

Parapneumonic effusion and thoracic empyema in adults. Clinical aspects, microbiology and frequency of surgical outcome

Empiema torácico en adultos. Aspectos clínicos, microbiología y frecuencia de desenlace quirúrgico

Renata Báez-Saldaña^{1,2*}, Héctor Molina-Corona^{1,2}, María E. Martínez-Rendón^{1,2}, Marco Iñiguez-García¹, Araceli Escobar-Rojas² and Teresa Fortoul-Vandergoes²

¹Instituto Nacional de Enfermedades Respiratorias; ²Postgraduate Division, Faculty of Medicine, Universidad Nacional Autónoma de México. Mexico City, Mexico

Abstract

Background: To date, information about the outcome of patients with parapneumonic effusion and empyema is limited. **Objective:** To describe the clinical characteristics, the microbiological study and the frequency and type of surgical treatment in adult patients with parapneumonic effusion or empyema. **Method:** A prospective cross-sectional study of patients admitted with parapneumonic effusion or empyema, from August 2011 to July 2014, in a reference hospital for respiratory diseases in Mexico City, was conducted. Clinical characteristics, microbiology, risk categories for poor prognosis in empyema and frequency and type of surgical treatment were studied. **Results:** We studied 284 patients whose median age was 47 years, 75% were men, and 57.7% were transferred from other hospitals. In 38.5% of the cases a microorganism was identified and there was a predominance of Gram negative. 153 (53.9%) required surgical treatment, of which 90% were thoracotomy with decortication. Hospital mortality was 5.63%. **Conclusions:** Most of the patients arrived in advanced stages of the disease, so more than half required surgery, of which 90% was decortication. It is desirable to favor mechanisms for early diagnosis and treatment to reduce the need for surgical treatment.

Keywords: Empyema. Microbiology. Surgery treatment.

Resumen

Antecedentes: La información sobre el tipo y la frecuencia del tratamiento quirúrgico en los casos de empiema torácico es escasa. **Objetivo:** Describir las características clínicas, el estudio microbiológico y la frecuencia y el tipo de tratamiento quirúrgico en pacientes adultos con derrame pleural paraneumónico o empiema. **Método:** Estudio transversal prospectivo de pacientes con diagnóstico de derrame pleural paraneumónico o empiema, de agosto de 2011 a julio de 2014, en un hospital de referencia para enfermedades respiratorias en la Ciudad de México. Se estudiaron las características clínicas, las categorías de riesgo para mal pronóstico en empiema y la frecuencia y el tipo de tratamiento quirúrgico. **Resultados:** Se estudiaron 284 pacientes cuya mediana de edad fue de 47 años y el 75% eran hombres. El 57.7% fueron trasladados de otros

*Correspondence:

Renata Báez-Saldaña

Tlalpan, 4502

Col. Sección XVI

C.P. 14080, Ciudad de México, México

E-mail: baezrd@unam.mx

Date of reception: 26-08-2019

Date of acceptance: 06-09-2020

DOI: 10.24875/CIRUE.M20000221

Cir Cir (Eng). 2021;89(1):61-68

Contents available at PubMed

www.cirugiaycirujanos.com

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hospitales. En el 38.8% de los casos se identificó un microorganismo, con predominio de gramnegativos. Requirieron tratamiento quirúrgico 153 pacientes (53.9%), de los cuales en el 90% fue toracotomía con lavado y decorticación. La mortalidad hospitalaria fue del 5.63%. Conclusiones: La mayor parte de los pacientes llegaron en etapas avanzadas de la enfermedad, y por ello más de la mitad requirieron cirugía, de los cuales en el 90% fue lavado y decorticación. Es deseable favorecer mecanismos para realizar un diagnóstico y un tratamiento tempranos con el fin de disminuir la necesidad de tratamiento quirúrgico.

Palabras clave: Empiema. Microbiología. Tratamiento quirúrgico.

Introduction

Patients with community-acquired pneumonia may develop pleural effusion, the frequency of which in the literature is highly variable. A study by Chalmers et al.¹ describes it to be 7.2%,¹ while other works, such as that by Falguera et al.², report it at 19%, and that by Feller-Kopman and Light³, at 40%. Among the cases that develop pleural effusion due to pneumonia, a minority are complicated with pleural empyema, which is associated with considerable morbidity and mortality, which can markedly decrease if the condition is early recognized and treated. In recent years, there has been an increase in the incidence of pleural infections in adults, as shown by studies carried out in Finland⁴, Denmark⁵, Canada⁶ and the United States of America⁷.

In adults, a study in a Canadian population observed a statistically significant 1.2-fold increase in the incidence of empyema over a 9-year period, between 1995 and 2003⁴, and another study in the United States of America showed a more than six-fold increase in empyema mortality rate over a 4-year period, between 2000 and 2004, in comparison with the 1950-1975 rate⁵.

Currently, empyema treatment includes antibiotics and pleural space drainage by placing an endopleural tube with or without the use of thrombolytics⁸. This treatment fails in 30% of cases, in which it is necessary for a surgical approach to be resorted to, either video-assisted thoracoscopy, cavity lavage and decortication, or cavity open drainage⁹.

In a study carried out in Mexican patients with empyema, the delay in decision-making and the time between the onset of the condition and the decision of treatment were identified to be the main factors that caused an adverse event, which ranged from hospital stay prolongation to death¹⁰. In Mexico, empyema continues to be one of the common pleural pathologies that cause significant morbidity and mortality; however, there is limited information available on the outcome

of patients with this disease. The purpose of this work was to describe the clinical characteristics, microbiological analysis and the frequency and type of surgical treatment in adult patients with thoracic empyema.

Method

The study was approved by the Research Ethics Institutional Committee with number C11-11. A prospective cross-sectional study of 284 consecutive patients aged 15 years and older diagnosed with parapneumonic pleural effusion and empyema (PPE/E) was carried out from 2011 to 2014 at a respiratory disease referral hospital in Mexico City. Cases with pleural effusion due to hospital-acquired pneumonia were excluded.

All patients underwent helical computed tomography (CT) of the chest and thoracentesis within the first 24 hours after admission. Patients who were transferred from another hospital and who already had an endopleural tube placed did not undergo thoracentesis. A pleural fluid sample was obtained under aseptic conditions and processed with standardized procedures by the institution's laboratory. Pleural fluid gross examination was carried out, and the sample was subsequently sent in 20-mL sterile syringes for aerobic microorganisms, mycobacteria and fungi cultures. In addition, the samples were systematically processed for cytological examination and biochemical analysis, which included cellularity differential, and pH, lactate dehydrogenase, adenosine deaminase, glucose and protein measurement. C-reactive protein or procalcitonin were not measured in pleural fluid, because in our institution these are not routine measurements for the evaluation and treatment of patients with PPE/E. In cases of empyema with viscous pleural fluid, the sample was sent to the lab only for microbiological examination.

PPE was defined as that with exudate characteristics and cellularity with predominance of polymorphonuclear neutrophils, due to pneumonia. The accepted criteria

for thoracic empyema diagnosis, regardless of its origin, were:

- Frank pus at the time of thoracentesis or finding of microorganisms with Gram staining or culture, or all the following positive tests on pleural fluid: pH < 7.2, glucose < 60 mg/dL, lactate dehydrogenase > 1000 IU/mL, protein > 3 g/mL, and total leukocytes at 15,000 cells/mm³.
- Physical, radiological and laboratory signs consistent with a clinical picture suggestive of empyema¹¹.

Surgery (type of surgery) and death were regarded as outcome variables. The independent variables were general, clinical (comorbidity, symptoms, disease duration) and radiological characteristics; type of empyema, primary or postpneumonic or secondary empyema (postpneumonectomy, hemothorax, trauma, esophageal rupture or secondary to malignant pleural effusion); presence and number of loculations; obesity (body mass index [BMI] > 30 kg/m²) or malnutrition (BMI < 18.5 kg/m² for women and < 20 kg/m² for men)¹²; laboratory and microbiology tests; time between onset of the condition and treatment decision; referral from another hospital and microorganisms isolated in pleural fluid.

Microbiological evaluation included pleural fluid samples for Gram staining and culture for aerobic microorganisms, expectoration, blood culture and bronchial lavage by fibrobronchoscopy. The indication to perform each one of the above tests was individualized according to the case, except for pleural fluid samples culture, for which obtaining material was attempted in all cases. The detection of respiratory pathogens was carried out according to standardized methods and microbiological guidelines at the institution's laboratory, which uses certified methods. In no case was molecular microbiology used for etiology confirmation.

All patients were treated with intravenous antibiotics with a double regimen that included, in most cases, a beta-lactam and another drug to cover anaerobes, such as clindamycin or piperacillin-tazobactam, intravenously administered throughout hospital stay or until completing 3-4 weeks of treatment. In all cases in which pus was obtained on thoracentesis, or in case of PPE with pH ≤ 7.2, an endopleural tube was placed for drainage of the cavity. Intrapleural fibrinolytics were not used in any patient because this type of treatment is not available in our institution. If a satisfactory drainage was not documented or if the patient did not improve, either clinically or

radiographically, the attending pulmonologist evaluated, together with the thoracic surgeon, the decision of surgical treatment, with the approach technique being decided by the surgeon.

Follow-up of the studied cases was until hospital discharge, either due to improvement or death.

Descriptive statistics were carried out. Continuous variables were expressed as medians (25-75 interquartile range [IQR]) and discrete dichotomous or polytomic variables were summarized as frequencies and percentages. The STATA 15.1 statistical package (College Station, Texas, USA) was used.

Results

Two-hundred and eighty-four patients were included in the study; median age was 47 years, 75% were men and low socioeconomic level predominated (89.4%). Among the study population, 60% reported current or past exposure to smoking, with a median smoking index of 5.3 pack-years. In addition, 39% of the cases reported exposure to wood smoke, with a median exposure index of 45 hours per year. Comorbidities were recorded in 82% of the population, with the most common comorbid conditions being diabetes (35.5%) and hypertension (22.9%). Most cases had received antibiotics prior to admission (72.9%) and more than half (57.7%) were transferred from other hospitals (Table 1).

Symptoms were highly variable, but those most frequently reported (> 60%) were self-reported fever, diaphoresis, productive cough, dyspnea, chest pain, and weight loss. In 35.6% of patients, diastolic blood pressure < 60 mmHg was recorded. In 60.5%, heart rate was > 90 beats per minute, and 15% had a respiratory rate > 30 breaths per minute. In 52%, oxygen saturation was < 90%. Median time of current complaint duration was 24 days, and median hospital length of stay was 19 days. There were 16 (5.63%) deaths from empyema during hospitalization, out of which only one was due to tuberculosis (Table 2).

Nearly half the patients had > 12,000 mm³ leukocytes and 66.5% had neutrophilia. Leukocytopenia and neutropenia were uncommon, and lymphocytopenia (lymphocytes < 1000/mm³) was documented in 26% of cases. Anemia and hypoalbuminemia (hemoglobin < 3 g/dL) were common, and were detected in 49.6% and 80% of the patients, respectively (Table 3).

The results of pleural fluid biochemical analysis were consistent with the PPE/E diagnosis, with acidic pH, decreased glucose values and markedly high

Table 1. General characteristics and medical history at admission in 284 patients with parapneumonic pleural effusion or empyema

Characteristics and medical history	n (%)
Age in years, median (IQR)	47 (36-58)
Age in years, upper-lower limits	15-96
Stratified age in years	
15-29	36 (12.7)
30-39	57 (20)
40-59	123 (43.3)
60-69	40 (14.1)
70-96	28 (9.9)
Male gender	213 (75.00)
Low socioeconomic level	254 (89.44)
Current or past smoking	172 (60.56)
Smoking index, median (IQR)	5.3 (2.0, 16.0)
Alcoholism (n = 279)	111 (39.78)
Wood smoke exposure	108 (39.27)
Wood smoke exposure index (hours/year), median (IQR)	45 (14.5-90)
Drug use (n = 284)	23 (8.10)
Any comorbidity	234 (82.39)
Diabetes	101 (35.56)
Hypertension	65 (22.89)
Obesity (BMI $\geq$ 30)	50 (17.60)
Lung cancer	12 (4.23)
Previous admission for empyema	44 (15.49)
Antibiotic prior to admission	207 (72.88)
Transfer from another hospital	164 (57.75)

BMI: body mass index; IQR: interquartile range.

lactate dehydrogenase figures. Regarding the PPE/E characteristics, locule formation was highly common (80.6%), ranging from 1 to 5 in number, with more than half the patients having two or more. Pachypleuritis was documented in 88%. Pus was obtained when thoracentesis was performed in 140 (56.7%) of the 247 cases. A risk category for empyema poor prognosis between moderate and high was identified in 97.5% of patients. Most cases were due to PPE (37.3%) and primary empyema (36.6%) (Table 4).

The microorganisms that were identified in pleural fluid were extremely variable and we only have data on aerobes. In 209 (73.6%) of 284 cases, pleural fluid culture was carried out, and in 81 cases (38.8%) were 89 pathogens isolated, out of which 38.5% were gram-positive and 44% were gram-negative. *Mycobacterium tuberculosis* was isolated in 13.2% and fungi were identified in 4.3%. The most common gram-positive microorganisms were *Staphylococcus aureus* and *Streptococcus constellatus*, and among gram-negative microorganisms, enterobacteria, such as *Escherichia coli*, predominated (Table 5).

In 153 cases (53.9%) a surgical procedure was carried out, and among them, in 138 (90.20%) the

Table 2. Type and frequency of symptoms referred in current condition

Signs and symptoms	Total population N = 284 n (%)
Self-reported fever	197 (69.4)
Chills	147 (51.8)
Diaphoresis	177 (62.3)
Cough	234 (82.4)
Expectoration	207 (72.9)
Dyspnea	242 (85.2)
Chest pain	235 (82.7)
Hemoptysis or hemoptoic sputum	52 (18.3)
Orthopnea	48 (16.9)
Weight loss	172 (60.6)
Myalgia or arthralgia	55 (19.4)
Headache	74 (26)
Fatigue	150 (52.8)
Nausea or vomiting	80 (28.47)
Confusion	21 (7.4)
Wheezing	85 (29.9)
Affected hemithorax	
Right	155 (54.6)
Left	120 (42.3)
Bilateral	6 (2.1)
Systolic blood pressure < 90 mmHg	13 (4.58)
Diastolic blood pressure < 60 mmHg	101 (35.56)
Heart rate > 110 beats per minute	69 (24.3)
Respiratory rate > 30 breaths per minute	42 (14.84)
Oxygen saturation < 90%	121 (51.93)
Disease duration (days), median (IQR) (n = 279)	26 (13-42)
Days of hospital stay, median (IQR)	19 (14-26)
Death	16 (5.63)

IQR: 25-75 interquartile range.

procedure was thoracotomy for lavage and decortication. Open pleurotomy was practiced in 12 cases (7.84%) and video-assisted thoracoscopy was carried out in 3 cases (1.96%). Median (IQR) time elapsed between patient admission and the day surgery was practiced was 8 (4-14) days, and between surgery and hospital discharge, it was 11 (8-20) days (Table 6).

Discussion

In the present study, we describe the clinical characteristics and the frequency and type of surgical treatment of patients with PPE/E, a pathology that is

Table 3. Selected clinical laboratory results in patients with parapneumonic pleural effusion and empyema

Parameters*	
Leukocytes/mm ³	11,600 (8,845-16,750)
Leukocytes > 12,000/mm ³ , n (%)	129 (45.42%)
Leukocytes < 4,000/mm ³ , n (%)	4 (1.41%)
Neutrophils/mm ³	9,000 (6,400-13,620)
Neutrophils > 7,500/mm ³ , n (%)	189 (66.55%)
Neutropenia < 2,000 mm ³ , n (%)	3 (1.06%)
Total lymphocytes	1300 (940-1,800)
Lymphopenia < 1,000 mm ³ , n (%)	74 (26.06%)
Hemoglobin (g/dL)	11.8 (10.4-13.3)
Anemia†, n (%)	141 (49.6%)
Albumin (g/dL)	2.4 (2.01-2.83)
Albumin < 3 g/dL	216 (80.30%)
Lactate dehydrogenase	183 (145-258)

*Results expressed as medians (25-75 interquartile range) unless otherwise specified.

†Anemia according to the World Health Organization cutoff points: women ≤ 11.9 g/dL; men ≤ 12.9 g/dL.

still prevalent in our setting and that in developed countries has shown an increase in incidence and mortality⁴⁻⁷. This is the first prospective study with an elevated number of consecutive patients with pleural infection of similar characteristics to be carried out in a research center in Mexico. The patient population was characterized for being made up of adults at productive stage, with a predominance of men (75%), with a high frequency of exposure to smoking or wood smoke, and with at least one concomitant disease in 80% of the population (the most common were diabetes, hypertension and obesity). More than half the cases were transferred from other hospitals, 73% had received antibiotics prior to hospital admission and 54% of cases did not resolve with chest drainage with endopleural tube and antibiotics, and thus they required surgery, which in 90% of patients consisted of cavity lavage and decortication.

Other studies report a predominance of men similar to that of our study and a median age of 57 years, which is older than that of our population (47 years)¹.

In a study on risk factors for the development of PPE/E, the frequency and type of comorbidity was highly variable¹. Diabetes was much less common than in our study (6.5 vs. 35.6%) and hypertension or obesity were not reported, which were other of the

Table 4. Parapneumonic pleural effusion or empyema characteristics in the study population

Pleural fluid biochemistry	n (%)
pH (n = 113), median (IQR)	7.02 (6.829-7.22)
Pleural fluid glucose (n = 170), median (IQR)	18 (5, 65)
Lactate dehydrogenase, U/L (n = 161), median (IQR)	2340 (700, 7665)
Parapneumonic pleural effusion or empyema characteristics	
Free	55 (19.37)
Loculated	229 (80.63)
Number of locules	
1	104 (36.62)
2	73 (25.70)
3	39 (13.73)
4	12 (4.23)
5	1 (0.35)
Two or more locules	125 (54.59)
Pachypleuritis	251 (88.38)
Pus	140/247 (56.7)
Risk categories for poor prognosis	
1 (very low)	1 (0.35)
2 (low)	6 (2.11)
3 (moderate)	137 (48.24)
4 (high)	140 (49.30)
Type of parapneumonic effusion or empyema	
Parapneumonic	106 (37.3)
Primary empyema	104 (36.6)
Secondary empyema	51 (18)
Tuberculous empyema	23 (8.1)

IQR: 25-75 interquartile range.

most common comorbid conditions in our study, but liver or heart disease are described with a frequency of approximately 10%.

The most common symptoms in the study population were productive cough, fever, pleuritic-type chest pain and dyspnea, which are variable and can occur alone or in combination; none is specific for distinguishing between pneumonia and pneumonia associated with pleural effusion or empyema. In the present study, the aforementioned symptoms, together with weight loss and fatigue, were referred by patients on more than 60% of occasions. Infections by anaerobes are described as having a more chronic course, with weight loss and anemia being more common; both were prevalent in our study, in 61% and 49.6% of patients, respectively, together with leukocytosis with neutrophilia and hypoalbuminemia. The above-described clinical and laboratory variables have been associated with the development of PPE/E in patients with pneumonia^{1,13}.

Table 5. Microorganisms most commonly identified in the pleural fluid of 89 patients with parapneumonic effusion and empyema

Identified microorganisms	n
Two microorganisms in one sample	
<i>Achromobacter dentrificans</i> , <i>Comamonas</i>	1
<i>Acinetobacter baumannii</i> , <i>Acinetobacter calcoaceticus</i>	1
<i>Enterobacter cloacae</i> , <i>Enterococcus faecalis</i>	1
<i>Escherichia coli</i> , <i>Stenotrophomonas maltophilia</i>	1
<i>Proteus mirabilis</i> , <i>Acinetobacter baumannii</i>	1
<i>Staphylococcus aureus</i> , <i>Achromobacter dentrificans</i>	1
Coagulase-negative <i>Staphylococcus</i> , <i>Escherichia coli</i>	1
Gram-positive bacilli, gram-negative bacilli	1
One type of microorganism identified	
<i>Actinomyces israelii</i>	1
<i>Aspergillus</i> sp.	1
<i>Burkholderia cepacia</i>	1
<i>Candida albicans</i>	1
<i>Candida glabrata</i>	1
<i>Enterococcus faecalis</i>	1
	20
<i>Enterococcus faecium</i>	2
<i>Escherichia coli</i>	5
ESBL <i>Escherichia coli</i>	1
<i>Klebsiella pneumoniae</i>	2
<i>Mycobacterium tuberculosis</i>	11
<i>Penicillium marneffei</i>	1
<i>Proteus mirabilis</i>	1
<i>Pseudomonas aeruginosa</i>	2
<i>Staphylococcus aureus</i>	12
<i>Staphylococcus hominis</i>	1
<i>Streptococcus agalactiae</i>	2
<i>Streptococcus intermedius</i>	1
<i>Streptococcus constellatus</i>	7
<i>Streptococcus constellatus</i> ssp.	1
<i>Streptococcus mutans</i>	1
<i>Streptococcus oralis</i>	2
<i>Streptococcus pneumoniae</i>	3
Gram-negative bacilli	11
Gram-positive cocci	1
Main species of gram-negative bacteria identified:	36
<i>Escherichia coli</i> , <i>Enterococcus faecalis</i> , <i>Enterococcus faecium</i> , <i>Pseudomonas aeruginosa</i> , <i>Acinetobacter baumannii</i> , <i>Klebsiella pneumoniae</i> , etc.	
Main species of gram-positive bacteria identified:	31
<i>Staphylococcus aureus</i> , <i>Streptococcus constellatus</i> , <i>Streptococcus pneumoniae</i> , etc.	
Gram-positive cocci and gram-positive and gram-negative bacilli without species identification	7
Fungi: <i>Candida albicans</i> , <i>Aspergillus</i> sp., <i>Penicillium marneffei</i>	4
<i>Mycobacterium tuberculosis</i>	11

The pathogenic microorganisms that have traditionally been identified as a cause of pleural infection are *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *S. aureus*¹³⁻¹⁷. In our study, gram-negative microorganisms were the most common (44%) and only three

Table 6. Frequency and type of surgery practiced in patients with parapneumonic pleural effusion or empyema

	n (%)
Surgery	153/284 (53.9)
Type of surgery	
Lavage and decortication	138/153 (90.20)
Open pleurotomy	12/153 (7.84)
Video-assisted thoracoscopy	3/153 (1.96)
Time between patient admission and surgery (days), median (IQR)	8 (4-14)
Time between surgery and discharge (days), median (IQR)	11 (8-20)

IQR: 25-75 interquartile range.

cases with *S. pneumoniae* were identified among 91 isolates. Our results contrast with previous studies and with that by Lardinois et al.¹⁸, who identified *S. pneumoniae* in 25%, *S. aureus* in 15% and other streptococci in 10%; on the other hand, gram-negative bacteria, such as *E. coli*, *Enterobacter cloacae*, *Proteus mirabilis* and *Pseudomonas aeruginosa*, were identified only in 6%.

Identification of pleural infection causative microorganism is known to tend to be difficult. Previous studies describe that, in 40-82% of cases, the etiological agent is not identified^{1,16,18}. We failed to identify the pathogen in 61.2% of cases, a figure that, though elevated, falls within the range described in the literature. The explanation for this high number of negative cultures has several reasons; among them, that no cultures were carried out for anaerobic microorganisms and neither were molecular methods additional to traditional culture media used for the present study and, on the other hand, a considerably high proportion of patients (72.9%) had received antibiotic treatment prior to obtaining the pleural fluid sample. In addition, it is possible that, in some cases, sterile inflammatory fluid adjacent to a loculus with bacteria was obtained.

There are several surgical techniques that have been employed for the treatment of PPE/E, including pleural decortication, video-assisted thoracoscopic surgery (VATS), thoracoplasty and Eloesser-type open pleurotomy⁸.

Surgery was practiced in 54% of our cases, with the most common type being thoracotomy with decortication on 90% of occasions. Due to a late arrival of most our patients, it is evident that they had the expected complications as a result of the empyema organization stage, such as locule formation and pachypleuritis¹⁹,

which caused, on one hand, incomplete drainage of the cavity, and on the other, pulmonary entrapment, which are complications that often can only be resolved by thoracotomy and decortication²⁰, a procedure that resolves pleural sepsis and allows the lung to expand by freeing it from pleural adhesions, which significantly improves forced vital capacity and forced expiratory volume in 1 second. Although it is a major surgery, median postoperative hospital stay is not that long; for example, in the study by Pothula and Krellenstein^{7,21} it was 7 days, although much shorter compared to our patients' hospital stay, which was 11 (8-20) days.

VATS debridement has gained popularity since the mid-1990s³, and this technique has therefore long been proposed for complicated cases with pleural cavity incomplete drainage, and has been shown to be useful for debridement in multiloculated or single-locule empyema that does not resolve with antibiotic treatment and drainage²². However, in our cases, it was the procedure that was least performed (1.96%), due to the advanced stage at patient presentation, since 97.5% had high categories of risk for complications³. Previous evidence obtained in retrospective studies on the efficacy of VATS as a definitive treatment method in these cases is variable, from 56% to up to 97%^{11,23}, and is highly dependent on the stage PPE/E is found at: the more advanced the organizational phase, the higher the frequency of failure. On the other hand, when this technique was compared with fibrinolytic therapy in a randomized clinical trial in patients with loculated PPE/E, VATS was shown to be more efficacious than fibrinolytic therapy and to be associated with shorter hospital stay and lower cost²⁴.

VATS is a minimally-invasive surgical procedure that can resolve empyema in cases that are not yet chronic; however, the possibility of freely choosing for thoracotomy to be carried out in chronic cases is suggested, especially in those patients in whom the referral procedure takes more than 2 weeks and when gram-negative microorganisms are documented as causing the disease¹⁸, as it occurred in our cases, in whom median time of current complaint evolution was 24 days and gram-negative bacteria predominated. However, it should be noted that the latter criterion was not taken into account to decide the type of surgical approach.

Definitive treatment of patients with PPE/E should be implemented within the first 10 days of hospitalization¹¹, which in our series occurred in 59% of cases, although median (IQR) time elapsed between patient

admission and the day surgery was practiced was 8 (4-14) days. However, hospital mortality was 5.63%, a figure that is at the lower limit of mortality reported in other studies of past decades, which is 4-24%^{18,25}; moreover, this occurred in most cases of bacterial etiology, since only in one of the 16 demises the patient had tuberculosis.

In none of our patients was fibrinolytic therapy used, a fact that we consider did not influence on the high frequency of surgery for pleural infection to be resolved. The use of intrapleural fibrinolytic agents has been described as not being a systematic treatment for PPE/E because it has not shown benefit on mortality reduction²⁶, and the results of a clinical trial carried out in 2005, which included 427 patients, did not show any benefit on mortality, surgery rate or hospital length of stay either²⁷.

Conclusions

Most patients arrived at advanced stages of the disease, and since this is correlated with its evolution time, more than half the cases required surgery to resolve the disease, among which in 90% was thoracotomy with lavage and decortication carried out. The results of this study reflect the need to favor mechanisms for early diagnosis and treatment in patients with PPE/E in order to reduce the need for surgical treatment and, if surgery is necessary, to increase the frequency VATS is practiced with.

Conflicts of interest

The authors declare that there is no conflicts of interests.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

1. Chalmers JD, Singanayagam A, Murray MP, Scally C, Fawzi A, Hill AT. Risk factors for complicated parapneumonic effusion and empyema on presentation to hospital with community-acquired pneumonia. *Thorax*. 2009;64:592-7.

2. Falguera M, Carratalá J, Bielsa S, García-Vidal C, Ruiz-González A, Chica I, et al. Predictive factors, microbiology and outcome of patients with parapneumonic effusion. *Eur Respir J*. 2011;38:1173-9.
3. Feller-Kopman D, Light R. Pleural disease. *N Engl J Med*. 2018;378:740-51.
4. Lehtomäki A, Nevalainen R, Ukkonen M, Nieminen J, Laurikka J, Khan J. Trends in the incidence, etiology, treatment, and outcomes of pleural infections in adults over a decade in a Finnish university hospital. *Scand J Surg*. 2020;109:127-32.
5. Søgaard M, Nielsen RB, Nørgaard M, Kornum JB, Schønheyder HC, Thomsen RW. Incidence, length of stay, and prognosis of hospitalized patients with pleural empyema: a 15-year Danish nationwide cohort study. *Chest*. 2014;145:189-92.
6. Nayak R, Loughheed MD, Brogly S, Lajkosz K, Petsikas D. Thoracic empyema — 20 year trends in management and outcomes in Ontario, Canada. *Am J Respir Crit Care Med*. 2018;197:A4215.
7. Grijalva CG, Zhu Y, Nuorti JP, Griffin MR. Emergence of parapneumonic empyema in the USA. *Thorax*. 2011;66:663-8.
8. Semenkovich TR, Olsen MA, Puri V, Meyers BF, Kozower BD. Current state of empyema management. *Ann Thorac Surg*. 2018;105:1589-96.
9. Reichert M, Hecker M, Witte B, Bodner J, Pöberg W, Weigand MA, et al. Stage-directed therapy of pleural empyema. *Langenbecks Arch Surg*. 2017;402:15-26.
10. Herrera-Kiengelher L, Báez-Saldaña R, Salas-Hernández J, Avalos-Bracho A, Pérez-Padilla R, Torre-Bouscoulet L. Frequency of adverse events and mortality in patients with pleural empyema in a public referral hospital in Mexico City. *Int J Tuberc Lung Dis*. 2010;14:1187-92.
11. Molnar TF. Current surgical treatment of thoracic empyema in adults. *Eur J Cardiothorac Surg*. 2007;32:422-30.
12. World Health Organization. Physical status: The use and interpretation of anthropometry. World Health Organization Technical report series 854. Geneva: WHO; 1995. (Consultado el 24 de octubre de 2018.) Disponible en: https://apps.who.int/iris/bitstream/handle/10665/37003/WHO_TRS_854.pdf.
13. Ahmed RA, Marrie TJ, Huang JQ. Thoracic empyema in patients with community-acquired pneumonia. *Am J Med*. 2006;119:877-83.
14. Burgos J, Luján M, Falcó V, Sánchez A, Puig M, Borrego A, et al. The spectrum of pneumococcal empyema in adults in the early 21st century. *Clin Infect Dis*. 2011;53:254-61.
15. Clark J. Microbiology and management of pleural empyema. *Adv Exp Med Biol*. 2009;634:61-8.
16. Maskell NA, Batt S, Hedley EL, Davies CW, Gillespie SH, Davies RJ. The bacteriology of pleural infection by genetic and standard methods and its mortality significance. *Am J Respir Crit Care Med*. 2006;174:817-23.
17. Marks DJB, Fisk MD, Koo CY, Pavlou M, Peck L, Lee SF, et al. Thoracic empyema: a 12-year study from a UK tertiary cardiothoracic referral centre. *PLoS One*. 2012;7:e30074.
18. Lardinois D, Gock M, Pezzetta E, Buchli C, Rousson V, Furrer M, et al. Delayed referral and gram-negative organisms increase the conversion thoracotomy rate in patients undergoing video-assisted thoracoscopic surgery for empyema. *Ann Thorac Surg*. 2005;79:1851-6.
19. Mutsaers SE, Prele CM, Brody AR, Idell S. Pathogenesis of pleural fibrosis. *Respirology*. 2004;9:428-40.
20. Rzyman W, Skokowski, Romanowicz G, Lass P, Dziadziuszko R. Decorication in chronic pleural empyema — effect on lung function. *Eur J Cardiothorac Surg*. 2001;21:502-7.
21. Pothula V, Krellenstein DJ. Early aggressive surgical management of paraneumonic empyemas. *Chest*. 1994;105:832-6.
22. Corcoran JP, Wrightson JM, Belcher E, DeCamp MM, Feller-Kopman D, Rahman NM. Pleural infection: past, present, and future directions. *Lancet Respir Med*. 2015;3:563-77.
23. Reichert M, Pösentrup B, Hecker A, Schneck E, Pons-Kühnemann J, Augustin F, et al. Thoracotomy versus video-assisted thoracoscopic surgery (VATS) in stage III empyema-an analysis of 217 consecutive patients. *Surg Endosc*. 2018;32:2664-75.
24. Wait MA, Sharma S, Hohn J, Dal Nogare A. A randomized trial of empyema therapy. *Chest*. 1997;111:1548-51.
25. Park C-K, Oh H-J, Choi H-Y, Shin HJ, Lim JH, Oh IJ, et al. Microbiological characteristics and predictive factors for mortality in pleural infection: a single-center cohort study in Korea. *PLoS One*. 2016;11:e0161280.
26. Altmann ES, Crossingham I, Wilson S, Davies HR. Intra-pleural fibrinolytic therapy versus placebo, or a different fibrinolytic agent, in the treatment of adult parapneumonic effusions and empyema. *Cochrane Database Syst Rev*. 2019;(10):CD002312.
27. Cameron R, Davies HR. Intra-pleural fibrinolytic therapy versus conservative management in the treatment of adult parapneumonic effusions and empyema. *Cochrane Database Syst Rev*. 2008;(16):CD002312.
28. Maskell NA, Davies CW, Nunn AJ, Hedley EL, Gleeson FV, Miller R, et al. U.K. Controlled trial of intrapleural streptokinase for pleural infection. *N Engl J Med*. 2005;352:865-874. DOI: 10.1056/NEJMoa042473