



# Predictors of outcome of chest tube drainage of nonpurulent exudative pleural effusions

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This study of predictors of outcome of chest drainage of nonpurulent pleural effusions found that the development of empyema, a prolonged duration of drainage and a prolonged duration of illness are predictive of a poor outcome of drainage <https://bit.ly/3tpK39Y>

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## Abstract

**Background** Although chest tube drainage is the primary management method for many pleural effusions, it has a failure rate of 9.4–48%. In this study, we examined the factors that predict the outcome of management of nonpurulent exudative effusions. The aim of this study was to determine the predictors of outcomes of chest tube drainage of pleural effusions.

**Methodology** Consecutive patients who had a chest tube drainage of nonpurulent exudative pleural effusions were followed up in a prospective observational cohort study until extubation and discharge. Data on the management of the patients were recorded, analysed and compared between groups of patients with good and poor outcomes.

**Results** Of the 52 patients studied, 38 had good outcomes, while 14 had poor outcomes. The mean±SD age was 39.7±15.9 years. Multivariate analysis demonstrated that empyema thoracis complicating drainage was an independent predictor of a poor outcome, while the duration of drainage ≤14 days and duration of illness before presentation <30 days were predictive of a good outcome.

**Conclusion** Our results show that the development of empyema thoracis during drainage, a long duration of drainage and a prolonged period of illness before presentation are predictive of the outcome of chest tube drainage.

## Introduction

Pleural effusion is an accumulation of fluid in the pleural space [1]. It occurs as a result of increased secretion or reduced reabsorption of fluid from the pleural space and can be classified as transudate or exudate according to its composition and underlying pathophysiology [1, 2]. Exudative effusions are usually due to increased vascular permeability or lymphatic obstruction [3]. Common causes of exudative nonpurulent pleural effusions are malignant neoplasms, parapneumonic effusions and empyema [3–5].

The prevalence of pleural effusion is about 400/100 000 population [6]. LIGHT [7] estimated that ~1.5 million people develop pleural effusion in the USA every year. Though the prevalence of pleural effusion in Nigeria is not known, it is nonetheless a cause of significant morbidity and mortality with varying outcomes of management.

The fluid is considered an exudate if it satisfies any of LIGHT's criteria [8]. Other criteria, which have sensitivity and specificity of 96% and 93% respectively, were proposed by ROMERO *et al.* [9].



ROMERO's criteria classify pleural fluid as exudates if: pleural fluid lactate dehydrogenase (LDH) is higher than  $307 \text{ IU}\cdot\text{L}^{-1}$  or pleural fluid cholesterol is higher than  $60 \text{ mg}\cdot\text{dL}^{-1}$ .

The goals of management of pleural effusion are: draining the pleural fluid, adequate lung re-expansion and management of the underlying disease.

Despite some studies showing video-assisted thoracoscopy surgery (VATS) to be of greater benefit in draining complicated exudative effusion, chest tube drainage is still widely used as a standard of care [10–12].

The failure rate of tube thoracostomy in the management of these conditions ranges from 9.4% to 48% [13–15] with attendant morbidities such as additional procedures, higher risk of complications, longer duration of hospital stay and increased cost of care, which negatively affects the social and economic output of patients and that of their dependants. A few studies have investigated the variables predictive of the outcome of chest tube drainage, but these studies have largely been on parapneumonic effusions [13, 16, 17]. It was on this premise that we set out to determine the factors that could predict the outcome of chest tube drainage for nonpurulent pleural effusions and thus identify situations that would require an alternative management approach.

### Methods

This was a prospective observational cohort study that was aimed at identifying the factors that predict the outcome of chest tube drainage of exudative nonpurulent pleural effusions, at the University of Calabar Teaching Hospital in Southern Nigeria. Ethical approval for the study was obtained from the University of Calabar Teaching Hospital Human Research Ethics Committee before the commencement of the study.

Consecutive consenting patients who had a chest tube drainage for nonpurulent exudative effusions were recruited over 12 months between April 2015 and March 2016. The sample size was calculated based on a retrospective review of exudative effusions seen in the year preceding the study. All patients who had post-operative chest tube insertion, empyema thoracis at the time of admission or who withheld consent to participate in the study were excluded from the study. Exudative pleural effusion was defined as having LDH levels  $>307 \text{ IU}\cdot\text{L}^{-1}$  and/or cholesterol levels  $>60 \text{ mg}\cdot\text{dL}^{-1}$  [9]. These criteria have shown equivalence to Light's criteria and are used in this study due to cost-efficiency and convenience in our low resource centre, where patients are often unable to pay for multiple tests or are unwilling to allow the multiple blood sampling that is needed to calculate the ratios in Light's criteria. Empyema was defined as the presence of purulent fluid on thoracocentesis [18, 19].

### Study procedure

Patients who had pleural effusion underwent a general clinical and investigative workup for pleural effusions, including a detailed history and physical examination, posteroanterior (PA) and lateral erect chest radiographs, and diagnostic thoracocentesis. Fifty millilitres of pleural fluid was sampled for biochemical analysis (pH, glucose, protein, LDH, cholesterol), microbiology (gram stain, cell count and bacterial culture; Ziehl–Nielsen staining for acid and alcohol fast bacilli (AAFB) and Genexpert for detection of *Mycobacterium tuberculosis*) and cytology for malignancy. Nonpurulent parapneumonic effusion was defined as pleural effusion associated with underlying pneumonia with the absence of purulent fluid on thoracocentesis [18, 19].

All subjects had 1 g of intravenous ceftriaxone as a prophylactic antibiotic. Under aseptic conditions in the ward procedure room, all patients had insertion of a 28 FG chest tube in the 5th intercostal space along the mid-axillary line under local anaesthesia with 2% lignocaine with adrenaline. The tube was directed posteriorly and upwards, so the tip rested in the paravertebral gutter. The chest tubes were anchored with Nylon 2 sutures with a horizontal mattress technique and connected to underwater sealed drainage without suction. The tube was confirmed to be functional if the fluid in the drainage tubing oscillated with the patient's breathing, towards the chest on inspiration. An erect PA chest radiograph was done on the same day to confirm the position of the tube and adjustments made to the tube position as necessary. Loculated effusion was defined by findings of an irregular scalloped contour of an effusion or fixed fluid in an abnormal location that was not basal on a chest radiograph.

All patients were initially placed on oral paracetamol 1 g every 8 h. The pain response was evaluated and medications adjusted accordingly.

The patients were managed in the thoracic surgery ward by speciality trained nurses. An erect PA chest radiograph was done before removing the chest tube to assess for the degree of drainage and lung

re-expansion and to identify failed drainage and the need for additional procedures. In patients with successful drainage of the effusion, the chest tube was removed if there was drainage of  $<200 \text{ mL}\cdot\text{day}^{-1}$  for three consecutive days with clinical and radiological evidence of full lung re-expansion.

The decision to remove the chest drain and commence with an additional procedure such as a thoracoscopy or thoracotomy was made based on clinical and radiological evidence of trapped lung or persistent complicated empyema with failure of lung re-expansion. Prolonged drainage was defined as a duration of chest drainage exceeding 14 days. In each case, the patient was followed for 1 month after discharge.

Patients were divided by outcome into two groups: good outcome (group 0) and poor outcome (group 1). Good outcome was defined as successful chest tube drainage characterised by: 1) radiological (chest radiograph) evidence of adequate lung re-expansion with aeration of the lung at the ipsilateral costophrenic angle on an erect PA chest radiograph – taken in full inspiration before chest tube removal – and/or blunting of the costophrenic angle that does not extend to the dome of the ipsilateral diaphragm with preserved ipsilateral cardiophrenic angle on an erect PA chest radiograph taken in full inspiration before chest tube removal; and 2) no need for an additional procedure.

#### Data collection and analysis

Data on the patient's clinical information, pleural fluid analysis, radiological investigations, course and complications of closed thoracostomy tube drainage (CTTD), total volume drained, the outcome of CTTD and additional therapeutic interventions were collected for analysis. The outcome measure was the success or failure of chest tube drainage. Data generated from the study were entered and analysed using the Statistical Package for Social Sciences (SPSS) IBM version 20. Univariate analysis was done, Continuous variables were presented as mean $\pm$ SD, while categorical variables were presented as percentages. Continuous and categorical variables were compared using t-test and the Chi-squared test (or Fisher's exact test, where appropriate) to identify factors associated with outcome. Multiple logistic regression was done to identify independent predictive factors of the outcome of CTTD of pleural effusions. Statistical significance was established as  $p<0.05$  and the confidence interval was fixed at 95%.

#### Results

A total of 55 patients were recruited at the commencement of the study; however, three died before any assessment was carried out. The analysis, therefore, was done for the 52 patients who were assessed consisting of 25 (48.1%) males and 27 (51.9%) females. The mean $\pm$ SD age of study participants was 39.7 $\pm$ 15.9 years. Of the three patients that died, two had stage IV breast cancer with pulmonary metastasis and malignant pleural effusion. The third patient was being managed for advanced lung cancer with malignant pleural effusion. They all died of respiratory failure while on chest tube drainage. All patients were followed up for one 1 month after discharge. The demographic, clinical, radiological, pleural fluid and aetiological characteristics of the studied subjects are summarised in table 1.

Bacterial culture was positive in 8 (33.33%) of the 24 pleural fluid aspirate samples taken from patients with parapneumonic effusion. Of these, six grew single isolates and three grew two organisms each. 12 organisms were isolated: 4 (33.3%) *Klebsiella pneumoniae*, 3 (25.0%) methicillin-resistant *Staphylococcus aureus*, 3 (25.0%) *Pseudomonas aeruginosa* and 2 (16.7%) *Proteus mirabilis*. Three (30.0%) of the 10 empyema samples were positive on bacterial culture: two (50.0%) yielded *Klebsiella pneumoniae* and one (25.0%) methicillin-resistant *Staphylococcus aureus*.

The outcome of chest tube drainage was based on the success (good outcome) or failure (poor outcome) of chest drainage. Of the 52 subjects, 38 had a good outcome while 14 had a poor outcome. Twelve of the 14 patients with a poor outcome had additional procedures, while two left the study against medical advice. Of the 12 that had additional procedures, six had thoracotomy and decortication, three had therapeutic thoracentesis, two had open thoracostomy window and one was treated by VATS. All additional treatments were successful and there was no mortality. The commonest complications of chest tube drainage were empyema (20.0%), followed by subcutaneous emphysema (12.7%) and blocked tube (10.9%). Tube dislodgement and malposition each occurred in 1.8% of patients.

Table 2 shows the relationship between study variables and the outcome of chest tube drainage among study participants. Among participants with a good outcome, the proportion of patients whose drainage was not complicated by empyema thoracis was higher than those who developed empyema (88.1% versus 9.1%,  $p<0.001$ ). The highest proportion of participants with good outcomes (91.2%,  $p=0.001$ ) was among those with a duration of illness of  $<1$  month.

**TABLE 1** Demographic, clinical, pleural fluid and radiological characteristics of the studied subjects

<b>Age years, mean±sd (range)</b>	39.67±15.9 (3–73)
≤19	5
20–49	31
50–79	16
<b>Sex, male/female</b>	25/27
<b>Location, rural/urban</b>	38/14
<b>Duration of illness days</b>	
<30	34
≥30	18
<b>Symptoms, frequency</b>	
Dyspnoea	39
Cough	32
Chest pain	30
Sputum	27
Fever	24
Weight loss	19
Haemoptysis	4
History of diabetes mellitus	2
<b>Body mass index kg·m<sup>-2</sup>, mean±sd</b>	22.6±4.8
Underweight	16
Normal weight	21
Overweight	15
<b>Pleural fluid biochemistry, mean±sd</b>	
Glucose mg·dL <sup>-1</sup>	53.88±16.6
Protein g·L <sup>-1</sup>	51.0±20.6
LDH IU·L <sup>-1</sup>	641.76±265.58
Cholesterol mg·dL <sup>-1</sup>	74.1±12.3
pH	7.26±0.27
Drainage duration days, mean±sd (range)	11.98±6.61 (5–36)
<b>Causes of effusion, n (%)</b>	
Pneumonia	24(46.2)
Tuberculosis	17 (32.7)
Malignancy	9 (17.3)
Pleural endometriosis	1 (1.9)
Undiagnosed pleural effusion	1 (1.9)

Data expressed as n unless otherwise indicated. LDH: lactate dehydrogenase.

Table 3 represents the result of multivariate analysis of variables that have a significant association with the outcome of chest drainage. Independent predictors of poor outcome were male sex (odds ratio: 0.04; 95% CI: 0.004–0.399,  $p=0.006$ ) and empyema complicating CTTD (odds ratio: 0.011; 95% CI: 0.001–0.151,  $p=0.001$ ). Patients with these variables were less likely to have good outcomes following CTTD for pleural effusion. However, duration of illness before presentation <30 days (odds ratio: 22.9; 95% CI: 2.154–203.351,  $p=0.001$ ) and duration of pleural fluid drainage <14 days (odds ratio: 13.2; 95% CI: 1.489–117.015,  $p=0.020$ ) were independent predictors of a good outcome.

### Discussion

The rate of good outcomes in this study was 73.1%. Fourteen (26.9%) of the patients in this study had a poor outcome. Of these, patients with nonpurulent parapneumonic effusions accounted for 57.1% of those with poor outcomes. Studies by Nwofor *et al.* [20] and Davies *et al.* [16] reported higher success rates of 86.2% and 85%, respectively. Unlike our study of nonpurulent pleural effusions, Nwofor and co-workers investigated the outcome of chest tube drainage for all pleural collections including traumatic haemothorax, pneumothorax and haemopneumothorax. Davies and co-workers [16] reported an impressive success rate of 85% with chest tube drainage of parapneumonic effusions. This higher rate of good outcome may be explained by their aggressive treatment protocol, which included the use of the radiologically guided chest intubation combined with antibiotic therapy and use of fibrinolytic agents (streptokinase or urokinase), in all cases of effusion they managed. In the study by Huang *et al.* [17], a success rate of 53% with chest tube drainage was reported, which is much lower than what was found in our study. Their study is not directly comparable with ours because it reported a selected series of patients managed in other centres before referral. All the effusions they studied were of pneumonic origin, unlike in this study.

TABLE 2 Relationship between study variables and outcome of chest tube drainage

Variable	Outcome			Chi-squared test	Fisher's exact test	p-value
	Good	Poor	Total			
<b>Subjects</b>	38 (73.1)	14 (26.9)	52 (100.0)			
<b>Age group</b>				0.297		0.862
≤19 years	4 (80.0)	1 (20.0)	5 (100.0)			
20–49 years	23 (74.2)	8 (25.8)	31 (100.0)			
50–79 years	11 (68.8)	5 (31.2)	16 (100.0)			
<b>Sex</b>				15.389		<0.001 <sup>#</sup>
Male	12 (48.0)	13 (52.0)	25 (100.0)			
Female	26 (96.3)	1 (3.7)	27 (100.0)			
<b>Location</b>					Fisher's exact	0.732
Rural	11 (78.6)	3 (21.4)	14 (100.0)			
Urban	27 (71.1)	11 (28.9)	38 (100.0)			
<b>History of diabetes mellitus</b>					Fisher's exact	0.470
Present	1 (50.0)	1 (50.0)	2 (100.0)			
Absent	37 (74.0)	13 (26.0)	50 (100.0)			
<b>Loculation</b>				16.737		<0.001 <sup>#</sup>
Present	0 (0.0)	6 (100.0)	6 (100.0)			
Absent	38 (82.6)	8 (17.4)	46 (100.0)			
<b>Bilateral effusion</b>				5.126		0.102
Present	0 (0.0)	1 (100.0)	1 (100.0)			
Absent	39 (74.5)	13 (25.5)	51 (100.0)			
<b>Colour of effusion</b>				3.577		0.311
Serous	10 (76.9)	3 (23.1)	13 (100.0)			
Serosanguinous	7 (77.8)	2 (22.2)	9 (100.0)			
Straw-coloured	12 (60.0)	8 (40.0)	20 (100.0)			
Bloody	9 (90.0)	1 (10.0)	10 (100.0)			
<b>Total volume drained</b>				0.03		0.863
≤2 L	9 (75.0)	3 (25.0)	12 (100.0)			
>2 L	29 (72.5)	11 (27.5)	40 (100.0)			
<b>Drainage duration</b>				8.047		<0.001 <sup>#</sup>
<7 days	5 (100.0)	0 (0.0)	5 (100.0)			
7–14 days	31 (86.1)	5 (13.9)	36 (100.0)			
>14 days	2 (18.2)	9 (81.8)	11 (100.0)			
<b>Empyema</b>				24.573		<0.001 <sup>#</sup>
Yes	1 (10.0)	9 (90.0)	10 (100.0)			
No	37 (88.1)	5 (11.9)	42 (100.0)			
<b>Blocked tube</b>					Fisher's exact	0.325
Yes	3 (50.0)	3 (50.0)	6 (100.0)			
No	35 (76.1)	11 (23.9)	46 (100.0)			
<b>Subcutaneous emphysema</b>					Fisher's exact	0.370
Yes	4 (57.1)	3 (42.9)	7 (100.0)			
No	34 (75.6)	11 (24.4)	45 (100.0)			
<b>Nerve injury</b>					Fisher's exact	0.470
Yes	1 (50.0)	1 (50.0)	2 (100.0)			
No	37 (74.0)	13 (26.0)	50 (100.0)			
<b>Body mass index</b> kg <sup>-1</sup> .m <sup>-2</sup>				1.110		0.292
Underweight	6 (37.5)	10 (62.5)	16 (100.0)			
Normal weight	17 (81.0)	4 (19.0)	21 (100.0)			
Overweight	15 (100.0)	0 (0.0)	15 (100.0)			
<b>Duration of illness before admission</b>				13.805		0.001 <sup>#</sup>
<30 days	31 (91.2)	3 (8.8)	34 (100.0)			
≥30 days	7 (38.9)	11 (61.1)	18 (100.0)			

Data expressed as n (%) unless otherwise indicated. #: statistically significant.

**TABLE 3** Independent predictors of outcome in chest tube thoracostomy (CTTD) for pleural effusion among study participants

Variable	Odds ratio of success	Odds ratio of failure	95% CI	p-value
<b>Duration of drainage</b>				
<14 days	13.2		1.489–117.015	0.020 <sup>#</sup>
≥14 days	1.0			
<b>Duration of illness before presentation</b>				
<30 days	20.9		2.154–203.351	0.009 <sup>#</sup>
≥30 days	1.0			
<b>Empyema complicating drainage</b>				
Present		0.01	0.001–0.151	0.001 <sup>#</sup>
Absent		1.0		
<sup>#</sup> : statistically significant.				

Similar to our results, DAVIES *et al.* [16] in Oxford, investigating a consecutive series of 85 patients who had chest tube drainage for parapneumonic effusions, found that the absence of purulence is predictive of a good outcome, but other studies [17, 20] did not find purulence to be predictive of outcome.

The review by GIRDHAR *et al.* [21] suggests that any delay in instituting drainage of pleural effusion increases morbidity and mortality. This agrees with our finding that a duration of illness <30 days was predictive of a good outcome but differs from findings by DAVIES *et al.* and other studies [16, 17, 22]. Our findings are, however, consistent with the pathophysiology of pleural effusions, as the longer an effusion is present in the pleural space and not drained, the greater the possibility that it progresses to a viscous fibrinopurulent phase or is complicated by empyema with a thickened pleura, lung entrapment and a poor drainage outcome.

The finding in this study that duration of drainage <14 days is predictive of good outcome differs from some other studies [16, 17, 22]. In the study by HUANG *et al.* [17], successful drainage was defined as either complete drainage of pleural effusion or incomplete drainage of pleural effusion but concomitant improvement in fever and leucocytosis with almost complete resolution of pleural effusion on chest radiograph 1 to 6 months later. This does not take into account that symptoms such as fever may resolve due to the resolution of the pneumonic process while the effusion persists. DAVIES and colleagues [16] allowed only a duration of 7 days before deciding failure of drainage in patients who showed no significant clinical or radiological improvement. TSAI *et al.* [22] retrospectively studied patients who had VATS and defined failure based on mortality. These studies were on parapneumonic effusions, and the definitions of outcome may not compare well with our study. In our study, the decision to remove the chest drain and commence with an additional procedure was made when there was evidence of trapped lung or complicated empyema with failure of lung re-expansion.

Our results show that for exudative nonpurulent pleural effusions, chest tube drainage alone can be done with a relatively high success rate. We found that the development of empyema thoracis during drainage, a long duration of drainage and a prolonged period of illness before presentation are predictive of the outcome of chest tube drainage.

We acknowledge that the current practice of thoracic ultrasound would have enabled us to better identify complicated effusions that would require aggressive treatment. We did not deploy the use of thoracic ultrasound in our study protocol as it was not available in our institution at the time. Our study was also performed in a single centre and may not be generalisable to the entire population of Nigeria. The small number of patients is also a limitation to this study.

We recommend a more aggressive management such as adjunctive fibrinolytic therapy, VATS or thoracotomy and decortication when empyema thoracis complicates chest tube drainage. Early referral of patients with pleural effusions should be encouraged to enable the institution of prompt and appropriate therapy.

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Conflict of interest: None declared.

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