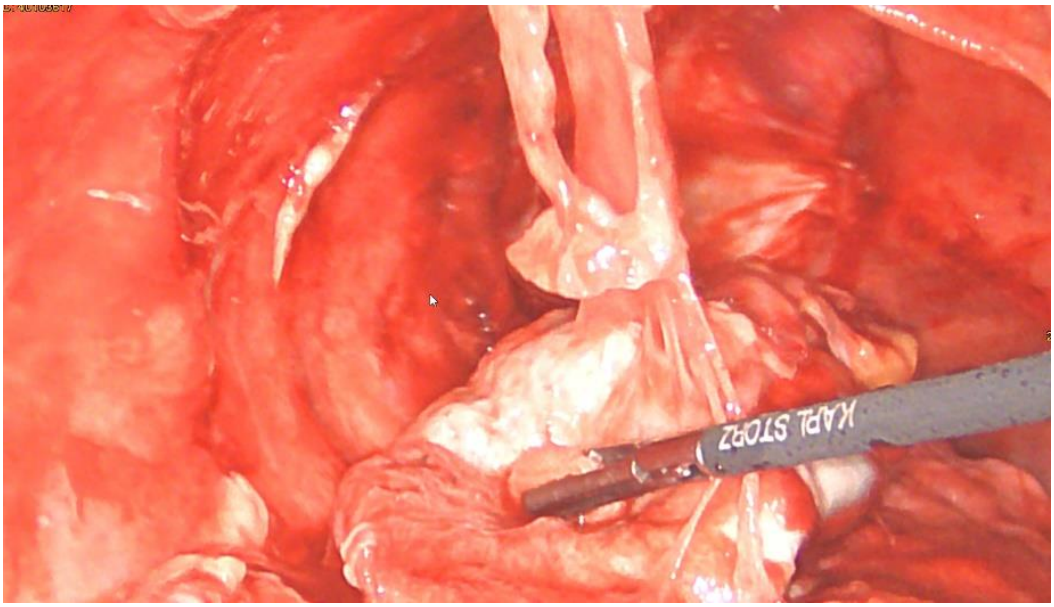


Figure 4. Decortication of fibrinous structures.
Source: Dr. Zsolt Sziklavari

Open Thoracotomy: The thoracotomy procedure starts by ensuring the patient's appropriate positioning, commonly in the lateral decubitus posture. This positioning optimizes access to the thoracic cavity while minimizing the potential for nerve injuries or complications associated with pressure (20). There are different approaches for thoracotomy posterolateral,

lateral or anterior. After the incision subcutaneous tissue and muscles are dissected and through the intercostal space access is gained into the thoracic cavity. Intrapleurally, the surgical principles are similar here as in VATS. The focus is on draining infected fluid and tissue, debridement, and decortication. Open thoracotomy is an invasive surgical procedure that provides good visibility and access for the surgeon. However, it also involves greater thoracic trauma and has largely been replaced by minimally invasive surgery (20). Even though VATS has widely replaced open thoracotomy in some cases it is indicated to use open thoracotomy or to convert from VATS to open thoracotomy. The decision to transition from minimally invasive surgery to open thoracotomy is highly individualized, and there are no set guidelines determining when this shift should occur. Therefore, it largely depends on the surgeon's judgment. However, there are clear indications for transitioning from laparoscopic to open surgery in cases of uncontrollable bleeding or structural injuries that cannot be repaired minimally invasively. Furthermore, insufficient surgical progress and failure to accomplish the primary objectives of empyema treatment, specifically, evacuation and lung expansion (2,8). At the end a pleural catheter is inserted into the pleural space (8).

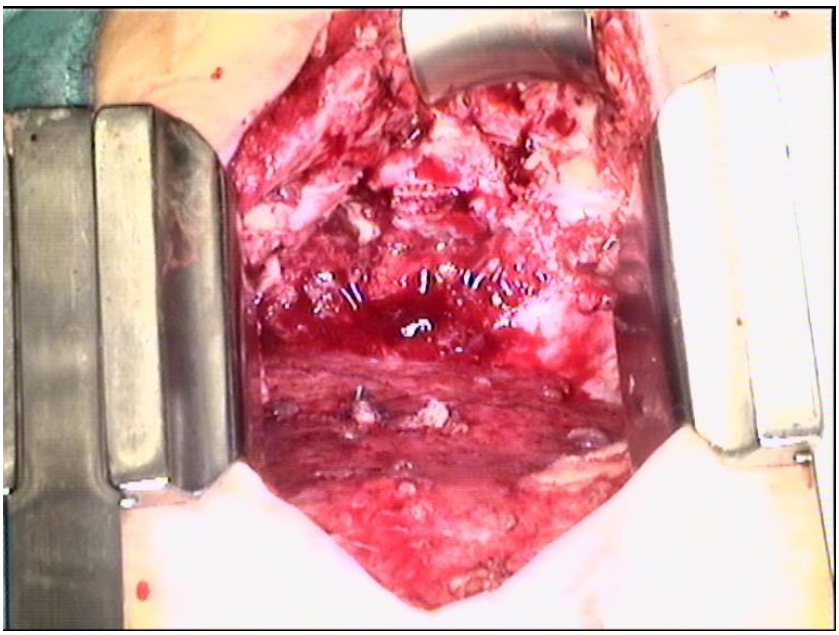


Figure 5. Open thoracotomy.
Source: Dr. Zsolt Sziklavari

Open window thoracostomy: The open-window thoracostomy is an additional drainage procedure for advanced empyema with necrotic deposits, bronchopleural fistulas, and purulent effusion. The thoracic window is placed at the site where the empyema is most prominent. The 8-10 cm long skin incision runs along the rib bone, followed by muscle dissection. The packing gauzes can be changed through the thoracic window once or twice daily. The empyema cavity can now be examined, typically aiming for a thoracic window with a target size of 5 cm in diameter. Depending on the findings, it must be decided whether and how many ribs need to be removed to achieve this size. The empyema wall is excised, after which the skin edge and empyema wall are sutured together. To reduce the empyema cavity, a muscle flap transposition is often performed. The muscle flap is introduced into the cleaned cavity and sutured to the surface of the empyema. A vacuum drain is placed to support healing (21).

VAC Treatment: The goal of VAC therapy is to enhance spontaneous wound healing. Initially, the wound is cleaned, and debridement is performed. Sterile sponges are inserted. Two types of foam are commonly used: black foam, made of polyurethane ether, is lightweight and hydrophobic, suitable for thoracic and abdominal cavity wounds; white foam, composed of polyvinyl alcohol, is denser and hydrophilic, ideal for superficial surface wounds. An evacuation tube is connected to a specialized pump that generates a vacuum. To seal the wound, it is essential to ensure thorough coverage for air and water tightness. Different pressures are applied, which are further categorized as continuous or intermittent. Various indications dictate the use of different pressures: higher pressures in the range of 150 mmHg or higher for large, exudative wounds, while lower pressures are used for painful chronic wounds (22).

Supportive Treatment: Patients suffering from pleural infection are characterized by elevated metabolic rates and malnutrition since they typically exhibit a systemic inflammatory response. Therefore, adequate attention should be given to nutritional support, as hypoproteinemia and other forms of malnutrition lead to a poorer prognosis and outcome. As well ensuring the maintenance of water, electrolyte, and acid-base balance (8).

2 OBJECTIVES

2.1 Aims

The aim of the presented study was to analyze clinical data of patients with symptomatic pleural empyema hospitalized at the REGIOMED clinics and to evaluate and compare outcomes of different surgical treatment methods.

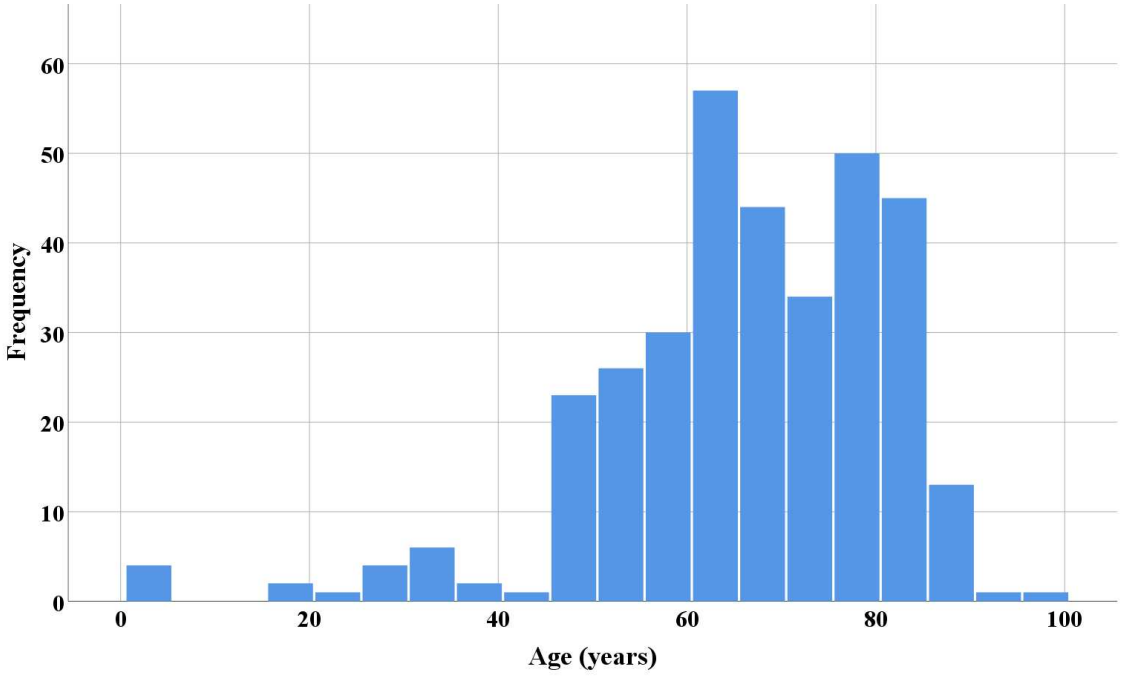
2.2 Hypotheses

1. The utilization of minimally invasive surgery demonstrates more favorable outcomes compared to open surgery and other treatment modalities concerning in hospital mortality.
2. Minimal invasive surgery demonstrates better outcomes concerning postoperative length of in hospital stay compared to open surgery and other treatment modalities.
3. Minimally invasive surgery demonstrates better outcomes concerning one year survival compared to open surgery and other treatment modalities.
4. The rate of hospital Readmission is reduced due to the use of minimal invasive surgery.

3 MATERIALS AND METHODS

The study included patients diagnosed with pleural empyema due to a variety of etiologies. The study encompassed the patient cohort treated at Regiomed Clinics from 2017 to 2023. The research project was approved by the Institutional Review Board (IRB) of the Medical School REGIOMED Coburg in accordance with §2 of its statutes. Due to the retrospective nature of this project, additional study registration was not considered necessary. Eligible patients were required to be aged 18 or older, have a confirmed diagnosis of pleural empyema, and have undergone treatment at a non-university institution within the REGIOMED Clinic Network. Patients who failed to meet these criteria, those with interventions outside the scope of interest, or those with incomplete data were excluded from the analysis.

The study included 344 patients. Out of the total 344 patients, there were 91/344 (26,5%) women and 253/344 (73,5%) men. The median age of this cohort diagnosed with pleural empyema was 66 years.



The parameter of diagnostic was subdivided into subgroups either diagnosed by CT, punctation, or clinical diagnosis which included sonography. Also, a combination of the former parameters was evaluated. CT diagnostic was performed in 203/344 (59%) patients, punctation in 21/344 (6,1%) CT and punctation in 4/344 (1,2%) patients, clinical diagnosis including

sonography in 17/344 (4,9%) patients, combination of CT and clinical diagnosis in 25/344 (7,3%) patients and the combination of diagnostics in 58/344 (16,9%) patients.

Another parameter is to identify the cause of the pleural empyema. We categorized the underlying causes into parapneumonic origin, superinfection, and others. Parapneumonic reasons were seen in 205/344 (59,6%) patients, superinfection in 98/344 (28,5%) patients and other causes in 193/344 (56,1%) patients.

The parameter "Pathogen" aims to identify the pathogens. The most common pathogens were Staphylococcus aureus (n=40), Escherichia coli (n=23), and Streptococcus pneumoniae (n=23), other pathogens in a smaller number were also identified. In a significant portion of cases, however, no specific pathogen could be identified and documented.

The initial antibiotic therapy was examined, in total we could evaluate 12 different antibiotics. An antibiotic switch was performed in 158/344 (45,9%) patients and not performed in 186/344 (54,1%).

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 are 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 was the timing of the initiation of therapy. Here, we defined initial surgical therapy, which was stated as surgical intervention in the time range of five days after primary presentation. 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 (0,06%) patients the data is not correctly documented so could not conclude when exactly the initial treatment started.

Multimorbidity was defined as a condition affecting three or more organ systems, including heart, lungs, kidney/bladder, liver, metabolic disorders, malignant diseases, sepsis, vascular diseases, neurological diseases, endocrine disorders gastrointestinal diseases, alcohol abuse, drug abuse, obesity, musculoskeletal disorders, mental health disorders, other diseases. 275/344 (79,9%) were classified as multimorbid patients.

We also investigated the immune status of our cohort. 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.

3.1.1 Statistical Analysis

Chi-square test was applied for in hospital mortality, hospital stay, hospital readmission and survival after one year. If there was maximum 5 in at least one of the cells of the crosstab then we use Fisher's test result. If the value was greater than 5 in each cell, we use Pearson chi-square asymptotic significance as *P*-value.

ANOVA test was conducted for the postoperative stay. To detect pairwise differences between subgroups Bonferroni post-hoc test was applied.

4 RESULTS

4.1 In-Hospital Mortality

In our analysis of hospital mortality, the three subgroups—conservative therapy, minimally invasive surgery, and open surgery—were examined to determine statistical significance. The overall mortality in our treated patient pool was 39 out of 332 patients, meaning that 11.7% of our treated patients died in the hospital.

The conservatively treated group showed that 24 out of 66 patients (36.4%) experienced hospital mortality. This represents 61.5% of the total group with hospital mortality. The chi-square test yielded a value of 48.151 with a degree of freedom of 1 and an asymptotic significance of 0.000. Thus, it was found that there is a statistical association between conservative therapy and hospital mortality (P<0.001).

Under minimally invasive surgery, 10 out of 225 patients treated with VATS (4.4%) died in the hospital. This represents 25.6% of the total group with hospital mortality. The chi-square test, with a value of 35.911, a degree of freedom of 1, and an asymptotic significance of 0.000, also showed statistical significance in the VATS-treated patient group. A P-value of <0.001 demonstrates the statistical association between hospital mortality and minimally invasive surgery.

The group of patients treated with open surgery showed that 5 out of 41 patients (12.2%) experienced hospital mortality. This corresponds to 12.8% of the total hospital mortality among all patients. The chi-square test yielded a value of 0.009 with a degree of freedom of 1 and an asymptotic significance of 0.924. The interpretation of this test suggests that there is no significant association between open surgery and hospital mortality (P>0.05).

In summary, it can be interpreted that our analysis shows a statistical association between hospital mortality and conservative treatment as well as minimally invasive surgery. This suggests that these patient groups experienced a higher mortality rate in the hospital. Conversely, open surgery did not demonstrate a statistically significant association with in-hospital mortality.

			In hospital mortality		Total
			no	yes	
Consevative surgery	No	Count	251	15	266
		% within Consevative surgery	94.4	5.6	100.0
		% within In hospital mortality	85.7	38.5	80.1
		% of Total	75.6	4.5	80.1
	Yes	Count	42	24	66
		% within Consevative surgery	63.6	36.4	100.0
		% within In hospital mortality	14.3	61.5	19.9
		% of Total	12.7	7.2	19.9
Total		Count	293	39	332
		% within Consevative surgery	88.3	11.7	100.0
		% within In hospital mortality	100.0	100.0	100.0
		% of Total	88.3	11.7	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	48.151[a]	1	0.000		
Fisher's Exact Test				0.000	0.000
N of Valid Cases	332				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 7.75.

b. Computed only for a 2x2 table

			In hospital mortality		Total
			no	yes	
Minimally invasive	No	Count	78	29	107
		% within Minimally invasive	72.9	27.1	100.0
		% within In hospital mortality	26.6%	74.4%	32.2
		% of Total	23.5	8.7	32.2
	Yes	Count	215	10	225
		% within Minimally invasive	95.6	4.4	100.0
		% within In hospital mortality	73.4	25.6	67.8
		% of Total	64.8	3.0	67.8
Total		Count	293	39	332
		% within Minimally invasive	88.3	11.7	100.0
		% within In hospital mortality	100.0	100.0	100.0
		% of Total	88.3	11.7	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	35.911[a]	1	0.000		
Fisher's Exact Test				0.000	0.000
N of Valid Cases	332				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 12.57.

b. Computed only for a 2x2 table

			In hospital mortality		Total
			no	yes	
Open surgery	No	Count	257	34	291
		% within Open surgery	88.3	11.7	100.0
		% within In hospital mortality	87.7	87.2	87.7
		% of Total	77.4	10.2	87.7
	Yes	Count	36	5	41
		% within Open surgery	87.8	12.2	100.0
		% within In hospital mortality	12.3	12.8	12.3
		% of Total	10.8	1.5	12.3
Total		Count	293	39	332
		% within Open surgery	88.3	11.7	100.0
		% within In hospital mortality	100.0	100.0	100.0
		% of Total	88.3	11.7	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0.009[a]	1	0.924		
Continuity Correction[b]	0.000	1	1.000		
Likelihood Ratio	0.009	1	0.925		
Fisher's Exact Test				1.000	0.545
Linear-by-Linear Association	0.009	1	0.924		
N of Valid Cases	332				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.82.

b. Computed only for a 2x2 table

4.2 Length of Postoperative Length of Stay

The analysis of postoperative stay duration was conducted and compared across groups. The overall average postoperative stay across all groups is 14.31 days.

Regarding the group of patients treated conservatively 66/332 (19,9%) the average stay was 12.05 days, with a standard deviation of 14.024 days.

The postoperative stay for patients treated with VATS (minimally invasive surgery) is 13.07 days, with a standard deviation of 14.167 days.

Patients who underwent open surgical procedures had the longest postoperative stay, averaging 23.39 days, with a standard deviation of 17.813 days.

ANOVA was conducted, confirming a significant variance in average postoperative stay duration among therapy groups ($F=9.139$, $P<0.001$). Using the Bonferroni post-hoc test, specific pairwise comparisons were conducted to examine differences between groups.

A significant difference ($P=0.001$) with a mean difference of 11.343 days was found between conservative and open surgery. Similarly, testing between minimally invasive and open surgery revealed a significant difference ($P<0.001$) with a mean difference of 10.319 days.

In summary, it can be noted that patients undergoing open surgical treatment had significantly longer average postoperative stays compared to patients treated conservatively or with minimally invasive surgery. There was no significant difference in postoperative stay between the conservative and minimally invasive groups.

Descriptives

Postoperative stay

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
conservative	42	12.05	14.024	2.164	7.68	16.42	0	68
minimally invasive	224	13.07	14.167	0.947	11.21	14.94	0	164
open surgery	41	23.39	17.813	2.782	17.77	29.01	4	84
Total	307	14.31	15.065	0.860	12.62	16.00	0	164

ANOVA

Postoperative stay

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	3939.085	2	1969.542	9.139	0.000
Within Groups	65512.518	304	215.502		
Total	69451.603	306			

Multiple Comparisons

Dependent Variable: Postoperative stay

Bonferroni

(I) Type of therapy	(J) Type of therapy	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
conservative	minimally invasive	-1.024	2.468	1.000	-6.97	4.92
	open surgery	-11.343*	3.223	0.001	-19.10	-3.58
minimally invasive	conservative	1.024	2.468	1.000	-4.92	6.97
	open surgery	-10.319*	2.494	0.000	-16.32	-4.32
open surgery	conservative	11.343*	3.223	0.001	3.58	19.10
	minimally invasive	10.319*	2.494	0.000	4.32	16.32

* The mean difference is significant at the 0.05 level.

4.3 One Year Survival

In the parameter 'survival after one year,' we analyze how many patients are still alive after one year of treatment. Since for 2/332 patients the year has not yet concluded, no information could be provided for them. Therefore, we are considering a total of 330 patients for this analysis. Across all treatment methods, the overall survival after one year was 256 out of 330 patients (77.6%). 74 out of 330 patients passed away within this year (22.4%).

In our conservative patient group, 29 out of 65 patients survived after one year (44.6%). In relation to the overall survival of all treatment methods, this corresponds to 11,3%. The Chi-square test was applied with a value of 50.550, one degree of freedom, and an asymptotic significance of 0.000. This demonstrated statistical significance ($P<0.001$) between conservative treatment and survival after one year.

The patients treated with minimally invasive methods showed that 192 out of 223 patients were still alive after one year (86.1%). This corresponds to 75% of the overall survival after one year. We obtained a value of 28.719 from the Chi-square test with 1 degree of freedom and an asymptotic significance of 0.000. This test also indicates that minimally invasive treatment demonstrates statistical significance with survival after one year.

The group of patients treated with open surgery showed that 35 out of 42 patients were still alive after one year (83.3%). This corresponds to the overall survival rate of 13,7 % after one year across all treatment. The Chi-square test yielded a value of 0.917 with 1 degree of freedom and an asymptotic significance of 0.338. This indicates that there is no statistical significance between open surgery and survival after one year.

Therefore, it can be statistically interpreted that both conservative and minimally invasive treatment methods have a positive effect on survival after one year. However, open surgical treatment of pleural empyema does not show this effect.

			Survival after one year		Total
			no	yes	
Consevative surgery	No	Count	38	227	265
		% within Consevative surgery	14.3	85.7	100.0
		% within Survival after one year	51.4	88.7	80.3
		% of Total	11.5	68.8	80.3
	Yes	Count	36	29	65
		% within Consevative surgery	55.4	44.6	100.0
		% within Survival after one year	48.6	11.3	19.7
		% of Total	10.9	8.8	19.7
Total		Count	74	256	330
		% within Consevative surgery	22.4	77.6	100.0
		% within Survival after one year	100.0	100.0	100.0
		% of Total	22.4	77.6	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	50.550[a]	1	0.000		
Fisher's Exact Test				0.000	0.000
N of Valid Cases	330				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 14.58.

b. Computed only for a 2x2 table

			Survival after one year		Total
			no	yes	
Minimally invasive	No	Count	43	64	107
		% within Minimally invasive	40.2	59.8	100.0
		% within Survival after one year	58.1	25.0	32.4
		% of Total	13.0	19.4	32.4
	Yes	Count	31	192	223
		% within Minimally invasive	13.9	86.1	100.0
		% within Survival after one year	41.9	75.0	67.6
		% of Total	9.4	58.2	67.6
Total		Count	74	256	330
		% within Minimally invasive	22.4	77.6	100.0
		% within Survival after one year	100.0	100.0	100.0
		% of Total	22.4	77.6	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	28.719[a]	1	0.000		
Fisher's Exact Test				0.000	0.000
N of Valid Cases	330				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 23.99.

b. Computed only for a 2x2 table

			Survival after one year		Total
			no	yes	
Open surgery	No	Count	67	221	288
		% within Open surgery	23.3	76.7	100.0
		% within Survival after one year	90.5	86.3	87.3
		% of Total	20.3	67.0	87.3
	Yes	Count	7	35	42
		% within Open surgery	16.7	83.3	100.0
		% within Survival after one year	9.5	13.7	12.7
		% of Total	2.1	10.6	12.7
Total		Count	74	256	330
		% within Open surgery	22.4	77.6	100.0
		% within Survival after one year	100.0	100.0	100.0
		% of Total	22.4	77.6	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0.917[a]	1	0.338		
Fisher's Exact Test				0.430	0.227
N of Valid Cases	330				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 9.42.

b. Computed only for a 2x2 table

4.4 Hospital Readmission

The parameter "Hospital Readmission" indicates how many patients had to be readmitted to the hospital due to their pleural empyema or respiratory disease. In our entire patient analysis, 60 out of 332 patients (18.1%) required readmission.

The subgroup of conservatively treated patients showed a readmission rate of 7 out of 66 patients (10.6%). When considering this in relation to the overall hospital readmission rate the value of conservatively is 11.7%. The Chi-square test yielded a value of 3.101 with 1 degree of freedom and an asymptotic significance of 0.078. These tests indicate that there is no statistical significance between the readmission rate and conservative treatment.

The analysis of minimally invasively treated patients shows that 38 out of 224 (17%) experienced hospital readmission. When considering this in relation to the total readmission rate of all patients, 63.3% were minimally invasively treated patients. The Chi-square test yielded a value of 0.571 with an asymptotic significance of 0.450. These tests thus prove that there is no statistical significance.

Among the patients treated with open surgery, 15 out of 42 (35.7%) were readmitted to the hospital. This corresponds to a proportion of 25% of all hospital readmissions being from patients treated with open surgery. The Chi-square test yielded a value of 10.107 with an asymptotic significance of 0.001. This confirms that there is a statistical significance between open surgical treatment and hospital readmission (P=0.001).

Overall, the examination of hospital readmission shows an association between readmission and open surgery, which is not reflected in minimally invasive and conservatively treated patients.

			Hospital readmission		Total
			no	yes	
Consevative surgery	No	Count	213	53	266
		% within Consevative surgery	80.1	19.9	100.0
		% within Hospital readmission	78.3	88.3	80.1
		% of Total	64.2	16.0	80.1
	Yes	Count	59	7	66
		% within Consevative surgery	89.4	10.6	100.0
		% within Hospital readmission	21.7	11.7	19.9
		% of Total	17.8	2.1	19.9
Total		Count	272	60	332
		% within Consevative surgery	81.9	18.1	100.0
		% within Hospital readmission	100.0	100.0	100.0
		% of Total	81.9	18.1	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.101[a]	1	0.078		
Fisher's Exact Test				0.106	0.052
N of Valid Cases	332				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 11.93.

b. Computed only for a 2x2 table

			Hospital readmission		Total
			no	yes	
Minimally invasive	No	Count	86	22	108
		% within Minimally invasive	79.6	20.4	100.0
		% within Hospital readmission	31.6	36.7	32.5
		% of Total	25.9	6.6	32.5
	Yes	Count	186	38	224
		% within Minimally invasive	83.0	17.0	100.0
		% within Hospital readmission	68.4	63.3	67.5
		% of Total	56.0	11.4	67.5
Total		Count	272	60	332
		% within Minimally invasive	81.9	18.1	100.0
		% within Hospital readmission	100.0	100.0	100.0
		% of Total	81.9	18.1	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0.571[a]	1	0.450		
Fisher's Exact Test				0.450	0.271
N of Valid Cases	332				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 19.52.

b. Computed only for a 2x2 table

			Hospital readmission		Total
			no	yes	
Open surgery	No	Count	245	45	290
		% within Open surgery	84.5	15.5	100.0
		% within Hospital readmission	90.1	75.0	87.3
		% of Total	73.8	13.6	87.3
	Yes	Count	27	15	42
		% within Open surgery	64.3	35.7	100.0
		% within Hospital readmission	9.9	25.0	12.7
		% of Total	8.1	4.5	12.7
Total		Count	272	60	332
		% within Open surgery	81.9	18.1	100.0
		% within Hospital readmission	100.0	100.0	100.0
		% of Total	81.9	18.1	100.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	10.107[a]	1	0.001		
Fisher's Exact Test				0.004	0.003
N of Valid Cases	332				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 7.59.

b. Computed only for a 2x2 table

5 DISCUSSION

Pleural empyema is one of the most serious complications of pneumonia and other thoracic diseases. A number of reports demonstrated an increasing incidence in infection rate, especially in the elderly population (BTS).

Empyema develops through three stages: the exudative (stage I), fibrinopurulent (stage II), and organized phases (stage III) over the course of 3–6 weeks. Treatment includes conservative therapy and surgery; antibiotics and complete drainage of the infected fluidcavity are the principles of the therapy, which can be accomplished with a range of interventions, including: tube thoracostomy, fibrinolytic therapy, VATS or thoracotomy for decortication.(16)

If not treated early and adequately, it presents a poor prognosis. Notably, frail, elderly, and immunocompromised individuals face a 1.5-fold higher risk of adverse outcomes (17). This study aimed to examine whether and in what way minimally invasive surgery is superior to other treatment methods.

Thanks to advances in minimally invasive surgery, the outcomes for surgically treated patients have improved. According to the American Association for Thoracic Surgery Guidelines, there is a clear recommendation to use VATS as the first-line treatment for the surgical management of pleural empyema (2). In the guidelines it is claimed that VATS holds an advantage over open surgery in terms of a shorter postoperative length of stay and a reduction of 30-day mortality. (2) Similarly, the British guidelines also describe a clear advantage of minimally invasive surgery compared to open surgery. However, these guidelines state that postoperative mortality and the need for reoperation show no significant difference (just slightly lower outcomes) between minimally invasive techniques and open surgery. They do highlight the benefits of reduced postoperative pain, shorter hospital stays, and fewer postoperative complications (1).

In our retrospective data collection, we examined the in-hospital mortality rates among different treatment options. Contrary to the assumption that minimally invasive surgery would result in lower in-hospital mortality, the numbers showed in our study a different outcome. A group of 225 patients underwent minimally invasive surgery, of whom 10/225 (4,4%) experienced in-hospital mortality. In comparison, our analysis included a group of 41 patients who underwent open surgery, with 5/41 (12.2%) experiencing in-hospital mortality.

In our study, statistical analyses indicated that minimally invasive surgery and conservative treatment have a negative impact on hospital mortality. In contrast, open surgery showed no statistical significance. This can be interpreted to mean that both VATS and conservative approaches result in higher hospital mortality, whereas this is not the case with open surgery. This finding was contrary to our assumption; we expected that minimally invasive

surgery would offer an advantage over open surgery regarding hospital mortality. However, some limitations must be considered when applying this statistical result to clinical practice. It is important to note that the number of patients who underwent open surgery in our study was significantly smaller. Additionally, there is no detailed analysis of patient data to determine if the deceased patients had an inherently higher risk of mortality. Examples of such factors include multimorbidity, advanced age, or other underlying conditions. Furthermore, it is difficult to classify the severity of the disease, which means that more patients with a more severe disease course may have been treated minimally invasively, leading to a higher risk of mortality. The BTS discusses that not every patient is considered suitable for undergoing surgical therapy. The precise criteria for determining when surgery should be performed, or which circumstances and parameters should guide this decision, are not clearly delineated (1).

In our study, we discovered that the postoperative hospital stay was shorter with VATS compared to open surgery. The mean post operative hospital stays of patients undergoing minimal invasive surgery were 13.07 days whereas the mean stay in patients undergoing open thoracotomy were 23.39 days. The statistical analysis revealed that open surgery, significantly influenced the longer duration of postoperative stay, while minimally invasive surgery did not. This aligns with international guidelines and reports, which also describe shorter hospital stays with minimally invasive surgery (1, 2).

In a very similar previous report (n=359) from Bavaria, Sziklavari et al. found that recovery following VATS was significantly shorter (in stage II) compared to thoracotomy (23). The reason for the reduced postoperative stay can be multifactorial. As described in the guidelines, reduced pain and decreased blood loss led to less need for pain management and faster mobility for the patient. Additionally, the reduced blood loss contributes to a faster healing rate. Moreover, the wound size is significantly smaller with minimally invasive surgery, necessitating shorter wound management. Shorter postoperative stays are greatly advantageous for patients as they reduce the risk of nosocomial infections and superinfections, and improve the patient's psychological well-being by allowing them to return to their familiar environment sooner. Aside from nosocomial infections, longer hospital stays can also increase the risk of thrombosis and therefore pulmonary embolism. In addition to all the positive factors for the patient, it is also a matter of cost-effectiveness. The healthcare system significantly reduces its costs with a shorter patient stay.

The one-year survival rate was another parameter we investigated. From our analysis no direct comparison could be made between open surgery and minimal invasive surgery. However, we could conclude that there is a statistical significance between the one year survival

rate and minimal invasive surgery, but no statistical significance between one year survival rate and open surgery. The data from our study clearly show that minimally invasive treatment methods (VATS) are superior in terms of survival after one year. The significant statistical evidence supports the adoption of minimally invasive approaches as the preferred treatment option for improving patient outcomes in the context of pleural empyema. However, it is important to note that the parameter "one-year survival" must be viewed critically, as it does not solely depend on the pleural empyema condition. Many patients have comorbidities, and with an average age of 66 years, they are additionally at risk for other diseases, such as comorbidities, advanced age, nutritional status, a weakened immune system which in turn increases the risk of further infections, smoking and alcohol consumption, and many other factors. It is crucial to state that the direct statistical numbers cannot be applied straightforwardly to clinical practice. Nevertheless, the data provide us with valuable indications and reinforce the use of minimally invasive surgery

Another factor that was crucial for us was hospital readmission. We included patients who required inpatient treatment again due to thoracic issues. In our evaluation, we observed significant association between open surgery and hospital readmission. This indicates that patients who underwent open thoracic surgery were significantly more likely to be readmitted to the hospital compared to those who did not undergo open surgery. One must ask what the underlying reasons are: Are postoperative complications, the invasiveness of the procedure, or the typically complex presentation of empyema in these patients the main factors? In any case, our analysis indicates that minimally invasive surgery is statistically superior in this regard. In a large empyema cohort study (n=4095), Semenkovich et al. reported a substantial 30-day readmission rate for empyema (chest tube: 7.3%, VATS: 3.8%, open: 4.1%), with reintervention at readmission significantly higher for chest tube (6.1%) versus surgical patients (VATS: 1.9%, open 2.1%) (24). In the paper by Semenkovich, a 30-day readmission rate was included. In our study, however, we considered a more general readmission rate related to respiratory diseases without a specific time limit, indicating a potential connection with the previous pleural empyema. The absence of a time restriction means that other factors might have contributed to the observed readmissions. Therefore, the higher percentages of readmission in our study can be explained In the British guidelines, it was found as well that VATS treatment reduces postoperative hospital stay and is associated with fewer postoperative complications compared to open surgery (1). Similarly, according to the American Association guidelines: "VATS treatment for acute empyema versus thoracotomy is associated with improved postoperative pain control, shorter hospital stays, reduced blood loss, decreased

respiratory compromise, and a decrease in postoperative complications including 30-day mortality."(2). These points are being discussed here because they could all be reasons for hospital readmission. The fact that patients were readmitted to the hospital is not necessarily due to poorer surgical outcomes with open surgical therapy, but rather to increasing complications, longer hospital stays, and postoperative pain.

Through our analysis and comparison with international guidelines such as those from the BTS and AATS, it was highlighted that minimally invasive surgery is statistically superior to conservative treatment and open surgery in terms of postoperative length of stay, one-year survival, and hospital readmission. Similarly, comparable results were achieved when comparing our findings with publications by Sziklavari and Semenkovich.

Our study offers valuable insights into the treatment of pleural empyema, but several limitations must be acknowledged that could affect the generalizability and accuracy of our findings. We had to exclude some patients from our initial pool of 500 due to incomplete data. Additionally, inter-clinic transfers and discrepancies in sample sizes and treatment protocols present further limitations.

There were notable differences in the sample sizes of the treatment groups, particularly with fewer patients undergoing open surgery compared to those receiving minimally invasive surgery or conservative treatment. Furthermore, the variability in patient comorbidities and disease severity, which we could not fully account for, may have impacted the statistical results.

Survival rates might have been influenced by factors such as patient comorbidities, which were not adequately controlled for in the analysis. The observed significant association between open surgery and higher readmission rates could also be influenced by the lack of a specific timeframe for readmissions. Nonetheless, we believed it was important to extend the timeframe and not limit it to a shorter period.

In conclusion, while our study provides important insights into the treatment of pleural empyema, these limitations should be considered when interpreting the results and their implications for clinical practice. Further research with larger patient groups, standardized data, and additional parameters is necessary to validate these findings and to gain a more comprehensive understanding of the optimal treatment strategies for pleural empyema.

6 CONCLUSION

The treatment of pleural empyema is extremely complex and difficult to clearly define. Nevertheless, our data show clear advantages for minimally invasive surgery. Although this method does not significantly improve mortality according to our results, there are still several benefits that support its use. Based on our analysis, we were able to demonstrate that our patients who received minimally invasive therapy had statistical advantages in terms of one-year survival, hospital readmission, and postoperative stay. These factors all contribute to helping patients reintegrate into their daily lives and familiar environments more quickly. This reintegration can lead to faster and better recovery, ultimately enhancing the patient's quality of life.

As in all areas of medicine, therapy should not be based solely on statistical figures but should treat the person as an individual. Many factors need to be considered to provide individualized and tailored treatment. A patient-centered approach is essential to ensuring optimal care and recovery.

7 REFERENCES

1. Roberts ME, Rahman NM, Maskell NA, Bibby AC, Blyth KG, Corcoran JP, et al. British Thoracic Society Guideline for pleural disease. Thorax. 2023;78(Suppl 3):s1-s42.
2. Shen KR, Bribriesco A, Crabtree T, Denlinger C, Eby J, Eiken P, et al. The American Association for Thoracic Surgery consensus guidelines for the management of empyema. J Thorac Cardiovasc Surg. 2017;153(6):e129-e46.
3. Sunder-Plassmann L. [Pleural empyema]. Chirurg. 1998;69(8):821-7.
4. Shen KR. Surgical management of pleural empyema. Shanghai Chest. 2018;2.
5. Yang W, Zhang B, Zhang ZM. Infectious pleural effusion status and treatment progress. J Thorac Dis. 2017;9(11):4690-9.
6. Charalampidis C, Youroukou A, Lazaridis G, Baka S, Mpoukovinas I, Karavasilis V, et al. Pleura space anatomy. J Thorac Dis. 2015;7(Suppl 1):S27-32.
7. Schünke M SE, Schumacher U, Voll M, Wesker K. Prometheus Lernatlas der Anatomie. Stuttgart: Georg Thieme; 2005.
8. Veronica G, Manju P. Empyema. [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. [cited 2024 July 06] Avaliable from: https://www.ncbi.nlm.nih.gov/books/NBK459237/
9. Yang W, Zhang B, Zhang Z-M. Infectious pleural effusion status and treatment progress. Journal of Thoracic Disease. 2017;9(11):4690-9.
10. Ewig S, Kolditz M, Pletz M, Altiner A, Albrich W, Drömann D, et al. [Management of Adult Community-Acquired Pneumonia and Prevention - Update 2021 - Guideline of the German Respiratory Society (DGP), the Paul-Ehrlich-Society for Chemotherapy (PEG), the German Society for Infectious Diseases (DGI), the German Society of Medical Intensive Care and Emergency Medicine (DGIIN), the German Viological Society (DGV), the Competence Network CAPNETZ, the German College of General Practitioneers and Family Physicians (DEGAM), the German Society for Geriatric Medicine (DGG), the German Palliative Society (DGP), the Austrian Society of Pneumology Society (ÖGP), the Austrian Society for Infectious and Tropical Diseases (ÖGIT), the Swiss Respiratory Society (SGP) and the Swiss Society for Infectious Diseases Society (SSI)]. Pneumologie. 2021;75(9):665-729.
11. Reamy BV, Williams PM, Odom MR. Pleuritic Chest Pain: Sorting Through the Differential Diagnosis. Am Fam Physician. 2017;96(5):306-12.
12. RD A, J B. Malignat Pleural Effusion. StatPearls Publishing: StatPearls [Internet]; 2024.

13. Liou AA, Anderson B, Whitehurst C, Roman S, Beltran C, Acton T, et al. The role of the RAPID score in surgical planning for empyema. J Thorac Dis. 2023;15(3):985-93.
14. Mukherjee S, Sonanini D, Maurer A, Daldrup-Link HE. The yin and yang of imaging tumor associated macrophages with PET and MRI. Theranostics. 2019;9(25):7730-48.
15. Presti T, Asghar A, Ravikumar N. Management of Pleural Infection: A Historical Review and Updates. Journal of Respiration. 2024;4(2):112-27.
16. Light RW. Parapneumonic effusions and empyema. Proc Am Thorac Soc. 2006;3(1):75-80.
17. M. IM, Mauricio D. Thoracic Emypema. StatPearls [Internet]: Treasure Island (FL): StatPearls Publishing; 2023.
18. Kumar A, Anand S. Lung Decortication. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
19. Samira S, Hans LJ. Thoracoscopy: medical versus surgical-in the management of pleural diseases. J Thoracic Disease; 2015;(Suppl 4):S339-51.
20. Lazopoulos A, Barbetakis N, Lazaridis G, Baka S, Mpoukovinas I, Karavasilis V, et al. Open thoracotomy for pneumothorax. J Thorac Dis. 2015;7(Suppl 1):S50-5.
21. Nakajima Y. [Open window thoracostomy and muscle flap transposition for thoracic empyema]. Kyobu Geka. 2010;63(8 Suppl):684-91.
22. Agarwal P, Kukrele R, Sharma D. Vacuum assisted closure (VAC)/negative pressure wound therapy (NPWT) for difficult wounds: A review. J Clin Orthop Trauma. 2019;10(5):845-8.
23. Sziklavari Z, Graml JI, Zeman F, Ried M, Grosser C, Neu R, et al. [Outcomes of Stage-Adapted Surgical Treatment of Pleural Empyema]. Zentralbl Chir. 2016;141(3):335-40.
24. Semenkovich TR, Olsen MA, Puri V, Meyers BF, Kozower BD. Current State of Empyema Management. Ann Thorac Surg. 2018;105(6):1589-96.

8 ENGLISH SUMMARY

Objectives: The aim of this study was to compare the treatment strategies of the original 500 pleural empyema patients from the REGIOMED clinics, in Germany, particularly regarding surgical management using minimally invasive surgery versus open thoracotomy. Specifically, the parameters of in-hospital mortality, postoperative stay, hospital readmission, and survival after one year were examined and compared.

Materials and Methods: Originally, 500 patient data with the diagnosis of pleural empyema from the REGIOMED clinic network, spanning the period from 2017 to 2023, were retrospectively compared. During the analysis, some patients had to be excluded due to incomplete data. Various parameters were examined, focusing on the treatment options used in this study. The therapies were categorized into conservative therapy, drainage, minimally invasive surgery, open thoracotomy, and VAC therapy.

Results: The study included a total of 344 patients with a median age of 66 years. In the examination of in-hospital mortality utilizing the Chi-square test, the findings revealed significant associations between conservative therapy and minimally invasive surgery with in-hospital mortality (P<0.001 and P<0.001, respectively). In terms of postoperative stay a significant difference (P=0.001) with a mean difference of 11.343 days was found between conservative and open surgery. Similarly, testing between minimally invasive and open surgery revealed a significant difference (P<0.001) with a mean difference of 10.319 days. The analysis of one-year survival rates revealed the overall one-year survival rate was 77.6% (256 out of 330 patients). While conservative and minimally invasive treatments showed statistically significant positive effects on one-year survival (P<0.001), open surgical treatment did not demonstrate a statistically significant impact. Overall, 18.1% (60 out of 332) of patients required hospital readmission due to pleural empyema or respiratory disease. While open surgical treatment showed a statistically significant association with higher readmission rates (P=0.001), conservative and minimally invasive treatments did not demonstrate any significant association with readmission rates.

Conclusion: The minimally invasive therapy demonstrates statistical superiority in terms of hospital readmission, postoperative stay, and survival after one year compared to other treatment options. Nevertheless, it does not show superiority in terms of in-hospital mortality. The optimal treatment for a patient should be individualized and tailored to potential comorbidities and prognoses to guarantee quality of life.

9 CROATIAN SUMMARY

Ciljevi: Cilj ove studije bio je usporediti strategije liječenja originalnih 500 pacijenata s pleuralnim empiemom iz REGIOMED klinika, posebno u pogledu kirurškog upravljanja korištenjem minimalno invazivne kirurgije u odnosu na otvorenu torakotomiju. Konkretno, ispitani su i uspoređeni parametri bolničke smrtnosti, postoperativnog boravka, ponovnog prijema u bolnicu i preživljavanja nakon jedne godine.

Materijali i metode: Izvorno je retrospektivno uspoređeno 500 podataka pacijenata s dijagnozom pleuralnog empiema iz mreže REGIOMED klinika, obuhvaćajući razdoblje od 2017. do 2023. Tijekom analize neki pacijenti morali su biti isključeni zbog nepotpunih podataka. Ispitani su različiti parametri, s fokusom na opcije liječenja korištene u ovoj studiji. Terapije su kategorizirane u konzervativnu terapiju, drenažu, minimalno invazivnu kirurgiju, otvorenu torakotomiju i VAC terapiju.

Rezultati: Studija je uključivala ukupno 344 pacijenta s medijanom dobi od 66 godina. U ispitivanju bolničke smrtnosti korištenjem Chi-square testa, rezultati su otkrili značajne veze između konzervativne terapije i minimalno invazivne kirurgije s bolničkom smrtnošću (P<0.001 i P<0.001). U pogledu postoperativnog boravka pronađena je značajna razlika (P=0.001) s prosječnom razlikom od 11.343 dana između konzervativne i otvorene kirurgije. Slično, testiranje između minimalno invazivne i otvorene kirurgije otkrilo je značajnu razliku (P<0.001) s prosječnom razlikom od 10.319 dana. Analiza stopa preživljavanja od jedne godine otkrila je ukupnu stopu preživljavanja od jedne godine od 77.6% (256 od 330 pacijenata). Dok su konzervativne i minimalno invazivne terapije pokazale statistički značajne pozitivne učinke na preživljavanje nakon jedne godine (P<0.001), otvorena kirurška terapija nije pokazala statistički značajan utjecaj. Ukupno je 18.1% (60 od 332) pacijenata zahtijevalo ponovni prijem u bolnicu zbog pleuralnog empiema ili respiratornih bolesti. Dok je otvorena kirurška terapija pokazala statistički značajnu povezanost s višim stopama ponovnog prijema (P=0.001), konzervativne i minimalno invazivne terapije nisu pokazale značajnu povezanost s stopama ponovnog prijema.

Zaključak: Minimalno invazivna terapija pokazuje statističku superiornost u pogledu ponovnog prijema u bolnicu, postoperativnog boravka i preživljavanja nakon jedne godine u usporedbi s drugim opcijama liječenja. Ipak, ne pokazuje superiornost u pogledu bolničke smrtnosti. Optimalno liječenje za pacijenta treba biti individualizirano i prilagođeno potencijalnim komorbiditetima i prognozama kako bi se osigurala kvaliteta života.