



Therapeutic strategy for acute pleural empyema: comparison between retrospective study and prospective study

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Abstract

Objectives The purpose of this study is to investigate the efficiency of therapeutic strategy for acute pleural empyema.

Methods We retrospectively reviewed 121 acute empyema patients and evaluated the therapeutic strategy for acute pleural empyema. Then, we prospectively reviewed 114 acute pleural empyema patients based on the strategy.

Results The duration from onset to hospitalization in our hospital is statistically shorter, and the mortality and the rate of stage 3 empyema patients are lower in the prospective study group (PSG) than in the retrospective study group (RSG). Retrospective study and prospective study found that surgical group (SG) had more favorable outcomes than non-surgical group (NSG). Although antibiotic treatment duration, hospital stay, and entire mortality were comparable in NSG of both study groups, mortality of patients with PS grade 4 was significantly lower in PSG. SG in PSG had more favorable outcomes than that in RSG, such as antibiotic treatment duration, hospital stay, complication, and mortality.

Conclusions The good outcomes may be mainly caused by shorter duration from onset to hospitalization and shorter duration from hospitalization to operation. Operative management is an effective procedure for selected patients, and it is important to refer for thoracic surgical consultation earlier.

Keywords Pleural empyema · Retrospective study · Prospective study · Therapeutic strategy

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Abbreviations

PS	Performance status
RSG	Retrospective study group
PSG	Prospective study group
SG	Surgical group
NSG	Non-surgical group
IPR	Incomplete pulmonary re-expansion
CPR	Complete pulmonary re-expansion

Introduction

The primary treatment of acute pleural empyema involves the administration of antibiotics and drainage, but surgical treatment often becomes a choice when infection cannot be controlled by antibiotics and drainage. Optimal management of this condition remains undefined and outcomes remain poor, with up to a 20% mortality within the first year, 20% requiring surgery due to failed medical therapy and an average hospital stay of 10 days [1]. This paper describes our experiences of the retrospective study and the prospective study for acute pleural empyema, then we investigate

the efficiency of our therapeutic strategy for acute pleural empyema.

Patients and methods

235 cases of acute pleural empyema thoracis admitted to our hospital between 2009 and 2018 were reviewed. Patients with lung abscess were excluded. We retrospectively reviewed 121 patients from January 2009 to June 2014, and evaluated the therapeutic strategy for acute empyema. Then, we prospectively reviewed 114 acute empyema patients from July 2014 to December 2018 based on the strategy. The definition of empyema was selected as septations or loculations identified in the pleural space by computed tomography, existence of gross pus or organisms demonstrated by Gram stain or culture, or positive biochemical methods. All empyemas were classified into three stages according to Light [2], namely, exudative phase (Stage I), fibrinopurulent phase (Stage II), and organized phase (Stage III). Chest drain was inserted by means of fluoroscope, ultrasonography, or single-trocar thoracoscopy under local anesthesia.

Statistical analysis

The analyses were performed using the statistical software program StatMate III (ATMS Co., Ltd., Tokyo, Japan). Patients' characteristics were compared using the Chi-square test or the Fisher's exact test for categorical data and *t* tests for continuous data. A two-sided *p* value < 0.05 was considered statistically significant.

Results

Results of RSG and the therapeutic strategy for PSG

Patients' characteristics and outcomes between NSG and SG in RSG are shown in Table 1. NSG had significantly higher age than SG, but no significant difference in gender, comorbidity, and Performance Status (PS) was observed among two groups. There was no significant difference in serum white blood cell (WBC) and C-reactive protein (CRP) of admission between NSG and SG, but these of 3 days after admission were significantly higher in SG. The rates of advanced empyema, multiloculated empyema, methicillin-resistant *Staphylococcus aureus* (MRSA) empyema, and empyema with fistula in SG were significantly higher than these in NSG. Furthermore, there was no survivor of multiloculated empyema or MRSA empyema in NSG. There was no significant difference in mortality between both groups, and patients with PS grade 4 in both groups had high mortality (NSG 58.5% vs SG 77.8%). According to the results

of the RSG, we evaluated the therapeutic strategy for acute empyema as follows. Early surgical procedures are recommended when any of the following applies: (1) multiloculated empyema; (2) MRSA empyema; and (3) patients who show no response to antibiotic or drainage treatment within 3 days. Exceptions: patients with PS grade 4. We shared the results of RSG with pulmonologists of our hospital and surrounding facilities. Then, treatment plan and chest drainage were made by pulmonologists and thoracic surgeons. Chest tube was inserted by means of fluoroscopy, ultrasonography, or single-trocar thoracoscopy under local anesthesia. Multiple chest tubes were frequently inserted for patients of NSG, because only one chest tube was inadequate. The first-line antibiotics were penicillins combined with β -lactamase inhibitors according to the British Thoracic Society (BTS) guidelines [3]. In addition, we made the protocol from surgery to discharge as follows. Operative technique: through the drain incision or new thoraco-port at the middle aspect of the 7th intercostal space, an endoscope was inserted for inspection of the pleural cavity. A transverse skin incision (about 5 cm) was made laterally at the largest empyema cavity level. The first step consisted of complete evacuation of the fluid component of empyema by suction, and disruption of fibrinous pleural septations and peeling off minimal adhesions until the empyema cavity became single space. The next step included repeated pleural lavage with hydrogen peroxide and subsequently with normal saline until the cavity was clean. Finally, 28-Fr chest tubes were placed at the apical position and on the diaphragm. In addition, 12-Fr chest tube for irrigation was inserted. To facilitate complete pulmonary re-expansion, the 28-Fr chest tubes were connected to a suction system of 20 cm H₂O. Patients underwent intermittent pleural lavage (normal saline, 1000 ml per hour, once or twice a day) through the 12-Fr chest tube from the next day after surgery. The chest tube as an injection site of normal saline was frequently changed according to the drainage volume of each chest tube. Pleural lavage was continued until the pleural fluid was sterilized. Antibiotic treatment was finished when serum CRP decreased under 5 mg/dl and discharged 2 days later. The purpose of this prospective study was to demonstrate the efficacy of our therapeutic strategy for acute pleural empyema. The primary endpoint of the prospective study was mortality.

Results of the PSG and comparison with RSG

Patients' characteristics and outcomes of RSG and PSG are shown in Table 2. There was no significant difference in age, gender, comorbidity, PS, and rates of multiloculated empyema and MRSA empyema. Duration from onset to hospitalization was significantly shorter and the rate of early stage empyema was higher in PSG. As for outcomes, there was no significant difference in the

Table 1 Patients' characteristics and outcomes between NSG and SG in RSG

Valuables	NSG (<i>n</i> = 69)	SG (<i>n</i> = 52)	<i>p</i> value
Age (years)	74 (25–92)	66 (15–85)	< 0.01
Gender (male/female)	56/13	41/11	0.75
Comorbidity, %	65 (94.2)	47 (90.4)	0.42
Performance Status (PS)	1 (0–4)	1 (0–4)	0.49
PS4, %	17 (24.6)	9 (17.3)	0.33
Duration from onset to hospitalization (days)	17 (0–37)	19.5 (9–40)	< 0.01
Laboratory findings			
Serum WBC (/ml)			
Admission	13,600 (7200–46,000)	13,550 (9200–31,300)	0.83
3 day later	8300 (3500–18,800)	13,400 (5200–25,600)	< 0.01
Serum CRP(mg/dl)			
Admission	15.5 (5.83–38.00)	17.0 (6.68–37.20)	0.36
3 days later	7.5 (2.59–30.90)	18.2 (4.56–28.90)	< 0.001
Pleural fluid analysis			
Ph			
Ph	7.098 (6.000–7.810)	7.145 (6.606–7.500)	0.89
LDH (IU/l)			
LDH (IU/l)	1239 (156–73,200)	1385 (128–19,381)	0.42
Total protein (g/dl)			
Total protein (g/dl)	4.8 (1.3–5.9)	5.2 (1.4–7.5)	0.99
Glucose (mg/dl)			
Glucose (mg/dl)	36 (0–197)	6 (0–104)	0.25
Stage of Empyema			
Stage I, %			
Stage I, %	31 (44.9)	2 (3.8)	< 0.001
Stage II, %			
Stage II, %	23 (33.3)	5 (9.6)	< 0.01
Stage III, %			
Stage III, %	15 (21.7)	45 (86.5)	< 0.001
Multiloculated, %			
Multiloculated, %	8 (11.6)	40 (76.9)	< 0.001
Cured, %			
Cured, %	0 (0.0)	37 (92.5)	< 0.001
MRSA infection, %			
MRSA infection, %	6 (8.7)	14 (26.9)	< 0.01
Cured, %			
Cured, %	0 (0.0)	11 (78.6)	< 0.01
Empyema with fistula, %			
Empyema with fistula, %	3 (4.3)	14 (26.9)	< 0.001
Cured, %			
Cured, %	2 (66.7)	11 (78.6)	0.66
Hospital stay (days)			
Hospital stay (days)	20 (7–45)	23 (8–49)	0.32
Complications, %			
Complications, %	13 (18.8)	17 (32.7)	0.08
Recurrence, %			
Recurrence, %	3 (4.3)	3 (5.8)	0.52
Mortality, %			
Mortality, %	13 (18.8)	7 (13.5)	0.43
Mortality of PS4/All PS4, %			
Mortality of PS4/All PS4, %	10/17 (58.5)	7/9 (77.8)	0.33

Values are number of patients (%), median or range values has been italicized

NSG non-surgical group, SG surgical group, *pH* power of hydrogen, WBC white blood cells, CRP C-reactive protein, LDH lactate dehydrogenase, MRSA methicillin-resistant *Staphylococcus Aureus*

rate of patients with incomplete pulmonary re-expansion (IPR) after drainage or surgery between RSG and PSG, but mortality was significantly lower in PSG. Patients with IPR after drainage or operation were significantly more likely to detect microbe from pleural effusion after drainage or operation than those with complete pulmonary re-expansion (CPR) in both study groups. Patients' characteristics and outcomes of NSG in both study groups are shown in Table 3. There was no significant difference in age, gender, comorbidity, and PS between RSG and PSG. Duration from onset to hospitalization was significantly shorter and the rate of early stage empyema

was higher in PSG. Outcomes such as recurrence, complication, and mortality were comparable in both study groups. However, mortality of patients with PS grade 4 was significantly lower in PSG. Perioperative characteristics of SG in both study groups are shown in Table 4. In RSG, 9 empyema patients with fistula cured by ligation or suture of fistula. Two empyema patients with fistula cured by wrapping the fistula with intercostal muscle pedicle. In PSG, one empyema patients with fistula cured by operation and endoscopic bronchial occlusion, and surgical procedure was performed for two young men who had suffered from amyotrophic lateral

Table 2 Patients' characteristics and outcomes of RSG and PSG

Valuables	RSG (<i>n</i> = 121)	PSG (<i>n</i> = 114)	<i>p</i> value
Age (years)	71 (15–92)	72.5 (31–93)	0.57
Gender (male/female)	97/24	91/23	0.95
Comorbidity, %	112 (92.6)	101 (88.6)	0.30
Performance Status (PS)	1 (0–4)	1 (0–4)	0.47
PS4, %	26 (21.5)	24 (21.0)	0.94
Duration from onset to hospitalization (days)	18 (0–40)	5.5 (0–30)	< 0.001
Laboratory findings			
Serum WBC (/ml)	13,600 (7200–46,000)	14,300 (2900–46,300)	0.20
Serum CRP (mg/dl)	16.1 (5.83–38.00)	19.7 (6.09–54.40)	< 0.05
Pleural fluid analysis			
pH	7.137 (6.000–7.810)	7.251 (6.000–7.714)	< 0.05
LDH (IU/l)	1239 (128–73,200)	1006 (25–38,120)	0.77
Total protein (g/dl)	4.8 (1.3–7.5)	4.5 (0.6–6.5)	< 0.01
Glucose (mg/dl)	22 (0–197)	45 (0–251)	< 0.01
Stage of empyema			
Stage I, %	33 (27.3)	54 (47.4)	< 0.01
Stage II, %	28 (23.1)	19 (16.7)	0.21
Stage III, %	60 (49.6)	41 (36.0)	< 0.05
Multiloculated, %	48 (39.7)	33 (28.9)	0.08
MRSA infection, %	20 (16.5)	14 (12.3)	0.35
Empyema with fistula, %	17 (14.0)	19 (16.7)	0.58
Patients with IPR, %	33 (27.3)	26 (22.8)	0.43
IPR and BDA/IPR, %	30/33 (90.1)	21/26 (80.8)	0.26
CPR and BDA/CPR, %	8/88 (9.1)	8/88 (9.1)	1.00
Complications, %	30 (24.8)	13 (11.4)	< 0.01
Recurrence, %	6 (5.0)	2 (1.7)	0.18
Mortality, %	20 (16.5)	7 (6.1)	< 0.05
Mortality of PS4/All PS4, %	17/26 (65.4)	3/24 (12.5)	< 0.001

Values are number of patients (%), median or range has been italicized

RSG retrospective study group, PSG prospective study group, IPR incomplete pulmonary re-expansion, CPR complete pulmonary re-expansion, BDA bacterial discharge after drainage or operation

sclerosis, because they had no organ failure, even though their PS was grade 4. There was no significant difference in age, gender, comorbidity, PS between RSG, and PSG. Duration from onset to hospitalization and duration from hospitalization to operation were significantly shorter in PSG. Outcomes such as antibiotic treatment duration, hospital stay, operating time, bleeding volume, complication, and mortality were lower in PSG. Patients' characteristics and outcomes of NSG and SG in of PSG are shown in Table 5. NSG had significantly higher age and PS than SG. There was no significant difference in serum laboratory findings and pleural fluid analysis. The rate of early stage empyema was higher in NSG, but antibiotic treatment duration and hospital stay were longer and mortality was higher in NSG than in SG.

Discussion

Recent epidemiologic studies have indicated that the incidence of empyema has been increasing in the last two decades [4]. Antibiotics and chest tube drainage remain to be the initial treatment modality in early phase of empyema. However, Nandeesh et al. [5] reported that mere chest tube insertion was associated with more morbidity and high chance of failure, requiring a longer stay and a second intervention to cure the disease. It is an attractive option for early and decisive treatment in patients who are good surgical candidates, but no randomized trial showed any major clinical benefits, except for a slightly shorter hospital stay [6]. It means that some patients' selection is

Table 3 Patients' characteristics and outcomes of NSG in both study groups

Valuables	RSG (<i>n</i> = 69)	PSG (<i>n</i> = 71)	<i>p</i> value
Age (years)	74 (25–92)	77 (28–93)	0.23
Gender (male/female)	56/13	55/16	0.59
Comorbidity, %	65 (94.2)	64 (90.1)	0.37
Performance Status (PS)	1 (0–4)	2 (0–4)	0.20
PS4, %	17 (24.6)	22 (31.0)	0.40
Duration from onset to hospitalization (days)	17 (0–37)	3 (0–28)	< 0.001
Laboratory findings			
Serum WBC (/ml)	13,600 (7200–46,000)	13,500 (2900–46,000)	0.87
Serum CRP (mg/dl)	15.5 (5.83–38.00)	19.9 (6.09–54.40)	0.06
Pleural fluid analysis			
pH	7.098 (6.000–7.810)	7.266 (6.500–7.714)	0.35
LDH (IU/L)	1239 (156–73,200)	936 (25–9442)	< 0.01
Total protein (g/dl)	4.8 (1.3–5.9)	4.6 (0.6–6.5)	0.31
Glucose (mg/dl)	36 (0–197)	78 (0–251)	0.70
Stage of Empyema			
Stage I, %	31 (44.9)	47 (66.2)	< 0.05
Stage II, %	23 (33.3)	10 (14.1)	< 0.01
Stage III, %	15 (21.7)	14 (19.7)	0.76
Multiloculated, %	8 (11.6)	6 (8.5)	0.54
MRSA infection, %	6 (8.7)	3 (4.2)	0.28
Empyema with fistula, %	3 (4.3)	9 (12.7)	0.08
Drainage treatment (days)	14 (4–46)	12.5 (5–61)	0.40
Antibiotic treatment (days)	19 (5–43)	20 (5–60)	0.31
Hospital stay (days)	20 (7–45)	25 (6–74)	< 0.05
Patients with IPR, %	12 (17.4)	15 (21.1)	0.58
Complications, %	13 (18.8)	11 (15.5)	0.60
Recurrence, %	3 (4.3)	1 (1.4)	0.30
Mortality, %	13 (18.8)	7 (9.9)	0.12
Mortality of PS4/All PS4	10/17 (58.5)	3/22 (13.6)	< 0.01

Values are number of patients (%), median or range has been italicized

NSG non-surgical group, RSG retrospective study group, PSG prospective study group, IPR incomplete pulmonary re-expansion, CPR complete pulmonary re-expansion, BD bacterial discharge after drainage or operation, PS4 performance status grade 4

needed, and decision-making protocol for operation may shorten the interval and offer a better outcome. Then, we evaluated the therapeutic strategy for acute empyema from the results of RSG and used these findings to better inform medical colleagues about the importance of early referral for thoracic surgical consultation.

Baek et al. [7] reported that early surgical treatment was necessary for patients with multiloculated empyema because of its rapid progression and difficulty to treat with percutaneous drainage. In our study, some patients with monoloculated empyema turned to multiloculated within 1 day and percutaneous drainage turned to be inadequate.

MRSA infection is still a major global healthcare problem. Although vancomycin is the first-line antibiotic for MRSA bacteremia treatment, it has a relatively slow onset of bactericidal activity and poorly penetrates some tissues

[8]. Delaney et al. [9] reported that MRSA infection was characterized by rapid evolution to complex empyema and vast involvement of the diaphragm and chest wall and treatment must proceed quickly to control sepsis, to evacuate pus, and to obliterate the pleural space, considering the high risk of mortality in this pathology.

Many reports accept operations when other therapies failed, but few reports concretely commented the timing to decide operation. Sato et al. [10] suggested that thoracoscopic treatment seems to be a promising procedure in patients who show no response to conservative therapy within 3 days. In our RSG, serum WBC and CRP 3 days after admission were significantly higher in SG. It means that patients who show no response to conservative therapy within 3 days tend to need surgical procedure.

Table 4 Perioperative characteristics of SG in both study groups

Valuables	RSG (<i>n</i> =52)	PSG (<i>n</i> =43)	<i>p</i> value
Age (years)	66 (15–85)	69 (31–88)	0.23
Gender (male/female)	41/11	36/7	0.55
Comorbidity, %	47 (90.4)	37 (86.0)	0.51
Performance Status (PS)	1 (0–4)	0 (0–4)	0.28
PS4, %	9 (17.3)	2 (4.7)	0.05
Duration from onset to hospitalization (days)	19.5 (9–40)	8 (2–30)	< 0.001
Duration from hospitalization to operation (days)	6 (1–22)	2 (0–5)	< 0.001
Laboratory findings			
Serum WBC (/ml)	13,550 (9200–31,300)	16,800 (9200–38,900)	0.08
Serum CRP (mg/dl)	17.0 (6.68–37.20)	19.6 (7.25–41.40)	0.21
Pleural fluid analysis			
pH	7.145 (6.606–7.500)	7.201 (6.000–7.566)	0.20
LDH (IU/l)	1385 (128–19,381)	1095 (76–38,120)	0.63
Total protein (g/dl)	5.2 (1.4–7.5)	4.5 (0.7–5.7)	0.56
Glucose (mg/dl)	6 (0–104)	22 (0–160)	0.07
Stage of Empyema			
Stage I, %	2 (3.8)	7 (16.3)	<0.05
Stage II, %	5 (9.6)	9 (20.9)	0.12
Stage III, %	45 (86.5)	27 (62.8)	<0.01
Multiloculated, %	40 (76.9)	27 (62.8)	0.13
MRSA infection, %	14 (26.9)	11 (25.6)	0.88
Empyema with fistula, %	14 (26.9)	10 (23.3)	0.68
Operating time (minutes)	127 (39–540)	68 (32–248)	<0.01
Bleeding volume (ml)	221 (0–2274)	27.5 (0–1214)	<0.01
Drainage treatment (days)	14 (3–37)	10 (2–28)	<0.01
Antibiotic treatment (days)	12 (3–34)	7 (3–28)	<0.01
Hospital stay (days)	23 (8–49)	17 (7–52)	<0.01
Patients with IPR, %	21 (40.4)	11 (25.6)	0.13
Complications, %	17 (32.7)	2 (4.7)	<0.01
Recurrence, %	3 (5.8)	1 (2.3)	0.41
Mortality, %	7 (13.5)	0 (0.0)	<0.05
Mortality of PS4/All PS4	7/9 (77.8)	0/2 (0.0)	0.21

Values are number of patients (%), median, or range has been italicized

SG surgical group, RSG retrospective study group, PSG prospective study group, IPR incomplete pulmonary re-expansion, PS4 performance status grade 4

The American Medical Association [11] summarized that the effervescent cleansing action of hydrogen peroxide may act as a chemical debriding agent to help lift debris and necrotic tissue from the wound surface when used at full strength. We use hydrogen peroxide solution to lift debris and necrotic tissue from lung surface without injury.

There are pros and cons regarding postoperative intrathoracic lavage. Gossot [12] reported that postoperative lavage was unnecessary, because empyema cavity was cleaned sufficiently by operation procedure. Mennander [13] reported that pleural lavage is a feasible method to clear pleural pus discharge without prolongation of hospitalization and may be recommended after thoracotomy for patients with

fibrinopurulent stage 2 empyema. Patients with IPR after drainage or operation were significantly more likely to detect microbe from pleural effusion after drainage or operation in our study. Therefore, pleural lavage after surgery or drainage may be available for patients with IPR.

Retrospective study and prospective study found that SG had more favorable outcomes than NSG. Almost all patients with PS grade 4 belong to NSG in PSG. The entire mortality was comparable in NSG between RSG and PSG. However, mortality of patients with PS grade 4 was significantly lower in NSG of PSG. The good outcomes may be caused by early and aggressive drainage treatment (multiple tubes insertion or single-trocar thoracoscopy under local anesthesia etc.).

Table 5 Patients' characteristics and outcomes of NSG and SG in of PSG

Valuables	NSG (<i>n</i> = 71)	SG (<i>n</i> = 43)	<i>p</i> value
Age (years)	77 (28–93)	69 (31–88)	< 0.01
Gender (male/female)	55/16	36/7	0.41
Comorbidity, %	64 (90.1)	37 (86.0)	0.98
Performance status (PS)	2 (0–4)	0 (0–4)	< 0.01
PS4, %	22 (31.0)	2 (4.7)	< 0.001
Duration from onset to hospitalization (days)	3 (0–28)	8 (2–30)	< 0.01
Laboratory findings			
Serum WBC (/ml)	13,500 (2900–46,000)	16,800 (9200–38,900)	0.07
Serum CRP (mg/dl)	19.9 (6.09–54.40)	19.6 (7.25–41.40)	0.85
Pleural fluid analysis			
pH	7.266 (6.500–7.714)	7.201 (6.000–7.566)	0.77
LDH (IU/L)	936 (25–9442)	1095 (76–38,120)	0.29
Total protein (g/dl)	4.6 (0.6–6.5)	4.5 (0.7–5.7)	0.34
Glucose (mg/dl)	78 (0–251)	22 (0–160)	0.13
Stage of empyema			
Stage I, %	47 (66.2)	7 (16.3)	< 0.001
Stage II, %	10 (14.1)	9 (20.9)	0.34
Stage III, %	14 (19.7)	27 (62.8)	< 0.001
Multiloculated, %	6 (8.5)	27 (62.8)	< 0.001
MRSA infection, %	3 (4.2)	11 (25.6)	< 0.001
Empyema with fistula, %	9 (12.7)	10 (23.3)	0.14
Drainage treatment (days)	12.5 (5–61)	10 (2–28)	0.41
Antibiotic treatment (days)	20 (5–60)	7 (3–28)	< 0.001
Hospital stay (days)	25 (6–74)	17 (7–52)	< 0.001
Patients with IPR, %	15 (21.1)	11 (25.6)	0.58
Complications, %	11 (15.5)	2 (4.7)	0.08
Recurrence, %	1 (1.4)	1 (2.3)	0.72
Mortality, %	7 (9.9)	0 (0.0)	< 0.05
Mortality of PS4/All PS4	3/22 (13.6)	0/2 (0.0)	0.58

Values are number of patients (%), median or range has been italicized

SG surgical group, RSG retrospective study group, PSG prospective study group, IPR incomplete pulmonary re-expansion, PS4 performance status grade 4

SG in PSG had more favorable outcomes than SG in RSG, such as antibiotic treatment duration, hospital stay, complication, and mortality. The good outcomes may be mainly caused by shorter duration from onset to hospitalization and shorter duration from hospitalization to operation.

Conclusion

Antibiotics and chest tube drainage remain to be the initial treatment modality in early phase of empyema. We can use our study to better inform medical colleagues that operative management is a relatively safe and effective procedure for selected patients, and it is important to refer for thoracic surgical consultation earlier.

Compliance with ethical standards

Conflict of interest The authors have declared that no conflict of interest exists.

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