Sonographic septation: a useful diagnostic predictor of complicated parapneumonic effusion

Shan-Yueh Chang ,[1,2,3] Ying-Chieh Chen,[1] Chen-Liang Tsai,[1] Shih-Wei Wu,[1,2] Chung-Kan Peng,[1,3] Chih-Hao Shen,[1,3] Yu-Ching Chou ,[4] Chih-Feng Chian [1]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan
[2]Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan
[3]Hyperbaric Oxygen Center, Division of Pulmonary Medicine and Critical Care Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan
[4]School of Public Health, National Defense Medical Center, Taipei, Taiwan

Correspondence to
Dr Chih-Feng Chian, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan; sonice3982@gmail.com

Accepted 25 May 2021
Published Online First 19 July 2021

To cite: Chang S-Y, Chen Y-C, Tsai C-L, *et al*. *J Investig Med* 2021;**69**:1447–1452.

ABSTRACT

Sonographic septation is associated with prolonged hospitalization and increased mortality in patients diagnosed with empyema. However, it is unknown whether sonographic septation is associated with complicated parapneumonic effusion (CPPE) or the need for invasive procedures among patients with pneumonia. In this retrospective study, we included 180 patients with non-purulent neutrophilic exudative pleural effusion secondary to pulmonary infections such as pneumonia and lung abscess. We performed univariate and multivariate logistic regression analyses, including baseline clinical characteristics, values from blood samples, and sonographic echogenicity, to identify variables correlated with CPPE and the need for invasive procedures. Seventy of the 180 included patients (38.89%) displayed sonographic septation. Multivariate logistic regression analysis identified that sonographic septation (adjusted OR (AOR)=3.38 (95% CI 1.64 to 6.98), p=0.001) and younger age (AOR=2.63 (95% CI 1.24 to 5.58), p=0.012) were independently associated with CPPE. With regard to treatment strategy, sonographic septation (AOR 9.06 (95% CI 3.71 to 22.11), p<0.001) and total serum protein level (AOR=1.80 (95% CI 1.13 to 2.86), p=0.013) were independently associated with the need for subsequent invasive procedures in patients with CPPE using multivariate logistic regression analysis. Sonographic septation is a useful predictor of CPPE and may imply the need for early invasive procedures.

Significance of this study

What is already known about this subject?

- 20%–40% of hospitalized patients with pneumonia have parapneumonic effusion (PPE) and the mortality rate of patients with pneumonia and PPE is as high as 15%.
- Treatment of complicated parapneumonic effusion (CPPE) consists of empiric antibiotic therapy and adequate drainage of the pleural fluid.
- Diagnosis and timing of drainage for patients with CPPE may be delayed due to similar clinical presentations to uncomplicated PPE, resulting in longer hospital stay and increased healthcare expenditure.
- Although the biochemical parameters of pleural effusion, Gram stain, and bacterial cultures are used to diagnose CPPE and determine treatment strategy, this process is time-consuming.

What are the new findings?

- Patients with sonographic septation had a 4.68-fold higher risk of having CPPE compared with those without septation (OR=4.68, 95% CI 2.45 to 8.91) using univariate logistic regression analysis.
- In multivariate logistic regression analysis, sonographic septation and younger age remained significantly correlated with CPPE.
- In multivariate logistic regression analysis, sonographic septation and total serum protein level were independently associated with invasive procedures.

INTRODUCTION

Pneumonia remains a major cause of death, even after years of research and the development of a broad spectrum of antibiotics.[1] In 2005, there were more than 60,000 people aged 15 years and above who died from pneumonia in the USA.[2] Parapneumonic effusion (PPE) is a type of effusion which usually occurs in patients with pneumonia or a lung abscess. It has been reported that 20%–40% of hospitalized patients with pneumonia have PPE and that the mortality rate of patients with pneumonia and PPE is as high as 15%.[3] Additionally, 20% of patients with PPE require hospitalization for more than 1 month.[4] Furthermore, a higher mortality rate has been reported in patients with bilateral PPE compared with those with unilateral PPE.[5] Complicated parapneumonic effusion (CPPE) is defined as PPE which only resolves after an invasive procedure, such as tube thoracostomy, or yields a positive Gram stain or bacterial culture.[6] Treatment of CPPE consists of empiric antibiotic therapy and adequate drainage of the pleural fluid. Several

Significance of this study

How might these results change the focus of research or clinical practice?

- Sonographic septation is a useful predictor of CPPE.
- Chest sonography may adjudicate on the decision of invasive procedures in patients with non-purulent PPE.
- Further studies are needed to investigate the association between sonographic septation and invasive procedures and its influence on prognosis in patients with non-purulent PPE.

guidelines have been proposed to accurately and rapidly diagnose CPPE to improve the outcomes by the early application of adequate drainage.

The American College of Chest Physicians (ACCP) and the British Thoracic Society (BTS) have proposed criteria to differentiate CPPE from non-CPPE and guide treatment.[7–9] The ACCP guidelines use plain chest radiograph of the pleural space, biochemical parameters, and bacteriology of the pleural effusion to categorize patients into four categories. Categories 3 and 4 are defined as moderate and high risk groups, respectively, and adequate drainage is recommended for these patients. The BTS guidelines use biochemical parameters of the pleural effusion and bacteriology to classify patients as having uncomplicated parapneumonic effusion (UPPE), CPPE, and empyema. Patients with empyema are recommended to receive empiric antibiotics as well as invasive procedures such as pigtail catheter drainage, chest tube thoracostomy, or video-assisted thoracoscopic surgery (VATS) to promptly control pleural infections. Importantly, the diagnosis and timing of drainage for patients with CPPE may be delayed due to similar clinical presentations to UPPE, resulting in longer hospital stay and increased healthcare expenditure.[10] Therefore, it is very important to accurately identify CPPE as early as possible. Although the biochemical parameters of pleural effusion, Gram stain, and bacterial cultures are used to diagnose CPPE and determine treatment strategy, this process is time-consuming.

Few studies have focused on identifying the predictive factors for CPPE/empyema. Falguera *et al*[11] identified five independent baseline characteristics, including age, alcoholism, pleuritic pain, tachycardia, and leukocytosis, in 882 patients diagnosed with community-acquired pneumonia with PPE. Although several clinical factors have been reported to predict CPPE/empyema, the application of imaging studies such as chest sonography has never been reported. Transthoracic sonography is a useful method to safely guide thoracentesis and the placement of a chest tube.[12 13] In patients with empyema, sonographic septation has been associated with longer hospital stay, longer duration of chest tube drainage, and higher probability of a need for fibrinolytic therapy or surgical interventions.[14] However, whether sonographic septation is a predictor of CPPE or a guideline for pleural drainage has never been investigated. Therefore, this study aimed to clarify the clinical significance of sonographic septation in patients with PPE.

METHODS

Study subject

All hospitalized patients with exudative pleural effusion secondary to pneumonia or lung abscess who underwent chest sonography and thoracentesis between January 2002 and April 2011 at the Tri-Service General Hospital, a tertiary referral center in Taiwan, were included in this study. All medical records, including the results of the pleural fluid analysis, cultures, biochemical parameters, cell counts, pH, cytology, baseline characteristics, and treatment strategy, from these patients were retrospectively reviewed. The inclusion criteria were age older than 20 years and those with exudative pleural effusion with neutrophil predominance concomitantly with pneumonia or a lung abscess.

The definition of exudate was determined according to Light's criteria.[15] Patients who had PPE were classified into UPPE or CPPE group according to the BTS guidelines (a case is defined as CPPE if it fits any of the following parameters: pleural fluid lactate dehydrogenase (LDH) >1000 IU/L, glucose <40 mg/dL, pH <7.2, positive Gram stain or bacterial culture).[7]

All patients were treated empirically with antibiotics, consisting of broad-spectrum penicillin with beta-lactamase inhibitor (amoxicillin-clavulanate, ampicillin-sulbactam, piperacillin-tazobactam), cephalosporin (ceftriaxone, ceftazidime, or cefepime), clarithromycin, fluoroquinolone (levofloxacin or moxifloxacin), or carbapenem (imipenem, meropenem, ertapenem). The antibiotics were changed in some cases according to the susceptibility evaluated with bacterial culture. Patients were excluded if the pleural fluid analysis showed transudative effusion, exudative effusion with lymphocyte predominance, malignant pleural effusion, post-traumatic pleural infection, tuberculosis-related effusion, or empyema (pus in the pleural fluid).[5] The decision to use invasive procedures or not was left up to the discretion of the attending physician. The most common causes of undergoing tube thoracostomy or VATS in this study were uncontrolled sepsis, large effusion with clinical symptoms such as dyspnea, or multiloculated effusion.

Imaging studies of the chest

The timing of chest ultrasound in this study is after the initial encounter of pneumonia or lung abscess with pleural effusion. All patients received chest ultrasound in an upright seated position or lying in the lateral decubitus position. A real-time ultrasound scanner (Toshiba SSA-340A; Tokyo, Japan) with a 3.75 MHz sector transducer under fixed parameters, such as a gain setting of 80 dB and a transmitted focal depth of 6 cm, was used to evaluate the pleural effusion, followed by a diagnostic thoracentesis if the width of the pleural effusion exceeded 10 mm. All sonographic images of the pleural fluid from the included patients were saved in JPG format. Sonographic septation was determined by two board-certified chest physicians blinded to patients' clinical information. If any disagreement existed between these two chest physicians, another senior board-certified chest physician was consulted. Sonographic septation was defined as the presence of hyperechoic strands (figure 1A) or web-like, branching fibrinous septa floating in the pleural effusion (figure 1B), as opposed to non-septated pleural effusion (figure 1C).[14 16]

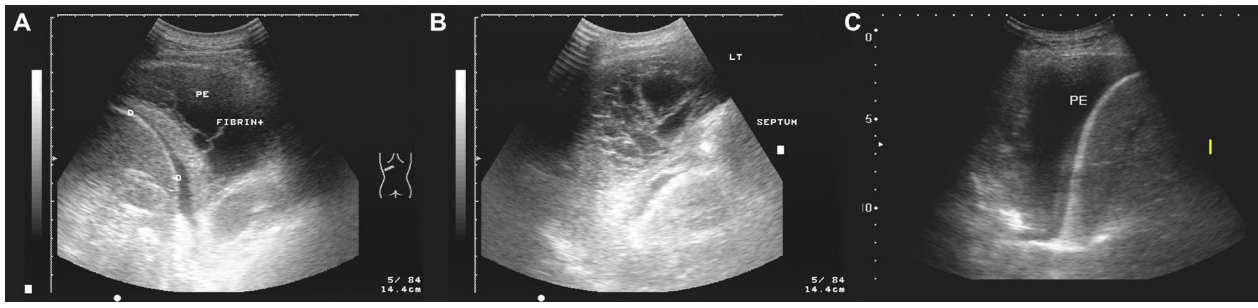

Figure 1 Sonography of chest demonstrated the presence of hyperechoic strands in the pleural fluid (A), branching fibrinous septa floating in the pleural effusion (B), and non-septated anechoic effusion (C). PE, pleural effusion; LT, left side.

Pleural effusion samples obtained with diagnostic thoracentesis were aliquoted into different collecting tubes using aseptic techniques. All specimens were sent to the laboratory for analysis of LDH, total protein, glucose, total leukocyte count, differential leukocyte count, Gram stain, bacterial culture, acid-fast stain, tuberculosis culture, cytology, and pH using a blood gas analyzer.

Statistical analysis

Data were expressed as mean±SEM. Continuous variables were compared between groups using the Student's t-test, and the χ^2 test was used to examine the differences between the two groups with respect to categorical variables. Fisher's exact test was used to compare differences between categorical variables among groups if the expected count of at least one cell was less than five. The positive predictive value, negative predictive value, sensitivity, and specificity of sonographic septation in predicting CPPE were calculated. OR, adjusted OR (AOR), and corresponding 95% CI of positive sonographic septation in predicting CPPE and invasive management were calculated using univariate and multivariate logistic regression analyses. Potential predictive factors including baseline characteristics which appeared to be significant in the univariate logistic regression analysis were entered into the multivariate logistic regression analysis in order to determine if the factors are independently associated with CPPE and the need for invasive management. Agreement between the two chest physicians in determining sonographic septation of the pleural fluid was evaluated by kappa statistics. All statistical analyses were performed using IBM SPSS Statistics V.22, and a two-tailed p value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Baseline characteristics and comorbidities

We included a total of 180 patients who had PPE and received thoracentesis from January 2002 to April 2011, of whom 97 (53.89%) were diagnosed with UPPE and 83 (46.11%) with CPPE. The baseline clinical characteristics, comorbidities, and sonographic echogenicity are shown in table 1. There were no significant differences in gender, smoking status, and comorbidities between the two groups; however, the CPPE group had a higher percentage of patients less than 60 years age, sonographic septation, and a lower rate of comorbid chronic obstructive pulmonary disease (COPD), compared with the UPPE group.

Bacteriology

Of the 180 patients, 21 (11.67%) of the effusion cultures were positive for micro-organisms. These findings consisted of 22

Table 1 Baseline characteristics of the study population

	Total	Parapneumonic effusion		
Baseline characteristics and comorbidities	(N=180)	UPPE (n=97)	CPPE (n=83)	P value
Age (years)	65.78±18.16	70.09±16.97	60.75±18.30	<0.001
Sex (male)	139 (77.2)	76 (78.4)	63 (75.9)	0.696
Smokers	96 (53.3)	55 (56.7)	41 (53.2)	0.649
Comorbidities				
Hypertension	72 (40.0)	44 (45.4)	28 (36.4)	0.231
Diabetes mellitus	40 (22.2)	25 (25.8)	15 (19.5)	0.327
COPD	28 (15.6)	22 (22.7)	6 (7.8)	0.008
Congestive heart failure	8 (4.4)	3 (3.1)	5 (6.5)	0.469
Chronic kidney disease	17 (9.4)	11 (11.3)	6 (7.8)	0.434
Malignancy	35 (19.4)	23 (23.7)	12 (15.6)	0.184
Cirrhosis	7 (3.9)	2 (2.1)	5 (6.5)	0.243
Atrial fibrillation	9 (5.0)	6 (6.2)	3 (3.9)	0.733
Sonographic septation	70 (38.9)	22 (22.7)	48 (57.8)	<0.001

Data are presented as mean±SD or n (%) unless otherwise stated.
Differences between continuous variables are assessed using Student's t-test. Fisher's exact test and χ^2 test are used for nominal variables.
COPD, chronic obstructive pulmonary disease; CPPE, complicated parapneumonic effusion; UPPE, uncomplicated parapneumonic effusion.

Table 2 Correlations between sonographic features and laboratory characteristics of pleural effusion and serum

	Sonographic septation		
Variables	**Positive (n=70)**	**Negative (n=110)**	**P value**
Pleural effusion			
LDH (IU/dL)	1654.10±232.99	960.5±191.84	0.024
Total protein (g/dL)	4.52±0.11	3.81±0.11	<0.001
Glucose (mg/dL)	72.91±10.98	118.95±6.53	<0.001
pH	7.46±0.64	7.83±0.47	<0.001
White cell count ('×10^9/L)	8.897±1.567	6.898±1.087	0.281
% neutrophils	82.23±1.52	75.00±1.47	0.001
% lymphocytes	11.21±1.32	13.77±1.22	0.171
Serum			
White cell count (×10^9/L)	13.994±0.820	13.803±0.686	0.859
CRP (mg/dL)	16.86±1.17	15.75±0.99	0.482
LDH (IU/dL)	282.53±20.79	281.70±17.17	0.975
Total protein (g/dL)	6.32±0.11	6.09±0.89	0.114
Glucose (mg/dL)	143.16±10.30	142.35±5.57	0.940
Albumin (g/dL)	3.09±0.78	3.00±0.58	0.354

Values are presented as mean±SEM.
P value is derived via Student's t-test, and p<0.05 is considered to be significant.
CRP, C reactive protein; LDH, lactate dehydrogenase.

organisms, including 13 aerobic Gram-positive bacteria, 5 aerobic Gram-negative bacteria, and 4 anaerobic bacteria. The most frequently isolated bacteria were *Streptococcus viridans* (n=5) and methicillin-resistant *Staphylococcus aureus* (n=3). The incidence of bacteria isolated from pleural effusion was much higher in the sonographic septated group than in the non-septated group (20% vs 4.5%, p=0.004).

Laboratory findings and sonographic septation

Table 2 shows the laboratory characteristics of pleural effusions with and without sonographic septation. The glucose level (p<0.001) and pH (p<0.001) of the pleural effusions were significantly lower in the sonographic septation group than in the non-septated group, whereas total protein level (p<0.001), LDH (p=0.024), and the percentage of neutrophils (p=0.001) were significantly higher in the sonographic septation group. The interobserver agreement of sonographic septation reached a κ of 0.77 between the two chest physicians.

Sonographic septation predicted CPPE

Patients with sonographic septation had a 4.68-fold higher risk of having CPPE compared with those without septation (OR=4.68, 95% CI 2.45 to 8.91) using univariate logistic regression analysis. In addition, CPPE was significantly associated with younger age, lower rate of COPD, and high serum total protein level in univariate logistic regression analysis. In multivariate logistic regression analysis, sonographic septation and younger age remained significantly correlated with CPPE (table 3).

Sonographic septation correlated with invasive procedures

In total, 101 patients received invasive procedures including tube thoracostomy (n=59) and VATS (n=42). Among the 70 patients with a septated effusion, 88.6% (62 of 70) received invasive procedures, compared with 35.5% (39 of 110) of those without sonographic evidence of septation.

Table 3 Univariate and multivariate logistic regression analyses for predictors of CPPE

	Univariate analysis			Multivariate analysis		
Variable	**OR**	**95% CI**	**P value***	**AOR**	**95% CI**	**P value**
Sonographic septation	4.68	2.45 to 8.91	<0.001	3.38	1.64 to 6.98	0.001
COPD	0.29	0.11 to 0.75	0.011	0.48	0.16 to 1.47	0.199
Sex (male)	0.87	0.43 to 1.75	0.697	–	–	–
Age (≤60)	2.83	1.51 to 5.32	0.001	2.63	1.24 to 5.58	0.012
Serum laboratory results				–	–	–
Leukocytes (>15 ×10^9/L)	1.40	0.75 to 2.61	0.298			
CRP (≤10 mg/dL)	0.59	0.30 to 1.18	0.138			
LDH (IU/dL)	1.001	0.998 to 1.004	0.389			
Glucose (mg/dL)	0.996	0.990 to 1.002	0.168			
Total protein (g/dL)	1.51	1.03 to 2.21	0.036	1.34	0.89 to 2.04	0.164
Albumin (≤3 g/dL)	0.92	0.49 to 1.72	0.782			

*P value is presented by univariate and multivariate logistic regression analyses.
AOR, adjusted OR; COPD, chronic obstructive pulmonary disease; CPPE, complicated parapneumonic effusion; CRP, C reactive protein; LDH, lactate dehydrogenase.

Table 4 Univariate and multivariate logistic regression analyses for predictors of invasive procedures

	Univariate analysis			Multivariate analysis		
Variable	**OR**	**95% CI**	**P value***	**AOR**	**95% CI**	**P value**
Sonographic septation	14.11	6.13 to 32.47	<0.001	9.06	3.71 to 22.11	<0.001
COPD	0.37	0.16 to 0.86	0.021	0.41	0.15 to 1.16	0.092
Sex (male)	2.16	1.06 to 4.38	0.033	2.57	0.99 to 6.63	0.051
Age (≤60)	1.84	0.98 to 3.47	0.057			
Diabetes mellitus	1.08	0.53 to 2.19	0.841			
Chronic kidney disease	1.49	0.53 to 4.21	0.455			
Malignancy	0.44	0.21 to 0.94	0.035	0.56	0.21 to 1.49	0.246
Serum laboratory results				–	–	–
White cell count (>15×10^9/L)	1.29	0.68 to 2.44	0.430			
CRP (>10 mg/dL)	1.5	0.79 to 3.01	0.203			
LDH (IU/dL)	1.00	0.99 to 1.00	0.775			
Glucose (mg/dL)	0.99	0.99 to 1.00	0.625			
Total protein (g/dL)	1.73	1.17 to 2.57	0.007	1.80	1.13 to 2.86	0.013
Albumin (≤3 g/dL)	1.50	0.85 to 2.64	0.160			

Invasive procedures included tube thoracostomy and video-assisted thoracic surgery.
*P value is presented by univariate and multivariate logistic regression analyses.
AOR, adjusted OR; COPD, chronic obstructive pulmonary disease; CRP, C reactive protein; LDH, lactate dehydrogenase.

Using sonographic septation as the predictor of invasive procedures, the sensitivity, specificity, positive predictive value, and negative predictive value were 61.4%, 89.9%, 88.6%, and 64.5%, respectively. The potential predictors of invasive procedures in univariate logistic regression analysis were sonographic septation (OR=14.11, CI 6.13 to 32.47, p<0.001), male gender (OR=2.16, CI 1.06 to 4.38, p=0.033), absence of COPD (OR=0.37, CI 0.16 to 0.86, p=0.021), absence of malignancy (OR=0.44, CI 0.21 to 0.94, p=0.035), and serum total protein level (OR=1.73, CI 1.17 to 2.57, p=0.007). In multivariate logistic regression analysis, sonographic septation and total serum protein level were independently associated with invasive procedures (table 4).

DISCUSSION

In the current study, we demonstrated that the sonographic findings of septation were useful for predicting CPPE and strongly correlated with subsequent invasive procedures such as tube thoracostomy or VATS. Patients with CPPE were significantly younger, had a lower rate of COPD, and a higher rate of sonographic septation than those with UPPE. Furthermore, we also demonstrated that sonographic septation was significantly associated with higher LDH, total protein level, percentage of neutrophils, and lower glucose and pH in the pleural effusion, compared with the non-septated group. Sonographic evidence of septation suggests the presence of overwhelming inflammation in the pleural fluid, which correlates with the fibropurulent stage of PPE. Importantly, patients with septated PPE had a significantly increased risk of receiving invasive procedures in our study subjects. The above findings suggest that sonographic septation is strongly correlated with CPPE and predicts the application of tube thoracostomy or VATS in patients with pneumonia and pleural effusion.

At baseline, our patients with CPPE were younger, had a higher rate of sonographic septation, and a lower rate of COPD compared with the patients with UPPE. Also, age younger than 60 years was an independent predictor of CPPE, and the AOR was 2.63. The relationship between younger age and CPPE may be related to the changes in innate immunity associated with aging; however, the exact mechanism remains unknown.[17 18]

Falguera *et al*[11] reported that leukocytosis was an important predictor of CPPE or empyema in a patient diagnosed with community-acquired pneumonia. Nevertheless, sonographic echogenicity was not included in previous studies as a possible predictor of CPPE. In the current study, leukocytosis was not significantly associated with CPPE when analyzed using univariate logistic analysis. We found that sonographic septation and age were better predictors of CPPE compared with COPD and leukocytosis. Moreover, the AOR was higher for sonographic septation than for age (AOR 3.38 vs 2.63).

The incidence of pleural space infection is increasing despite continuous improvements in diagnostic and therapeutic modalities.[19] Accurate diagnosis and appropriate antibiotic treatment can prevent progression from UPPE to CPPE.[10] However, the most commonly used scoring systems to assess the severity of pneumonia, such as the Pneumonia Severity Index, CURB-65 (consciousness, urea nitrogen, respiratory rate, blood pressure, and age (above or below 65)), and Acute Physiology and Chronic Health Evaluation (APACHE II), are of no prognostic value for the development of CPPE.[20] The imbalance of fibrinogenesis and fibrinolysis increases fibrin deposition and septum formation, which then envelops the infected area and leads to regional heterogeneity in the composition of the pleural fluid. Chest sonography allows for better characterization of a pleural fluid collection with septation than CT.[21] Based on our findings, we suggest that chest sonography can be used to detect pleural fluid septation, which can be considered to represent the formation of CPPE and the risk of invasive procedures.

Early treatment with antibiotics has been reported to prevent the development of UPPE and progression

to empyema in patients with pneumonia.[10] Conversely, delayed pleural drainage for patients with CPPE has been reported to result in prolonged hospital stays and increased medical costs.[22] Feller-Kopman and Light[23] pointed out that in patients with septated or loculated PPE, early VATS should be considered if the patient is a good surgical candidate, or alternatively treated with 14-French chest tube thoracostomy or tissue plasminogen activator and deoxyribonuclease (t-PA-DNase) in a poor surgical candidate after multidisciplinary discussion. Our results disclosed that sonographic septation has good specificity (89.9%) and a high positive predictive value (88.6%) in predicting the need for invasive procedures in patients with infectious lung diseases and pleural effusion, which were in line with the statement of Feller-Kopman and Light.[23] For the decision of chest tube placement, it is very challenging without biochemical analysis of the pleural effusion during the initial thoracentesis. Our results suggest that it is possible to consider an early chest tube placement during the initial thoracentesis in patients with clinically suspected PPE and sonographic septation.

There are several limitations to the current study. First, this study focused on the correlation between clinical parameters and sonographic septation with the development of CPPE and the subsequent need for an invasive procedure. We did not investigate the influence of treatment such as antibiotics on clinical outcomes in this study. Second, although we found that physicians performed invasive procedures more frequently for patients with sonographic septation, we still could not conclude that the clinical application of sonographic septation may affect the prognosis. Further studies are needed to investigate the association between sonographic septation and invasive procedures and its influence on prognosis in patients with non-purulent PPE.

In conclusion, sonographic septation is a useful predictor of CPPE. Chest sonography may adjudicate on the decision of invasive procedures in patients with non-purulent PPE.

Contributors S-YC wrote the first draft of this article. All authors contributed to acquisition, analysis, and interpretation of data. The principal author takes full responsibility for the data presented in this study, analysis of data, conclusions, and conduct of the research.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the Tri-Service General Hospital Institutional Review Board (TSGHIRB: 2-103-05-108).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

ORCID iDs
Shan-Yueh Chang http://orcid.org/0000-0001-8944-174X
Yu-Ching Chou http://orcid.org/0000-0003-4823-6541
Chih-Feng Chian http://orcid.org/0000-0001-8282-2056

REFERENCES

1 Musher DM, Thorner AR. Community-acquired pneumonia. *N Engl J Med* 2014;371:1619–28.
2 File TM, Marrie TJ. Burden of community-acquired pneumonia in North American adults. *Postgrad Med* 2010;122:130–41.
3 Davies CW, Kearney SE, Gleeson FV, *et al*. Predictors of outcome and long-term survival in patients with pleural infection. *Am J Respir Crit Care Med* 1999;160:1682–7.
4 Maskell NA, Davies CWH, Nunn AJ, *et al*. U.K. controlled trial of intrapleural streptokinase for pleural infection. *N Engl J Med* 2005;352:865–74.
5 Light RW. Parapneumonic effusions and empyema. *Proc Am Thorac Soc* 2006;3:75–80.
6 Light RW, Girard WM, Jenkinson SG, *et al*. Parapneumonic effusions. *Am J Med* 1980;69:507–12.
7 Colice GL, Curtis A, Deslauriers J, *et al*. Medical and surgical treatment of parapneumonic effusions : an evidence-based guideline. *Chest* 2000;118:1158–71.
8 Davies CWH, Gleeson FV, Davies RJO, *et al*. Bts guidelines for the management of pleural infection. *Thorax* 2003;58 Suppl 2:18ii–28.
9 Davies HE, Davies RJO, Davies CWH, *et al*. Management of pleural infection in adults: British Thoracic Society Pleural Disease Guideline 2010. *Thorax* 2010;65 Suppl 2:ii41–53.
10 Sahn SA. Diagnosis and management of parapneumonic effusions and empyema. *Clin Infect Dis* 2007;45:1480–6.
11 Falguera M, Carratalà J, Bielsa S, *et al*. Predictive factors, microbiology and outcome of patients with parapneumonic effusion. *Eur Respir J* 2011;38:1173–9.
12 Diacon AH, Brutsche MH, Solèr M. Accuracy of pleural puncture sites: a prospective comparison of clinical examination with ultrasound. *Chest* 2003;123:436–41.
13 Feller-Kopman D. Ultrasound-Guided Thoracentesis. *Chest* 2006;129:1709–14.
14 Chen KY, Liaw YS, Wang HC, *et al*. Sonographic septation: a useful prognostic indicator of acute thoracic empyema. *J Ultrasound Med* 2000;19:837–43.
15 Light RW, Macgregor MI, Luchsinger PC, *et al*. Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med* 1972;77:507–13.
16 Yang PC, Luh KT, Chang DB, *et al*. Value of sonography in determining the nature of pleural effusion: analysis of 320 cases. *AJR Am J Roentgenol* 1992;159:29–33.
17 Gomez CR, Nomellini V, Faunce DE, *et al*. Innate immunity and aging. *Exp Gerontol* 2008;43:718–28.
18 Kim S-K, Kang CU, Song SH, *et al*. Factors predictive of the failure of medical treatment in patients with pleural infection. *Korean J Intern Med* : 2014;29:603.
19 Farjah F, Symons RG, Krishnadasan B, *et al*. Management of pleural space infections: a population-based analysis. *J Thorac Cardiovasc Surg* 2007;133:346–51.
20 Chalmers JD, Singanayagam A, Murray MP, *et al*. Risk factors for complicated parapneumonic effusion and empyema on presentation to hospital with community-acquired pneumonia. *Thorax* 2009;64:592–7.
21 Kearney SE, Davies CW, Davies RJ, *et al*. Computed tomography and ultrasound in parapneumonic effusions and empyema. *Clin Radiol* 2000;55:542–7.
22 Heffner JE, McDonald J, Barbieri C, *et al*. Management of parapneumonic effusions. An analysis of physician practice patterns. *Arch Surg* 1995;130:433-8.
23 Feller-Kopman D, Light R. Pleural disease. *N Engl J Med* 2018;378:740–51.