Predicting Factors for Outcome of Tube Thoracostomy in Complicated Parapneumonic Effusion or Empyema*

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Study objectives: **To determine the predicting factors for outcome of tube thoracostomy in patients with complicated parapneumonic effusion (CPE) or empyema.**
Design and settings: **Retrospective chart review over a 55-month period at a tertiary referred medical center.**
Patients and measurements: **The medical charts of patients with empyema or CPE were reviewed. Data including age, gender, clinical symptoms, important underlying diseases, leukocyte count, duration of preadmission symptoms, interval from first procedure to second procedure, the time from first procedure to discharge (recovery time), the amount of effusion drained, administration of intrapleural streptokinase, chest tube size and position, loculation of pleural effusion, and characteristics and culture results of pleural effusion were recorded and compared between groups of patients with successful and failed outcome of tube thoracostomy drainage.**
Results: **One hundred twenty-one patients were selected for study. One hundred of these patients had received tube thoracostomy drainage with 53 successful outcomes and 47 failed outcomes of chest tube drainage. Nineteen patients received decortication directly, and the other two received antibiotics alone. Univariate analysis showed that pleural effusion leukocyte count, effusion amount, and loculation of pleural effusion were significantly related to the outcome of chest tube drainage. Multiple logistic regression analysis demonstrated that loculation and pleural effusion leukocyte count ≤ 6,400/μL were the only independent predicting factors related to failure of tube thoracostomy drainage.**
Conclusions: **Loculation and pleural effusion leukocyte count ≤ 6,400/μL were independent predicting factors of poor outcome of tube thoracostomy drainage. These results suggest that if the initial attempt at chest tube drainage fails, early surgical intervention should be considered in good surgical candidates with loculated empyema or pleural effusion with leukocyte count ≤ 6,400/μL.**
(CHEST 1999; 115:751–756)

Key words: complicated parapneumonic effusion; empyema; predicting factors; tube thoracostomy

Abbreviations: AROC = area under the receiver operating characteristic curve; CI = confidence interval; CPE = complicated parapneumonic effusion; D24 = the volume of pleural effusion drained from the chest tube within the first 24 h; LDH = lactate dehydrogenase; PMN = polymorphonuclear leukocyte; TNF = tumor necrosis factor

Despite the widespread availability of antibiotics and multiple options for drainage of the infected pleural space, the best methods for treating complicated parapneumonic effusions (CPEs) and thoracic empyemas remain debatable. Some reports[1,2] have suggested the most appropriate therapy for empyema or CPE depends on the stage of the disease. Infection of pleural spaces can be divided into three stages. The exudative stage commonly resolves with antimicrobial therapy alone,[2] fibrinopurulent parapneumonic effusion often requires tube thoracostomy drainage, and the organizational stage virtually always requires more aggressive surgical drainage. The evolution of pleural infection is not sharply defined, but rather represents a continuous spectrum of events. The decision for surgical intervention after failure of first tube thoracostomy is always empiric. Very few studies have focused on the predicting factors for outcome of tube thoracostomy drainage. LeMense et al[3] reported no significant

For editorial comment see page 612

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Manuscript received July 28, 1998; revision accepted October 28, 1998.
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difference in procedure success rate or hospital stay between multiloculated and uniloculated empyemas, parapneumonic and nonparapneumonic empyemas, and culture proved and biochemically proved empyemas. Other studies[4,5] suggest that failures of tube thoracostomy drainage were usually due to improper tube positioning, loculated or inaccessible collections, kinking of the thoracostomy tubes, or the presence of highly viscous fluid. None of these previous studies, however, had control groups, and their patient numbers were small. In this study, we reviewed our experience with thoracic empyema and CPE over a 55-month period at our hospital, a tertiary referred medical center, with special focus on the factors influencing the outcome of tube thoracostomy drainage.

Materials and Methods

Patient Characteristics

We retrospectively analyzed the medical records of 121 patients with empyema or CPE treated from January 1993 to July 1997 at National Cheng Kung University Hospital, a tertiary referred medical center in southern Taiwan. Empyema was defined as pleural effusion that met one or more of the following criteria: (1) grossly purulent fluid; (2) positive effusion culture; and (3) positive Gram's stain for bacteria. CPEs were defined as parapneumonic effusion with one or more of the following criteria[6]: (1) pH < 7.00; (2) lactate dehydrogenase (LDH) level $> 1{,}000$ U/L; or (3) glucose level < 40 mg/dL.

Data Collection

The following data were collected for each patient: age, gender, clinical symptoms, important underlying diseases, leukocyte count, duration of preadmission symptoms, the size and loculations of pleural effusions, interval from first procedure to second procedure (second chest tube or decortication), and time from first procedure to hospital discharge (recovery time). The characteristics of pleural effusion, including gross appearance, cell count, pH, glucose, protein, LDH, Gram's stain, acid-fast stain, and culture findings, were also recorded. Data related to tube thoracostomy were also recorded, including the volume of effusion drained from the chest tube within the first 24 h (D24), chest tube size and position, and intrapleural streptokinase administration.

In our hospital, we used water-seal drainage after chest tube insertion and applied low-pressure suction (-20 cm H_2O) if the drainage was not satisfactory. Good chest tube position was defined as chest radiograph or CT scan evidence of tube tip placement within the dependent part of the effusions. Large-amount effusion was defined as a height of the meniscus or size of the effusion reaching more than one third of the chest height or volume. Loculations were defined as the presence of one or more of the following criteria: (1) failure of the effusion to layer on decubitus x-ray films; (2) fixed fluid in an abnormal location; (3) septations seen on ultrasound or CT scan; or (4) irregular scalloped appearance of the effusion contour. Chest tube drainage success was defined as either complete drainage of pleural effusion or incomplete drainage of pleural effusion but concomitant improvement in fever and leukocytosis with almost complete resolution of pleural effusion on chest radiograph 1 to 6 months later. Chest tube drainage failure was defined as incomplete drainage of pleural effusion concomitant with persistent fever, leukocytosis, or fatal outcome. The sizes of the chest tubes inserted were 24F, 28F, or 32F.

Statistical Analysis

The primary end point of the present study was the success or failure of tube thoracostomy for the treatment of empyema or CPE. Possible predicting factors for the success or failure of therapy were assessed against this end point. For comparison of means, the Wilcoxon rank-sum test was used for continuous variables when they departed from a normal distribution; otherwise, Student's t test was used; and the χ^2 (Fisher's Exact Test when needed) test was used for discrete data. Moreover, the area under the receiver operating characteristic curve (AROC) and its 95% confidence interval (CI) were calculated for the continuous variables.[7] Continuous variables with an AROC significantly different from 0.5 were categorized with the cutoff values from the receiver operating characteristic curve analysis and selected for multivariate analysis. For the multivariate analysis, multiple logistic regression analysis was applied to adjust for confounding variables in order to assess the possible predicting factors. Data were reported as mean $\pm$ SEM. All reported p values are two tailed, and a p value < 0.05 was considered to be statistically significant. A software program (JMP; SAS Institute Inc; Cary, NC) was used for the analysis.

Results

Patients Characteristics

One hundred twenty-one patients were included in the present study. The mean $\pm$ SD age of the study population was 59 ± 15 years. Male gender was more frequent (99 men vs 22 women). Among the 121 patients, the most common causes of empyema or CPE were pneumonia (65%) and lung abscess (16%) (Table 1). The most frequent clinical symptoms were fever (76%), chest pain (65%), cough (55%), and dyspnea (44%). The most frequent underlying conditions were diabetes mellitus (29%), malignancy (12%), alcoholism (12%), and liver cirrhosis (10%). Bacteria were isolated or identified in pleural effusion of 69 patients (57%), including 65 from cultures and 4 from Gram's stain. The most frequently isolated bacteria were *Klebsiella pneu-*

Table 1—*Causes of Empyema or CPE*

Cause	No. of Patients
Pneumonia	79
Lung abscess	19
Liver abscess	5
Cancer	4
Postthoracotomy	4
Esophageal leakage	4
Postthoracentesis	1
Miscellaneous	5

moniae (20), mixed culture with viridans streptococci (17), and *Pseudomonas aeruginosa* (Table 2).

Outcome of Tube Thoracostomy

Of the 121 patients, 100 received tube thoracostomy as a first-line therapy. Successful tube thoracostomy drainage was achieved in 53 of these patients, and failure of tube thoracostomy drainage was encountered in 47 patients. Among the 53 patients with successful tube drainage, 6 died (one of Aspergillus meningitis, 1 of hepatorenal syndrome, 1 of pneumonia, and the other 3 of septic shock). Among the 47 patients with failure of tube drainage, 31 received decortication and 22 died. Among the other 21 patients who did not receive tube thoracostomy as first-line therapy, 19 received decortication directly, and 2 received systemic antibiotics alone with complete resolution of pleural infection (Fig 1). The mortality of patients with empyema or CPE in our study was 24% (29/121). Underlying diseases or associated medical condition were present in 26 (90%) of the 29 patients who died. All of the 18 patients with intrapleural streptokinase treatment received 250,000 IU streptokinase per day for 3 consecutive days, and 9 of these 18 patients had successful tube thoracostomy drainage.

Comparison of Success and Failure Groups of Tube Thoracostomy Drainage

A comparison of the two groups of patients is shown in Table 3. The group of patients with successful tube thoracostomy drainage had a significantly higher value of pleural effusion WBC count ($p = 0.04$), and the group of patients with tube drainage failure had a significantly longer interval from the first to the second procedure ($p = 0.03$) and a higher mortality rate ($p = 0.0001$). The recovery time was longer in the tube drainage failure group (27.6 ± 4.2 days) than that of the direct decortication group (16.4 ± 2.9 days; $p = 0.002$) and the group with successful drainage (19.4 ± 1.2 days; $p = 0.06$). No significant differences were found between the two groups with regard to age, gender, pleural effusion pH, protein, glucose, LDH, RBC count; preadmission symptom duration, blood WBC count, underlying diseases, D24, and number of chest tubes inserted.

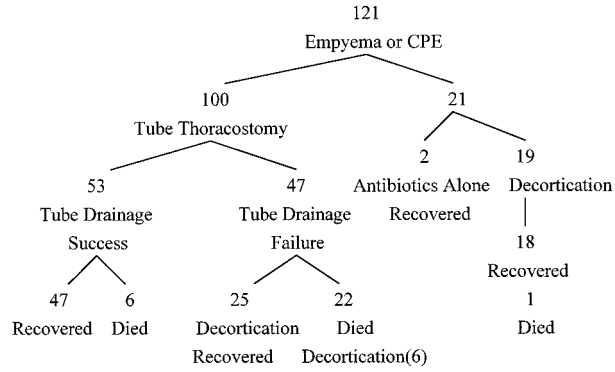

FIGURE 1. Outcome of 121 patients with empyema or CPE.

Table 2—*Bacteria Isolated from Pleural Effusion of 65 Patients**

Organism	Positive Pleural Fluid Culture
K pneumoniae	20
Mixed culture with viridans streptococci	17
P aeruginosa	5
Viridans streptococci	5
S pneumoniae	3
Staphylococcus coagulase negative	3
OSSA	3
ORSA	1
Aeromonas sobria	1
Escherichia coli	1
Group G streptococcus	1
Group D streptococcus	1
Nocardia asteroides	1
Propionibacterium acnes	1
Streptococcus intermedius	1
Yeast	1

*OSSA = oxacillin-sensitive *S aureus;* ORSA = oxacillin-resistant *S aureus.*

Table 3—*Characteristics of Patients in Success and Failure Groups of Tube Thoracostomy Drainage**

Patient Characteristics	Success (n = 53)	Failure (n = 47)	p Value
Age, yr	59.8 ± 1.8	58.0 ± 2.6	0.55
Gender, F/M	12/41	7/40	0.32
Pleural effusion			
PH	6.86 ± 0.05	6.90 ± 0.06	0.85
Protein, mg/dL	3,822 ± 194	3,866 ± 194	0.87
Glucose, mg/dL	72 ± 11	67 ± 14	0.38
LDH, IU/L	5,687 ± 1,653	6,890 ± 2,125	0.20
WBC count, /μL	20,579 ± 4,174	7,822 ± 2,941	0.04
RBC count, /μL	21,234 ± 5,940	73,421 ± 44,134	0.44
Preadmission symptom duration, d	8.8 ± 1.0	8.1 ± 1.1	0.29
Blood WBC count, /μL	15,996 ± 1,149	17,079 ± 1,097	0.33
Underlying disease† (%)	32 (60)	34 (72)	0.20
D24, mL	424 ± 69	445 ± 63	0.50
Recovery time, d	19.4 ± 1.2	27.6 ± 4.2	0.06
Interval from 1st to 2nd procedure, d	2.9 ± 1.1	6.6 ± 0.9	0.03
Mortality (%)	6 (11)	22 (47)	0.0001
No. of chest tubes	1.2 ± 0.1	1.3 ± 0.1	0.32

*Values given as mean ± SEM, unless otherwise indicated.
†Underlying diseases included malignancy, diabetes mellitus, alcoholism, chronic lung diseases, liver cirrhosis, chronic renal failure, and immunosuppression.

Predicting Factors for the Outcome of Tube Thoracostomy

Among all the discrete variables, univariate analysis revealed that only loculations of pleural effusion (odds ratio, 4.72) and large-amount effusion (odds ratio, 2.41) were significantly related to the failure of tube drainage (Table 4), but there was no significant difference in success rates of chest tube drainage between uniloculated and multiloculated empyemas or CPE (33.3% vs 41.2%, $p = 0.75$). For continuous variables, only the pleural fluid WBC count had an AROC significantly different from 0.5 (AROC = 0.66; 95% CI, 0.53 to 0.78) and a cutoff value $\leq 6{,}400/\mu L$ was established. Table 5 shows the results of multiple logistic regression analysis of all the variables tested for possible association with the outcome of chest tube drainage. Multiple logistic regression analysis demonstrated that loculation (odds ratio, 10.29; 95% CI, 2.18 to 79.65; $p = 0.008$) and pleural fluid WBC count $\leq 6{,}400/\mu L$ (odds ratio, 5.53; 95% CI, 1.37 to 28.05; $p = 0.02$) were the only two independent predicting factors related to failure of chest tube drainage.

Table 5—*Results of Multivariate Analysis of Factors Predicting Chest Tube Drainage Outcome*

Predicting Factors	Odds Ratio of Failure	95% CI	p Value
Loculations	10.29	2.18–79.65	0.008
Pleural fluid			
WBC $\leq 6{,}400/\mu L$	5.53	1.37–28.05	0.02

Discussion

The success rate for conventional tube thoracostomy drainage is 32 to 71%.[4] Mandal and Thadepalli[8] reported a 93% cure rate for patients treated by chest tube drainage alone. Their study was limited to patients with bacterial empyemas and excluded effusions caused by trauma, surgical intervention, esophageal diseases, or malignant diseases. The overall success rate of 53% in our study is comparable to that reported from other studies.[9–11] Substantial mortality rates from empyema have been reported, ranging from 1 to 61%.[8,12–14] In the present study, the overall mortality rate was 24%, and 12 fatalities (10%) were directly related to empyemas.

In the present study, *K pneumoniae* was the most common pathogen isolated in empyemas or CPE. This is contrast to recent studies in the West,[3,15,16] in which *Streptococcus pneumoniae* and *Staphylococcus aureus* were usually the predominant organisms. In our study, 10 of the 20 patients with *K pneumoniae* isolated from pleural fluid had diabetes mellitus. This result is similar to other reports[17–19] from Taiwan, in which *K pneumoniae* is the major pathogen of diabetics. The predilection of *K pneumoniae* infection for diabetics remains unexplained.

Very few studies have focused on the predicting factors for outcome of tube thoracostomy drainage. The review of Moran[20] suggests that the duration of the pleural infection, the characteristics of the pleural fluid, the presence or absence of loculations, and

Table 4—*Results of Univariate Analysis of Factors Predicting Chest Tube Drainage Outcome for Discrete Data*

Predicting Factor	Success, No. (%) (n = 53)	Failure, No. (%) (n = 47)	Odds Ratio of Failure	95% CI	p Value
Male	41 (77)	40 (85)	1.67	0.61–4.90	0.32
Pleural fluid					
Positive effusion culture or Gram's stain	28 (53)	28 (60)	1.32	0.60–2.93	0.49
Loculations	25 (47)	38 (81)	4.72	1.97–12.21	0.0005
Large amount effusion	17 (32)	25 (53)	2.41	1.07–5.51	0.03
Pus-like effusion	13 (25)	17 (36)	1.74	0.74–4.20	0.20
Good tube position	29 (55)	20 (43)	0.61	0.28–1.35	0.22
Chest tube size					0.53
24F	9 (17)	12 (26)			
28F	38 (72)	29 (62)	1.75	0.65–4.82	
32F	6 (11)	6 (13)	0.76	0.22–2.67	
Streptokinase	9 (17)	9 (19)	1.16	0.41–3.26	0.77
Chest pain	35 (66)	26 (55)	0.64	0.28–1.43	0.27
Fever	41 (77)	36 (77)	0.96	0.38–2.46	0.92
Alcoholism	5 (9)	7 (15)	1.68	0.50–6.06	0.40
Diabetes mellitus	13 (25)	16 (34)	1.59	0.67–3.84	0.29
Uremia	3 (6)	1 (2)	0.36	0.02–2.94	0.36
Liver cirrhosis	4 (8)	7 (15)	2.14	0.60–8.67	0.24

the overall condition of the patient are the four critical important factors to be considered in the selection of a pleural drainage method. It is reasonable to think that these four factors also influence the tube thoracostomy drainage outcome. The duration of the pleural infection may be difficult to determine because of the indolent nature of many infections and the potential for rapid progression of empyemas. In the study of LeMense et al,[3] no difference in procedure success rates or hospital stay was observed between multiloculated and uniloculated empyemas, parapneumonic and nonparapneumonic empyemas, and culture proved and biochemically proved empyemas. Their success rate of tube thoracostomy drainage was only 11%, because all patients had loculated pleural fluid at presentation. Other studies[4,5] have suggested that improper tube positioning, loculated or inaccessible collections, kinking of the thoracostomy tubes, or the presence of highly viscous fluid were possible causes of tube thoracostomy drainage failure. However, none of these previous studies was controlled and their patient numbers were small.

In the present study, multivariate analysis revealed that loculation of pleural effusion and pleural fluid WBC count $\leq$ 6,400/μL were both independent predicting factors for poor outcome of tube thoracostomy drainage. The success rates of tube drainage in loculated and nonloculated empyema were 40% and 76%, respectively; and in empyema with pleural fluid WBC count $\leq$ 6,400/μL and $>$ 6,400/μL, rates were 52% and 85%, respectively. The finding that pleural fluid WBC count $\leq$ 6,400/μL was a predictor of poor outcome of tube thoracostomy drainage contrasted with the general concept that the degree of leukocytosis is related to the disease severity. The reason for this apparent discrepancy is not clear, but one possible explanation may be related to the release of tumor necrosis factor (TNF) during pleural infection. Interleukin-8 and TNF are the major chemoattractants in the pleural liquid of patients with empyema.[21] Polymorphonuclear leukocytes (PMNs) stimulated with TNF adhere and form zones of close apposition to fibrin, so PMN migration through fibrin gels is inhibited.[22] In addition, fibrin formation is the predominant biological activity of TNF for survival of experimental septic peritonitis.[23] Idell et al[24] also reported that TNF increases plasminogen activator inhibitors 1 and 2 expression or release from human pleural mesothelial cells *in vitro.* Our hypothesis is that if a large amount of TNF surges into the pleural fluid of patients early in the course of empyema or CPE, fibrin will form rapidly and PMNs will adhere firmly to fibrin over the pleural surface. This model can explain why in our study pleural fluid WBC count $\leq$ 6,400/μL was a predictor of poor outcome of tube drainage.

To our knowledge, no previous study has compared the effect of different chest tube sizes on drainage outcome. In our study, the concern that a small-size chest tube may become plugged more easily than larger sizes was not a major factor in drainage outcome, although only chest tube sizes of 24F, 28F, and 32F were used in the study. Tube malposition was also reported as a cause of tube drainage failure.[5] However, in that study, the major causes of tube malposition occurred in tubes exiting from infected pleural space, such as in major fissures, anterior or posterior to the empyema. Today, the use of echo-guided chest tube insertion can avoid these events. However, Duponselle[25] reported that hemothoraces in ambulatory patients seemed to drain adequately regardless of the site of tube insertion. The result of our study was similar to that report, with nondependent tube position not being a major determinant of tube drainage failure.

Many studies[26–32] have reported on the safety and efficacy of intrapleural thrombolysis in the treatment of thoracic empyema, with success rates ranging from about 44 to 100%. The strategies used by these studies appeared to be more aggressive with placement of several tubes in most patients[27] and the use of CT scan guidance during placement.[27,28] Some studies included only early-stage (stage I and II) empyema[29] or empyema related to pneumonia.[30–33] In the present study, although the success rate was only 50% (9/18), our results were similar to those of Chin and Lim[30] in that intrapleural streptokinase did not influence the need for further surgical intervention.

Pothula and Krellenstein[34] reported that prolonged unsuccessful tube drainage is associated with increased morbidity and mortality. The present study showed the recovery time of tube drainage failure patients (27.6 $\pm$ 4.2 days) was significantly longer than that of direct decortication patients (16.4 $\pm$ 2.9 days; $p = 0.002$). The interval from first procedure to second procedure was significantly longer in patients with tube drainage failure than that of patients with successful tube drainage. The mortality was also significantly higher in patients with tube drainage failure than in those with successful tube drainage or direct decortication. Early thoracotomy also has the additional advantage that if decortication is accomplished within 2 weeks of pleural infection, the visceral pleural rind usually is easily extricated from the lung.[35] Several recent studies[36,37] have reported that video-assisted thoracoscopic surgery has the same rate of success as formal thoracotomy but offers substantial advantages over formal thoracotomy in terms of hospital stay and cosmetics in the treatment of loculated or tube thoracostomy-resistant empyemas. Although video-assisted thoracoscopic surgery may fail in cases of extensive pleural adhesions or

late-stage empyema,[38] it may be a safe and effective alternative in the treatment of empyema with loculations or pleural fluid WBC count ≤ 6,400/μL.

In conclusion, our results showed that loculation of pleural effusion and pleural fluid WBC count ≤ 6,400/μL were independent predicting factors for poor outcome of tube thoracostomy in this series. These results suggest that surgical intervention should be considered early after failure of first chest tube drainage in good surgical candidates with loculated empyema or pleural fluid with WBC count ≤ 6,400/μL to minimize the mortality and morbidity associated with thoracic empyema or CPE.

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