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# Prognostic factors influencing the outcome of empyema surgical management: prospective study in a Moroccan University Center.

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## ORIGINAL

### Abstract

Background: Pleural empyema is a public health problem, and is the most frequent complication of pleural infection with significant morbidity and mortality worldwide. Our study aims to highlight the management of pleural empyema and evaluate its prognosis factors involved especially in surgical treatment.

Patients and Methods: A prospective analysis of 53 patients who underwent surgical treatment of pleural empyema, from January 2015 to December 2019 at the thoracic surgery department in a tertiary referral university teaching hospital. Our study included patients who required surgical treatment for pleural empyema and were excluded patients with destroyed lungs associated with pyothorax.

Results: The mean age of patients was 39.24±15.89 years and 79,24% of them were males. In 85.7% of the cases, the etiology was undetermined in 34%, parapneumonic in 1.9%, of tuberculosis in 54.71%, post-traumatic in 11, 3%, postoperative in 7.5% and iatrogenic in 1.9%. 45 patients were treated with broad-spectrum antibiotics therapy adapted after antibiogram 14.38±21.76 days before the operation. A complete debridement and decortications were performed by VATS in 28 and by PLT in 22 patients. No major complications occurred. At a mean term follow-up of 20 months (3months—3 years); all patients were alive with no recurrence. The analysis of the results showed 4 factors of poor prognosis: delay of diagnosis and surgery (P = 0.02), chronic alcoholism (P = 0.034), preoperative ventilation disorder/COPD (P = 0.04) and active tuberculosis (P= 0, 05).

Conclusion: The success of surgical management of pleural empyema depends on several factors, which predict the prognosis, but can be prevented.

**Keywords :** Empyema, Pyothorax, Thoracic surgery, prognostic.

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## Introduction

Pleural Empyema or pyothorax, defined as the presence of bacteria or pus in the pleural cavity, is a serious infection. Despite adapted medical management, empyemas are still associated with high mortality and it ranges between 6%-24% in people with comorbidities with increasing incidence worldwide (1). In our country (Morocco), it remains a real public health problem. The development of pyothorax is conditioned by the precocity and the quality of treatment, but also by the general conditions in which they occur and the morbidity and mortality risk are highly reduced. In this prospective study, we report our 5 years of experience with pleural empyema.

## Patients and Methods

This is a prospective descriptive and analytical study of 53 patients; performed at the thoracic surgery department of Ibn Rochd University Hospital Center, from January 2015 to December 2019. Our study included patients who required surgical treatment for pleural empyema and were excluded patients with destroyed lung associated with pyothorax. All patients are initially seen by a pulmonologist who sometimes determines the etiology of pyothorax and installs a chest tube. The research of Koch's Bacillus (BK) in the sputum was systematic and the patients were operated on after their negativation. All patients underwent a check-up radiological examination performed with a standard chest x-ray and thoracic computed tomography (CT) scan. Preoperative preparation was performed in all of our patients, with the placement of a chest tube to allow an improvement of the respiratory functions and collect pleural effusion samples to perform microbiological and chemical examinations to set targeted antibiotic therapy and incentive physiotherapy. Endoscopy was not performed systematically. The surgical indication was retained due to the failure of medical treatment with the persistence of a trapped lung or several locations of pleural fluid or pleural thickening.

A complete debridement and decortication by VATS approach was the preferred procedure but thoracotomy was due to intolerance to selective intubation or lack of complete evacuation or complete lung expansion. The evolution was considered favorable in view of the complete perioperative pulmonary re-expansion, the stay in intensive care not exceeding 24 hours, the disappearance of the infectious signs, the absence of atelectasis and prolonged air leakage in the immediate postoperative, improvement of respiratory function, absence of sequelae pleural thickening or recurrence of pyothorax, and weight gain in the long-term course. The information was collected from a data collection sheet completed since admission, during hospitalization, and in postoperative. The qualitative values are presented by numbers and percentages. The quantitative values are presented by the medians, the means, and standard deviations. For univariate analyses, the Chi-square test and Fisher's exact test were used, when appropriate. For the outcome analyses, the above-mentioned potential prognostic factors were included in a multiple logistic regression analysis using a backward selection technique SPSS version 17.0 software (SPSS, Inc., Chicago, IL, USA). The level of significance was set at  $p < 0.05$ .

## Results

The mean age of patients was  $39.24 \pm 15.89$  years and 79, 24% of them were males. The main demographical and clinical characteristics of the patients are reported in ( Table 1). Chest pain was the main symptom in the 66%( $n=35$ ) of the series, 50,94%( $n=27$ ) patients presented dyspnea, cough 16,2%( $n=30$ ) high fever 22,6%( $n=12$ ), overall health deterioration 18,9%( $n=10$ ), purulent sputum 13,2%( $n=7$ ), hemoptysis 9,4%( $n=5$ ) and Fluid effusion syndrome 73.9% ( $n=39$ ) at the admission. chest x-ray was performed in all patients showing gas level 37.7%( $n=20$ ), Free pleural effusion 35.8% ( $n=19$ ), Septic pleurisy 18.9% ( $n=10$ ), Thickened pleura 1.9% ( $n=1$ ), Pleural calcifications 1.9%( $n=1$ ) Lung abscess 1.9%( $n=1$ ).

All patients were treated with antibiotic therapy and subsequent target therapy (after determination of responsible germs by bronchoalveolar lavage in 9 cases or analysis of pleural effusion in 23 cases) for  $14.38 \pm 21.76$  days prior to operation. The duration of antibiotic therapy depended on the condition of infectious disease of the patient; C-reactive protein (CRP), the efficacy and response of the treatment. The main etiologic agents were: Streptococcus pneumoniae and Mycobacterium tuberculosis. All patients needed the placement of a chest tube until the effusion was completely drained, and was guided by ultrasound in 18,9% ( $n=10$ ). The median time from admission to drainage was 4 days (range 1 – 10 days), No fibrinolytic therapy had been administered.

A preoperative CT chest for the evaluation of condition was achieved in all patients. 42 patients (79.24%) stage II, 8 patients (15.09%) presented with stage III and 3 patients (5.66%) stage I empyema ( Figure 1). In 43.4% ( $n=23$ ), the etiology was of tuberculous origin, undetermined in 34% ( $n=18$ ), post traumatic in 11,3% ( $n=6$ ), postoperative in 7.5% ( $n=4$ ) and post iatrogenic in 1.9% ( $n=1$ ), parapneumic in 1.9% ( $n=1$ ). The average delay between onset of symptoms and surgery

was 67.5 days (range 15-120).

For the operation, all patients were under general anesthesia with the use of double-lumen endotracheal tubes for selective ventilation and then placed in the lateral position. A complete debridement and decortications were performed in 50 cases by VATS in 28 cases and by PLT in 22 cases and pleuropneumonectomy in 3 cases after the first decortication through PLT. The mean operation time was 180 min. The intraoperative and 30-day mortality was null. The average length of stay in intensive care was 36 +/- 18 hours. Incentive respiratory physiotherapy was performed on all our patients. The last drainage was removed after 7.13±9.05 days and patients were discharged after 15.37±8.67 days. Antituberculosis treatment was administered to patients in whom tuberculosis was diagnosed histologically in the postoperative period. The regimen was isoniazid and rifampin for 6 months, with ethambutol and pyrazinamide for the first 2 months. The outcome was favorable in 90.56% of cases but the following postoperative complications were noted: Persistent pyothorax in 1.88% prolonged air leakage in 7.54% of patients and these five patients had trapped lung were not responsive to surgical treatment of which 2 cases kept the chest drain for an average of 30.45/-15 days and 3 patients were treated with Open window thoracostomy with good evolution. At a mean follow-up of 20 months (3 months–3 years), all patients were alive with no recurrence. The univariate analysis of the results of the surgery allowed to determine 4 factors of bad prognosis: delay between onset of symptoms and surgery > 45 days (P = 0.02), history of chronic alcoholism (P = 0.034), preoperative ventilation disorder: COPD (P = 0.04), active tuberculosis (P = 0.05) (Table 2).

**Table 1.** Demographical and clinical characteristics of the patients

Characteristics	N=53(%)
Age (years) Gender	39.24±15.89
Male	42(79,24)
Female	11(20,75)
Smoking	23(43,3)
Chronic Alcoholism	2(3,8)
COPD	20(37,73)
Heart Disease	2(3,8)
Arterial Hypertension	3(5,66)
Diabetes	6(11,3)
TBK	29(54,71)
Progressive Neoplasm	3(5,7)
Lung Cancer	1(1,9)
Thoracic Traumatism	6(11,3)
Preoperative White Blood Cell Count	13(24,5)
Preoperative C-reactive Protein(>100mg/L)	8(15,2)
Empyema Stage	
I	3(5,66)
II	42(79,24)
III	8(15,09)
Surgical Approach	
PLT	25(47,17)
VATS	28(52,83)
Operating Time (min) Side	120
Right	25(47,16)
Left	28(52,83)
Number Of Chest Tubes	2(100)
Length Of Hospital Stay(days)	15.37 +/-05,67

**Table 2.** the prognostic factors of our series

Prognostic Factors	Favourable Evolution	Unfavourable Evolution	P Value
Diabetes	35(67,6%)	17(32,7%)	0,349
Progressive Neoplasia	35(66%)	18(34%)	0,234
Old Tuberculosis	35(66%)	18(34%)	0,475
Active Tuberculosis	35(66%)	18(34%)	0,05
Lung Cancer	35(66%)	18(34%)	0,359
Smoking	35(66%)	18(34%)	0,634
Chronic Alcoholism	35(66%)	18(34%)	0,034
Thoracic Surgery	33(66%)	17(34%)	0,685
Delay Between Onset Of Symptoms And Surgery >45 Days			0,02
Pleural thickening	31(64,6%)	17(34%)	0,347
Preoperative Ventilation Disorder:COPD	35(66,7%)	18(34%)	0,04

## Discussion

Pyothorax or pleural empyema is a health care problem in many regions of the world; its incidence has increased since 1990, and it has affected more than 65,000 patients each year in the United States and the United Kingdom (2; 3). From 1996 to 2008, the hospitalization for pyothorax increased from 3.0 to 5.9 per 100,000 in the United States population. Pyothorax in recent years might be associated with an increasingly aging, high morbidity in a population (4), the average age of our population was young  $39.24 \pm 15.89$  years which has a good prognostic factor with a low rate of comorbidities ( Table 1). Treatment of these pus collections include surgical drainage and intra-pleural fibrinolytic agents.

Postpneumonic pleural empyema, which is the most common form of pleural empyema (60%), is increasing in North America and Europe and is recognized as a major cause of morbidity and prolonged hospital stay. The second most common cause of pleural empyema is postsurgical (30%), in our study, In 43.4%, the etiology was due to tuberculosis ,undetermined in34% ,post-traumatic in 11,3%, postoperative in 7.5% (5), and post iatrogenic in 1.9% (1), parapneumonic in 1.9%.

In our series, 43.3% were active smokers with a preoperative ventilatory disorder/COPD (P = 0.004) in 37.73% and a history of chronic alcoholism (P = 0.034) in 3.8%. We retained them as 2 significant poor prognosis factors. Unlike simple pleural effusion, empyema shows a rapid clinical progression, and any delay initiating effective drainage may result in increased morbidity and mortality. The importance of early surgical involvement in the management of lobulated pleural effusion and empyema has been reported in many recent studies. According to these studies, early application of VATS drainage or decortication has shown better early results than those in cases managed with fibrinolytic or thoracotomy alone. Presently, VATS has become one of the most important treatment modalities in the management of early stages of empyema, especially during the fibrinopurulent stage. However, because of the lack of sufficient data regarding the optimal timing of operation in the management of loculated pleural effusion and empyema, many physicians and surgeons are still debating when to perform surgical interventions in these patients. In most clinical situations the decision for surgical intervention is based solely on the patient's clinical status (for example, fever, leukocytosis, chest X-ray, and chest CT), and mainly relies on the physician's clinical experience and subjective opinion. Consequently, delays in the decision to perform surgical intervention may lead to deterioration in the patient's status and a worse postoperative outcome (4). In our series, the average delay between the onset of symptoms and surgery was  $54,36 \pm 65,55$  days and was retained as a factor of poor prognosis when it's exceeded 45 days with a P=0,02.

Before surgery it is mandatory, to have the correct empyema stage assessment, which must be done with a clear description of the radiographic aspect and with a CT scan, which can help to locate the presence of a thick pleura, which is a pathognomonic sign of stage 3 empyema ( Figure 1). The American Thoracic Society divides pleural empyema into 3 stages. Diagnosis usually is performed during the first stage with thoracentesis and the treatment is generally medical. The second or fibrinopurulent stages are characterized by a thick fluid and thick fibrin strands positive culture or presence of suppuration and increased loculations in the pleural cavity. Fibrinopurulent empyema changes into pleural fluid collection(stage III) within 7 days to 10 days of symptom onset. In addition, lung entrapment should be suspected when the pleural infection process is known to have been ongoing for longer than 10days to 14 days. The 3 stages of pleural empyema require individualized treatment, but only the second and third stages are definitely for thoracic surgeons. The guidelines produced by the British Thoracic Society suggest surgical treatment in patients with nonresolved pleural empyema with a maximum period of 7 days without resolution. surgical management is different according to the findings of stage II empyema: debridement and stage III empyema: lung decortication. The specimen is always sent for microbiological and pathologic examinations because cancer and mesothelioma could be hidden by an empyema. (6; 5; 7) the preoperative preparation of these patients is an essential step, it begins with the installation of a chest tube. This attitude must be a rule before any surgical intervention, in our series, all the patients received preoperative thoracic drainage. it is the therapeutic key in the management of pyothorax and constitutes a therapeutic emergency. Its interest lies above all in the control of the local and general infectious state to avoid pre- and postoperative septicemia which can be life-threatening. (8) succeeds in all her patients and demonstrates an improvement in respiratory function after decortication. But this improvement was less marked in pyothorax of tuberculous origin due to the pre-existing tuberculous pneumonia, active tuberculosis was a factor of poor prognosis in our study with  $P = 0.05$ .

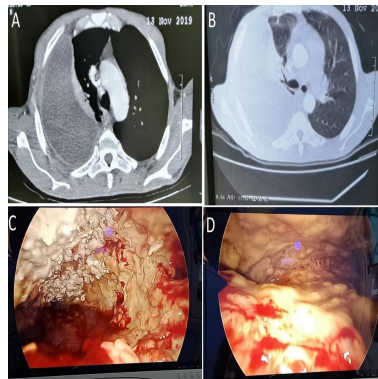
In our study, complete debridement and decortications were the most widely used surgical method: 94.33% (  $n=50$ ) cases benefited from this gesture, through VATS 52, 83% (  $n=28$ ) with good evolution. The PLT was performed in 41,50% (  $n= 22$ ) due to intolerance to selective intubation 50% ( $n=11$ ) or lack of complete evacuation 22,72% ( $n=5$ ) or complete lung expansion 27,27% ( $n=6$ ). In some cases, decortication alone is not sufficient and failed due to the existence of a broncho-pleural fistula and the existence of a severely damaged pathological pulmonary territory or completely destroyed therefore unable to spread and occupy the cavity thoracic. Thoracic surgeons are required to perform a pleuropneumonectomy; an intervention that eliminates the infectious focus and possible threatening fistula. It is a heavy intervention endowed with a risk of mortality of 1 to 9.5% and recurrent pyothorax from 16 to 40%. In our series 3(5,7%) patients had undergone a pleuropneumonectomy through PLT due to the existence of broncho-pleural fistulas. The average length of hospital stay was 15.37 days.

VATS has been demonstrated to be superior to open decortication (or chest tube drainage) for the management of adults with primary empyema in terms of postoperative morbidity, complications, and length of hospital stays and has equivalent resolution compared with open decortication. Additionally, VATS resulted in reduced postoperative pain ( $P<.0001$ ) and complications, including atelectasis( $P=0 .006$ ), prolonged air-leak ( $P= 0.0003$ ), sepsis ( $P= 0.03$ ), and 30-day mortality ( $P=0.02$ ). (9) another study performed in 106 patients demonstrated that patients treated with VATS debridement or decortications spent less time in the hospital, and the conversion rate to open procedure for stage III empyema was only 19%, which encourages considering VATS debridement/decortication as a first-choice treatment. The guidelines produced by the British Thoracic Society suggest surgical treatment in patients with nonresolved pleural empyema with a maximum period of 7 days without resolution. Early referral to surgery is a key factor for a successful operation of pleural empyema by the VATS approach. Conversion from VATS to thoracotomy range from 5.6% to 61% but increases from 22% to 86% between day 12 and day 16 of presentation, and patients with a symptom duration of fewer than 4 weeks had better early results compared with a symptom duration of more than 4 weeks. Stefani and colleagues demonstrated that the probability of thoracotomy increased from 28% to 81% if the operation was performed within 10 days or after a delay of 30 days to 40 days (10; 11).

The guidelines proposed by the European Association for Cardio-Thoracic Surgery preferred VATS in patients with stages II to III pleural empyema with the omission of stage III empyema with more than 5 weeks symptomatic clinical history. VATS decortication has also been reported to successfully manage tuberculous empyema. Irrespective of the pleural empyema stage, some patients have a hidden chest malignancy. (10; 11; 12) According to The American Association for Thoracic Surgery (AATS) consensus guidelines for the management of empyema, the choice of the initial approach in stage III of empyema is dictated based on the condition of the patient, pleural space, and underlying lung parenchyma (13). The development of pyothorax is conditioned by the precocity and the quality of treatment, but also by the underlying lesions and general conditions in which they occur, several factors including predisposing diseases, delay in targeted antimicrobial or surgical treatment, the choice of treatment, and the bacterial aetiology may affect the outcome. A short delay in the diagnosis and treatment of pleural empyema is associated with a superior outcome and a low mortality rate of 4.3 –15%. A difference in mortality from 3.4% to 16% has been described with a delay in chest tube drainage of more than 3 days, and the detrimental effect on the outcome of a further 1-day delay in chest tube drainage has been shown in animal models. Towe and his colleagues noticed that every daily surgery was delayed from admission to day 5 of hospitalization was associated with a 20% relative increase in mortality in these patients. (14) To improve unnecessary delays in patients receiving the most appropriate interventions, surgeons should extend widely their scope of responsibility beyond the operating room. Thoracic surgeons have an obligation to defend the management of empyema in the establishments where they practice and guide early treatment decisions to improve outcomes and reduce resource use in this clinically complex area disease. Thus recent guidelines have concluded that a multidisciplinary approach is recommended (15).

The evolution was favorable in 88.67% of our patients, the outcome was unfavorable in 5 patients who presented postoperative complications, either 9.5% of cases (persistent pyothorax, prolonged air leakage) and the mortality rate was zero.

In our series, the predictors of unfavorable evolution were: long delay between the onset of symptoms and surgery >45 days  $p = 0.02$ , chronic alcoholism  $p = 0.034$ , active tuberculosis  $p = 0.05$ , and finally a preoperative ventilation disorder: COPD  $p = 0.04$ .



**Figure 1.** VATS decortication in pleural empyema stage III of tuberculous origin. A,B) Pre-operative CT of the thorax; and C,D) operative views with thick fibrin layer over the parietal pleura and cortex overlying the lung.

## Conclusion

Pleural empyema remains a major complication of pleural infection with a great challenge for physicians for its treatment. The morbidity and mortality are high in elderly people and patients with co-morbidities but can be reduced to zero in the young population without co-morbidities and risk factors when diagnosis and therapeutic management are made at early time.

## Availability of data and materials

Data available on request from the authors

## Abbreviations

VATS: Video-assisted thoracic surgery, PLT: Postero lateral thoracotomy, COPD: Chronic obstructive pulmonary disease

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## Competing interests

The authors declare that they have no competing interests.

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