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A 10-year surgical outcome comparison between subphrenic-origin and parapneumonic empyema: a retrospective study

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Abstract

Background:

Empyema thoracis remains a significant clinical challenge with a rising incidence. While video-assisted thoracoscopic surgery (VATS) decortication is an established treatment, the clinical characteristics and outcomes of specific subgroups of subphrenic-origin empyema remain poorly defined in the current literature.

Methods:

To evaluate the clinical characteristics and surgical outcomes of subphrenic-origin and parapneumonic empyema, a retrospective analysis was conducted on patients who underwent VATS decortication at a single medical center between 2012 and 2021. To minimize selection bias, 1:4 propensity score matching (PSM) was performed, and 38 patients with subphrenic-origin empyema were compared with 152 patients with parapneumonic empyema. The primary outcomes included mortality (in-hospital, 30-day, and 1-year), length of ICU and hospital stay, and recurrence rates.

Results:

Compared with the parapneumonic group, the subphrenic-origin empyema group demonstrated a predilection for the right hemithorax (79.0% vs. 64.5%, $p = 0.003$) and was associated with a significantly longer duration from diagnosis to surgical intervention (7.8 ± 6.8 vs. 4.4 ± 6.0 days, $p = 0.003$). Postoperatively, subphrenic-origin empyema was an independent predictor of prolonged ICU stay (10.6 ± 12.6 vs. 6.4 ± 11.7 days, $p = 0.049$) and total hospital stay (37.6 ± 19.4 vs. 22.7 ± 19.3 days, $p < 0.001$). However, there were no statistically significant differences between the two groups in terms of in-hospital mortality, 30-day mortality, 1-year mortality, or recurrence rates.

Conclusions:

Although subphrenic-origin empyema is associated with longer diagnostic delays and requires more intensive postoperative resource utilization, timely VATS decortication yields survival and recurrence outcomes comparable to those of parapneumonic empyema. A multidisciplinary approach and a high index of clinical suspicion are essential for managing this complex subgroup.

1. Introduction

Empyema thoracis remains a severe, life-threatening suppurative infection of the pleural space that presents a formidable challenge to thoracic surgeons and pulmonologists alike [1, 2]. Despite advances in antimicrobial therapy and critical care, modern epidemiological studies indicate a persistent rise in empyema-related hospitalizations globally over the past few decades, impacting tens of thousands of patients annually [1–3]. Empyema is also associated with substantial morbidity, prolonged hospitalizations, high medical costs, and overall mortality rates ranging from 5% to 15% [1, 4, 5].

Pathophysiologically, empyema progresses sequentially from an early exudative stage with free-flowing fluid into a fibrinopurulent stage characterized by heavy fibrin deposition and loculations, ultimately evolving into a chronic organizing stage with a thick pleural peel that encases the lung and impairs pulmonary function. These processes correspond to the three-stage classification of the American Thoracic Society [1, 2, 6]. While early exudative effusions may respond to systemic antibiotics and tube thoracostomy alone, conservative medical drainage frequently fails in

advanced stages (Stages II and III), resulting in trapped lung and persistent sepsis [2, 6, 7]. For these complex cases, surgical debridement and decortication represent the definitive treatment to evacuate loculated collections, achieve effective source control, and facilitate complete lung re-expansion [1, 7, 8]. Over the past two decades, VATS decortication has largely superseded traditional open thoracotomy as the primary surgical modality, offering comparable or superior therapeutic success alongside markedly reduced tissue trauma, less postoperative pain, shorter chest tube duration, and expedited functional recovery [7–10].

Etiologically, the vast majority of empyema cases arise as parapneumonic empyema secondary to the contiguous progression of bacterial pneumonia [1, 2, 11]. However, a distinct and clinically intricate empyema subset originates from subphrenic-origin pathologies [12, 13]. These secondary pleural infections predominantly stem from pyogenic liver abscesses, peritonitis, or iatrogenic interventions [12–16]. The upward spread of abdominal sepsis into the negative-pressure pleural cavity occurs via transdiaphragmatic extension, rich diaphragmatic lymphatic channels, or congenital and acquired diaphragmatic defects [13, 17, 18].

Despite its clinical relevance, comparative data elucidating the clinical characteristics and surgical outcomes of subphrenic-origin empyema versus the more common parapneumonic empyema remain remarkably limited. Major international guidelines and large cohort studies predominantly focus on parapneumonic empyema, leaving subphrenic-origin empyema confined to sporadic case reports or small retrospective descriptions [1, 2, 12, 14]. Patients with subphrenic-origin empyema may present with atypical or misleading symptoms and subtle pulmonary findings, which frequently lead to diagnostic delays. [16]. Explore these differences is essential for establishing diagnostic suspicion and optimizing multidisciplinary care for these patients. To address this knowledge gap, we present a 10-year comprehensive surgical experience comprising 1,086 consecutive patients who underwent VATS decortication for empyema thoracis at a single tertiary medical center. Our primary objective was to compare the clinical presentation and surgical outcomes between subphrenic-origin empyema and parapneumonic empyema. Second, we evaluated the decade-long longitudinal dynamics in microbiological distribution to provide contemporary epidemiological insights for clinical management.

2. Methods

This retrospective study included patients undergoing VATS decortication for Empyema thoracis in our medical center from January 1, 2012 to December 31. The inclusion criteria were as follows: (I) diagnosed empyema, (II) receipt of VATS decortication, (III) follow up for at least one year, and (IV) availability of pleural effusion analysis data and culture data. The exclusion criteria were etiologies other than parapneumonic and subphrenic-origin.

Empyema thoracis was suspected when chest X-ray, computed tomography or ultrasonography revealed loculated or septated pleural effusion, with regular thickening and enhanced pleura. The diagnosis of empyema was confirmed with at least one of the following: pus effusion noted from chest tube drainage or during surgery, positive Gram stain or positive culture of the pleural effusion, or pleural fluid analysis with pH < 7.2 and glucose levels < 40 mg/dL. Empyema of subphrenic origin was defined in patients with pleural infection that was less likely attributable to primary pneumonia and associated with recent or concurrent acute abdominal episodes, recent surgery, or a known source of sepsis within the abdominal, pelvic, or retroperitoneal regions. The presence of identical bacteria or intestinal flora in pleural fluid cultures may also suggest a subphrenic-origin source.

Video-assisted thoracoscopic surgery with decortication was performed for those who were suspected of having stage II or III empyema and those who received chest tube drainage as initial treatment but had poor treatment response or deterioration. Pleural fluid was collected for laboratory analysis either before or during operation. Pathogen culture of the pleural fluid and pleural peels was also performed if possible. At the end of the operation, irrigation of the pleural cavity with normal saline and povidone-iodine solution was performed, and up to two chest tubes were inserted under

thoracoscopic visualization. All patients were prescribed empiric intravenous antibiotics for infection control. Removal of the chest tube was achieved once the drainage contents became serosanguinous, and a relatively small amount was noted.

Patient variables, including age, sex, smoking index, comorbidities, the empyema side, ATS classification of empyema stage, empyema origin, pleural fluid analysis, and pathogen results in pleural fluid and tissue cultures, were documented. Surgical outcomes included the diagnostic-to-surgical interval, operative time, length of intensive care unit (ICU) and hospital stays, recurrence rate and mortality rate. Short-term survival was described as in-hospital death and the 30-day mortality rate. The 1-year mortality rate of mid-term survival is also presented.

This study was approved by the Institutional Review Board of Changhua Christian Hospital (Institutional Review Board No. 241014), and informed consent was waived because of the retrospective study design.

Statistical analysis

The patients were categorized into two groups according to the source of infection: subphrenic origin and parapneumonic origin. Baseline characteristics were summarized using means ± standard deviations for continuous variables and frequencies with percentages for categorical variables. Between-group comparisons were performed via Student's t-test for continuous variables and the chi-square test or Fisher's exact test, as appropriate, for categorical variables.

Propensity scores were estimated via a logistic regression model including age, sex, smoking status, and the Charlson Comorbidity Index (CCI). A 1:4 propensity score matching was then performed via greedy nearest-neighbor matching. Cumulative survival rates for mortality were estimated via the Kaplan–Meier method, and differences between groups were assessed via the log-rank test. Univariate and multivariate Cox proportional hazards regression analyses were conducted to evaluate the association between infection origin and mortality. The multivariable model was adjusted for baseline covariates and further refined via backward stepwise selection. The results are reported as hazard ratios (HRs) with 95% confidence intervals (CIs).

Secondary outcomes, including recurrence risk, were analyzed via logistic regression, and the results are presented as odds ratios (ORs) and 95% CIs. Tertiary outcomes, including length of hospital stay and length of ICU stay, were analyzed via linear regression models adjusted for baseline covariates with backward selection. All the statistical analyses were performed via SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA). A two-sided p-value < 0.05 was considered statistically significant.

3. Results

During the 10-year study period from January 1, 2012 to December 31, 2021, a total of 1,086 patients were included in the analysis. A total of 848 (78.1%) patients were male, and 238 (21.9%) were female. A total of 496 (45.7%) of the patients were aged 65 and above, and 590 (54.3%) were less than 65 years old. A personal history of smoking was mentioned in 326 (30%) patients. Among all the patients, the most prevalent comorbidity was hypertension (52.9%), followed by liver disease (35.1%), diabetes mellitus (35.1%), and cancer (29.1%). Right-sided and left-sided empyema accounted for 659 (60.7%) and 412 (37.9%) of the patients, respectively; meanwhile, bilateral empyema simultaneously had the lowest occurrence in 15 (1.4%) patients. A total of 853 (78.5%) of the patients were classified as stage II, 229 (21.1%) as stage III, and 4 (0.4%) as Stage I. Most empyema cases were community acquired, accounting for 1,021 (94%) of the patients. The most common etiologies were parapneumonic (877 patients, 80.8%), cancer-related (67 patients, 6.2%), and subphrenic (38 patients, 3.5%). Subphrenic origins included liver abscess for 13 patients, cholangitis

for 7 patients, intra-abdominal abscess for 7 patients, cholecystitis for 5 patients, retroperitoneal abscess for 4 patients, hepatic hydrothorax for 2 patients, and peritoneal dialysis-associated peritonitis for 1 patient.

Analysis was performed between patients of parapneumonic origin and patients of subphrenic origin. After 1:4 propensity score matching, 38 patients with subphrenic-origin empyema were matched with 152 patients with parapneumonic empyema, and no significant differences in baseline characteristics, such as age, sex, smoking index, or comorbidity profiles, except for liver disease and COPD, were detected, as shown in Table 1. Patients with subphrenic-origin empyema had a greater prevalence of underlying liver disease (50.0% vs. 31.6%, P = 0.034), whereas patients with parapneumonic empyema presented with a greater prevalence of COPD (20.4% vs. 5.3%, P = 0.028). With respect to disease status, right-sided involvement was more common in patients with subphrenic disease (79.0% vs. 64.5%, P = 0.003). There was no significant difference in the empyema stage, pleural analysis results (including pH, glucose level, and LDH level), microbiological profile or positivity rates.

The overall mean interval from the diagnosis of empyema to surgery with VATS decortication was 5 ± 6.5 days for all patients. A total of 341 patients (31.4%) had received chest tube drainage before the operation. A total of 1080 patients (99.4%) received VATS decortication, and 4 patients (0.4%) converted to open decortication. The average operation time was 120.5 ± 43.8 minutes. The average ICU length of stay was 6.5 ± 11.5 days, and the average length of hospital stay was 24.0 ± 20.5 days. The 30-day mortality rate was 6.7%, with septic shock being the most common cause of mortality (37%). The in-hospital mortality rate was 10.9%, and the 1-year mortality rate was 21.7%. Recurrent empyema was found in 45 patients within one year, and among those, 40 (3.7%) patients received a second surgical intervention.

The surgical outcomes of the subgroup analysis are presented in Table 2. The mean diagnostic-to-surgical interval was significantly longer in the subphrenic origin group (7.8 ± 6.8 vs. 4.4 ± 6.0 days, P = 0.003), whereas the operative time did not differ between the two groups. Patients with subphrenic-origin empyema had longer ICU stays (10.6 ± 12.6 vs. 6.4 ± 11.7 days, P = 0.049) and prolonged total hospital stays (37.6 ± 19.4 vs. 22.7 ± 19.3 days, P < 0.001). Moreover, the in-hospital mortality, 30-day mortality, 1-year mortality and recurrence rates did not differ between the two groups. The Kaplan—Meier survival curves of all patients and subgroup patients are presented in Fig. 1.

Table 3 summarizes the results of the univariate and multivariate Cox regression analyses comparing mortality outcomes between patients with empyema of subphrenic origin and those with parapneumonic origin. In the univariate analysis, there were no significant differences in in-hospital mortality (cHR 0.81, 95% CI 0.30–2023, P = 0.683), 30-day mortality (cHR 1.34, 95% CI 0.30–6.05, P = 0.705), or 1-year mortality (cHR 1.79, 95% CI 0.86–3.72, P = 0.122) between the two groups. After adjustment for potential confounders in the multivariable model, no statistically significant associations were observed for in-hospital or 1-year mortality. Logistic regression revealed no difference in recurrence between patients with subphrenic and parapneumonic origins, as shown in Table 4. Linear regression analysis revealed that subphrenic-origin empyema independently predicted longer ICU and hospital stays. A longer interval from diagnosis to surgery, the presence of COPD, and the advanced stage of the disease were also significant predictors of both the ICU and hospital length of stay and are presented in Table 5.

Pleural fluid culture was performed for 967 patients, and 426 patients (44.1%) experienced microbiological growth. Tissue culture of the pleural peel was performed in 898 patients, and 392 (43.7%) had positive results. The most common pathogen in pleural fluid and pleural peel cultures was Streptococcus species in 221 patients, followed by Staphylococcus species in 108 patients and Klebsiella species in 87 patients. Prevotella species, Mycobacterium tuberculosis, and Pseudomonas aeruginosa were isolated from 45, 45 and 43 patients, respectively. Candida species were detected in 25 patients. Staphylococcus species were the most frequently identified pathogens in the subphrenic origin group and were found in 6 patients. The cultured microorganisms are presented in Table 6. The distribution of microorganisms according to time frame revealed an increase (28% to 35%) in the percentage of Streptococcus during the 10-year follow-up period, as shown in Fig. 2.

4. Discussion

Empyema evolves through three distinct stages according to the American Thoracic Society classification: the exudative, fibrinopurulent, and organizing stages. Therapy was prescribed according to the stage of empyema and patient condition, including thoracocentesis, tube thoracostomy drainage, intrapleural fibrinolytic agents, and decortication. In severe disease with inadequate pleural space obliteration or bronchopleural fistula, open window thoracostomy, vacuum-assisted closure therapy, omentopexy or thoracomyoplasty should be considered. [2, 6] In patients with stage II or III empyema, surgical debridement or decortication offers advantages in terms of the treatment success rate and length of hospital stay compared with barely tube thoracostomy. [7] The essential concepts to perform effective decortication are adequate drainage of the infected or loculated pleural effusions and removal of the fibrous tissue to enable full expansion of the affected lung. Previous studies have indicated that decortication performed via the VATS approach has comparable [6, 7, 19, 20, 21] or even better [8, 9] outcomes than the conventional open thoracotomy approach does and that similar or lower complication rates have been reported [9, 19]. Patients may also benefit from a decrease in surgical time, postoperative pain, prolonged air leakage, chest drainage duration, and length of hospital stay [6–9, 20, 21]. Almost all of our patients received decortication via the VATS approach.

Surgical outcomes and resource utilization

Multiple contemporary studies evaluating the outcomes of video-assisted thoracoscopic surgery (VATS) decortication for the treatment of empyema have demonstrated generally favorable perioperative outcomes, with variations reflective of patient selection and disease severity. In a large cohort analysis, 4,435 patients underwent VATS decortication, which was associated with a median operative time of 85 minutes, a median length of stay of 11.5 days, a 13.9% major morbidity rate, and a 2.8% mortality rate [10]. Another cohort study reported 1,313 patients with a similar median hospitalization duration of 12 days but higher in-hospital, 30-day, and 90-day mortality rates of 4.7%, 5.4%, and 6.3%, respectively, along with a 4.4% readmission rate and 3.0% reintervention rate within 90 days [5]. One meta-analysis further synthesized outcomes for VATS decortication, demonstrating pooled morbidity, mortality, and recurrence rates of 16.4%, 4.1%, and 7.2%, respectively [8]. A smaller single-center observational study of 644 patients in the VATS group reported a mean operative time of 112 minutes, a mean length of ICU stay of 3 days, a mean postoperative length of stay of 8 days, and lower recurrence (0.93%) and mortality rates (0.77%) [22]. These studies reinforced the overall safety and effectiveness of VATS decortication while highlighting variability across clinical contexts.

Compared with previous reports, our cohort presented a longer mean operative time (120.5 ± 43.8 minutes), longer ICU stay (6.5 ± 11.5 days) and hospital stay (24.0 ± 20.5 days). The above studies revealed an average patient age of 31.1 to 56 years, and our average patient age was 61 years. A total of 46% of our patients had a Charlson Comorbidity Index of ≥ 3, which reflected the complexity of the underlying comorbidities. Furthermore, our study included patients initially admitted for diseases other than empyema thoracis and patients with cancer, who were usually excluded from other studies. These factors may account for the longer hospitalization needed to continue treatment and rehabilitation programs for underlying diseases after the removal of chest drainage. The relatively high in-hospital mortality (10.9%) and 30-day mortality (6.7%) rates also reflect patient characteristics and comorbidity severity. Despite the outcomes mentioned above, the recurrence rate (4.1%) was favorable in our study, indicating effective surgical intervention. According to the subgroup analysis of parapneumonic and subphrenic-origin empyema, the longer diagnostic-to-surgical interval may be due to the time consumed to stabilize the patient for optimization of anesthesia and operative risk. The higher prevalence of comorbidity with liver disease could have limited the options for treatment and likely contributed to disease progression. The longer length of ICU and hospital stay after 1:4 propensity score matching indicated that the increased clinical variability in patients poses significant challenges to initial diagnosis and management. The disease complexity of subphrenic-origin empyema may also elongate and complicate postoperative recovery. This underscores the need for a multidisciplinary approach to patient care. Despite the increased clinical complexity, our propensity score-

matched analysis revealed no significant differences in in-hospital, 30-day, or 1-year mortality between the subphrenic and parapneumonic groups. These findings suggest that timely surgical intervention can mitigate the increased risks associated with infections of subphrenic origin.

Etiology and Pathophysiology of Subphrenic-origin Empyema

The most common etiology for subphrenic-origin empyema was liver abscess in our study, which accounted for 34.2% (13/38) of the patients. Hepatobiliary diseases such as liver abscess, cholecystitis, and cholangitis caused 65.7% (25/38) of the cases of subphrenic-origin empyema. Table 1 shows that as many as 79% (30/38) of subphrenic-origin empyema cases developed in the right-sided pleural cavity. Pleuroperitoneal communication (PPC) refers to the transmission of gas, fluids, cells or even microbes between the pleural cavity and the peritoneal cavity through the diaphragm. It is associated with foraminal defects and anatomic differences, including the area nuda hepatis on the right and the fibrous pericardium on the left, lymphoid drainage, intestinal peristalsis, and the piston effect of the liver [13]. Porous diaphragm syndrome (PDS) is related to the PPC and typically affects the central tendinous diaphragm on the right side [13, 17]. The incidence of subphrenic abscess is approximately 50% on the right side, 40% on the left side, and 25% on both sides [23]. Similarly, the right-sided tendency of subphrenic-origin empyema may be attributed to these various factors affecting the upward spread of infectious diseases.

In a retrospective cohort study, 234 patients developed liver abscess, and the incidence rate of empyema in these patients was 4.27% (10 patients). The risk factors for empyema were the presence of liver abscess combined with biliary tract inflammation or bilateral pleural effusion. [12] Another study reported that pyogenic liver abscess substantially increased the risk of empyema by 18 times. Recently, Klebsiella pneumoniae was found to be the primary causative pathogen for liver abscesses, resulting in a relatively high hazard ratio of pulmonary abscess and pleural empyema and leading to other metastatic infections. [14] However, in our study, Staphylococcus species were the most common pathogens associated with subphrenic-origin empyema, possibly because of the relatively small cohort size (n = 38) and the high negative culture rate (55.3%) after antibiotic use. A diaphragmatic defect, either an acquired perforation or a congenital abnormality, facilitates the spread of the infection. [18, 24] Rare pathophysiologies include hepatopleural fistulas, colopleural fistulas, iliopsoas abscesses [25–27], and even migrating appendicoliths existing in the thorax cavity [24]. Iatrogenic injury, which causes a connection between the abdominal and pleural cavities, can also lead to empyema, which has been described as a rare complication of percutaneous transhepatic gallbladder drainage (PTGBD), percutaneous drainage of infected intraabdominal fluid, and percutaneous nephrolithotomy [15, 18, 28].

Microbiological landscape

The most common pathoetiology for thoracic empyema is bacterial pneumonia, specifically as a complication resulting in parapneumonic effusion that progresses to empyema. [1, 11] The American Association for Thoracic Surgery states that bacterial pneumonia is the predominant precursor, with other less frequent causes, including bronchogenic carcinoma, esophageal rupture, chest trauma, mediastinitis, infected congenital cysts, extension from subphrenic sources, and postsurgical infections. [1] Pleural infection has been described differently from pneumonia in terms of bacteriologic distribution, which may be due to the acidic and hypoxic characteristics of the pleural space. [29] Common pathogens of gram-positive bacteria identified included Streptococcal species and Staphylococcus species. [29, 32, 33, 34] Methicillin-resistant S. aureus (MRSA) has emerged as a significant concern, with studies showing increasing prevalence, especially in children. [35, 36] Among gram-negative bacteria, Pseudomonas aeruginosa, Klebsiella pneumoniae and Escherichia coli are frequently encountered. [37–39] The most common anaerobes are Bacteroides, Fusobacterium, and Prevotella, which are thought to be associated with high aspiration risk patients and dental infections. [30, 40, 41] Anaerobes have been described in 5.7% to 27.3% of patients diagnosed with empyema [29–34, 39], which represent an unignorable portion. Fungal empyema is another rare but severe condition in which Candida species are commonly isolated and are related mostly to intra-abdominal and intrathoracic sources. [42, 43] It tends to

occur in patients with underlying immunocompromising conditions [30] and is characterized by high mortality rates, ranging from 38.5% to 73% in different studies. [42, 44, 45] Polymicrobials were obtained from 8.4% to 29% of cultures. [29, 33, 37, 39] The cultured species in our study were generally consistent with the findings of previous studies mentioned above, with Streptococcus species being the most prevalent pathogen, and multiple pathogens were noted in 172 (15.8%) patients.

The observed increase in Streptococcus prevalence over the 10-year period (from 28% to 35%) in our study may reflect changes in local epidemiology, increased antibiotic resistance and vaccine promotion. Two types of pneumococcal vaccines are available in our public healthcare policy: the 13-valent pneumococcal conjugate vaccine (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPV23). The PCV13 has been provided to high-risk and economically disadvantaged children under 5 years of age since 2008 and was introduced to the national children's routine immunization program in 2015. The infants were administered the first primary dose at 2 months of age, a second dose 2 months apart, and a booster dose at 12–15 months of age. In addition, PPV23 has been used in elderly individuals aged ≥ 75 years since 2007. Both PCV13 and PPV23 are recommended for people 2 years or older at high risk and all adults 65 years or older. A domestic study indicated that the number of infections caused by serotype 19A Streptococcus pneumoniae continuously increased after vaccine promotion, making it the most prevalent serotype. This strain presented a high rate (81.6%-97.2%) of nonsusceptibility to amoxicillin, penicillin, cefepime, cefotaxime, and meropenem, which could explain the increased prevalence of Streptococcus infection. [46]

Tuberculous empyema is a significant complication of tuberculosis. Its prevalence varies across different regions and populations and is often influenced by the local incidence of tuberculosis. In developing countries, where tuberculosis is relatively common, tuberculous empyema constitutes a notable proportion of empyema cases. For example, studies from India reported tuberculosis as the leading cause of empyema thoracis, accounting for more than half of the cases reported in surgical settings. [47, 48] Notably, tuberculous patients experienced a significantly increased need for surgical interventions, longer hospital stays, and higher rates of complications and recurrence. [47, 49] Fungal empyema is another rare but severe condition in which recent studies revealed Candida species to be the most commonly isolated pathogen and was mostly related to intra-abdominal and intrathoracic sources. [42, 43] It tends to occur in patients with underlying immunocompromising conditions [30] and is characterized by high mortality rates, ranging from 38.5% to 73% in different studies. [42, 44, 45]

Strengths and Limitations

There are several strengths to our study. First, this research presents a substantial cohort of 1,086 patients who underwent VATS decortication over a continuous 10-year period, providing a robust longitudinal perspective on the surgical management of empyema thoracis within a single institutional framework. Second, our study specifically focused on empyema of subphrenic origin, a clinical entity that is relatively underrepresented in the current literature compared with parapneumonic empyema. This study provides insights into the etiology and outcomes of this unusual clinical situation. Furthermore, the inclusion of comprehensive microbiological data from both pleural fluid and pleural peel tissue cultures enhances our understanding of the evolving pathogen landscape.

Nevertheless, some limitations should be acknowledged. This study is retrospective and was conducted at a single medical center with a selected operable population, which may limit the generalizability of our findings to other regions or healthcare settings with variable patient demographics. Additionally, the subset of patients of subphrenic origin remained relatively small despite the large overall sample size. Although the implementation of 1:4 PSM was performed to minimize potential confounding variables and selection bias, potentially limiting statistical power could exist. Finally, the high proportion of culture-negative results, likely due to prior antibiotic administration, remains a common challenge in the microbiological characterization of thoracic empyema.

5. Conclusions

VATS decortication provides effective source control and lung re-expansion with minimal need for conversion and a low recurrence rate. Compared with patients with parapneumonic origins, those with empyema of subphrenic origin presented longer intervals from diagnosis to surgery and prolonged ICU and total hospital stays. However, the PSM analysis in our study revealed that the adjusted mortality risk and recurrence rates are comparable to those associated with parapneumonic empyema, which suggests that timely surgical intervention can mitigate the increased risks associated with infections of subphrenic origin. Our findings encourage clinicians to maintain a high index of suspicion for subphrenic etiologies when evaluating empyema of obscure origin, thereby facilitating early optimization of preoperative management and timely multidisciplinary consultation. Minimizing diagnostic delays is paramount, and clinicians should anticipate a more intensive postoperative recovery trajectory for this complex patient subgroup. Additionally, future studies are warranted to further refine optimal management strategies for nonparapneumonic empyema.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Changhua Christian Hospital (Institutional Review Board No. 241014), and informed consent was waived because of the retrospective study design.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

Conception and design: Chien-Yu Lee, Bing-Yen Wang; Provision of study materials or patients: Ching-Yuan Cheng, Chang-Lun Huang, Ya-Fu Cheng, Ya-Fu Cheng; Collection and assembly of data: Chien-Yu Lee, Pei-Ru Lin, Yi-Ling Chen; Data analysis and interpretation: Chien-Yu Lee, Pei-Ru Lin, Yi-Ling Chen, Bing-Yen Wang; Manuscript writing: Chien-Yu Lee, Pei-Ru Lin, Yi-Ling Chen; Review and final approval of manuscript: All authors

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Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to privacy policy, but are available from the corresponding author on reasonable request.

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Tables

Table 1
Demographic characteristics

	Before Matching			After Matching (1:4)		
	Subphrenic origin	**Para-pneumonia**	**P-value**	**Subphrenic origin**	**Para-pneumonia**	**P-value**
Sample size	38	854		38	152	
Age	61.9 ± 13.9	62.8 ± 15.5	0.733	61.9 ± 13.9	61.9 ± 16.6	0.998
Gender, Male	22(57.9%)	674(78.9%)	0.002	22(57.9%)	88(57.9%)	1.000
Smoking index	9(23.7%)	269(31.5%)	0.309	9(23.7%)	35(23.0%)	0.932
Comorbidity						
Hypertension	19(50.0%)	482(56.4%)	0.434	19(50.0%)	76(50.0%)	1.000
CAD	3(7.9%)	137(16.0%)	0.253	3(7.9%)	24(15.8%)	0.213
COPD	2(5.3%)	182(21.3%)	0.013	2(5.3%)	31(20.4%)	0.028
DM	12(31.6%)	294(34.4%)	0.718	12(31.6%)	58(38.2%)	0.452
Liver disease	19(50.0%)	301(35.2%)	0.064	19(50.0%)	48(31.6%)	0.034
ESRD	4(10.5%)	79(9.3%)	0.774	4(10.5%)	13(8.6%)	0.751
Cancer	13(34.2%)	204(23.9%)	0.147	13(34.2%)	47(30.9%)	0.696
Connective tissue disease	2(5.3%)	29(3.4%)	0.385	2(5.3%)	10(6.6%)	1.000
Hemiplegia	1(2.6%)	37(4.3%)	1.000	1(2.6%)	6(3.9%)	1.000
Dementia	2(5.3%)	79(9.3%)	0.569	2(5.3%)	18(11.8%)	0.375
CCI ≥ 3	19(50.0%)	386(45.2%)	0.561	19(50.0%)	75(49.3%)	0.942
Empyema						
Side			< 0.001			0.003
Right	30(79.0%)	496(58.1%)		30(79.0%)	98(64.5%)	
Left	6(15.8%)	352(41.2%)		6(15.8%)	54(35.5%)	
Bilateral	2(5.3%)	6(0.7%)		2(5.3%)	0(0%)	
Stage			0.366			0.490
I	0(0%)	2(0.2%)		0(0%)	1(0.7%)	
II	33(86.8%)	674(78.9%)		33(86.8%)	120(79.0%)	
III	5(13.2%)	178(20.8%)		5(13.2%)	31(20.4%)	
Pleural analysis						
pH	7.3 ± 0.3	7.3 ± 0.4	0.454	7.3 ± 0.3	7.3 ± 0.3	0.688
Glucose	81.3 ± 51.4	69.5 ± 62.1	0.256	81.3 ± 51.4	76.3 ± 72.4	0.638

	Before Matching			After Matching (1:4)		
	Subphrenic origin	**Para-pneumonia**	**P-value**	**Subphrenic origin**	**Para-pneumonia**	**P-value**
LDH	2418.9 ± 7065.4	3277.7 ± 5297	0.338	2418.9 ± 7065.4	3049 ± 5408.3	0.613
Positive tissue or pleural culture	16(42.1%)	462(54.1%)	0.147	16(42.1%)	83(54.6%)	0.168
Pathogen			0.165			0.268
No identified	22(57.9%)	392(45.9%)		22(57.9%)	69(45.4%)	
Single	14(36.8%)	332(38.9%)		14(36.8%)	64(42.1%)	
Multiple	2(5.3%)	130(15.2%)		2(5.3%)	19(12.5%)	

Table 2
Surgical outcomes

	Before Matching			After Matching (1:4)		
	Subphrenic origin	**Para-pneumonia**	**P-value**	**Subphrenic origin**	**Para-pneumonia**	**P-value**
Diagnostic-to-surgical interval	7.8 ± 6.8	3.9 ± 6	< 0.001	7.8 ± 6.8	4.4 ± 6	0.003
Operative time (min)	117.8 ± 36.7	118.7 ± 39.9	0.891	117.8 ± 36.7	118.3 ± 39.6	0.944
ICU length of stay	10.6 ± 12.6	5.8 ± 11.4	0.012	10.6 ± 12.6	6.4 ± 11.7	0.049
Length of hospital stay	37.6 ± 19.4	21.8 ± 18.7	< 0.001	37.6 ± 19.4	22.7 ± 19.3	< 0.001
In-hospital mortality	6(15.8%)	84(9.8%)	0.233	6(15.8%)	15(9.9%)	0.383
30-day mortality	2(5.3%)	50(5.9%)	1.000	2(5.3%)	7(4.6%)	1.000
1-year mortality	10(26.3%)	158(18.5%)	0.228	10(26.3%)	24(15.8%)	0.130
Recurrence	1(2.6%)	35(4.1%)	1.000	1(2.6%)	6(3.9%)	1.000

Table 3
Hazard ratio for in-hospital, 30-day, and 1-year mortality

	Univariate cox regression		Multivariable cox regression	
	cHR (95% CI)	***p* Value**	**aHR (95% CI)***	***p* Value**
In-hospital mortality				
Subphrenic origin vs. Para-pneumonia	0.81 (0.30,2.23)	0.683	0.68 (0.24,1.89)	0.457
30-day mortality				
Subphrenic origin vs. Para-pneumonia	1.34 (0.30,6.05)	0.705	--	--
1-year mortality				
Subphrenic origin vs. Para-pneumonia	1.79 (0.86,3.72)	0.122	1.28 (0.61,2.69)	0.522

Table 4
Logistic regression for recurrence

Univariate logistic regression		
	cOR (95% CI)	***p* Value**
Subphrenic origin vs. Para-pneumonia	0.66 (0.08,5.63)	0.702

Table 5
Linear regression mode for length of stay

	ICU length of stay				**Hospital length of stay**			
	Crude β (95% CI)	***p* Value**	**Adjusted β (95% CI)**	***p* Value**	**Crude β (95% CI)**	***p* Value**	**Adjusted β (95% CI)**	***p* Value**
Subphrenic origin vs. Para-pneumonia	4.27 (0.03,8.51)	0.049	4.58 (0.58,8.57)	0.025	14.85 (7.94,21.76)	< 0.001	13.98 (7.41,20.56)	< 0.001
Interval from diagnosis to surgery	0.57 (0.31,0.83)	< 0.001	0.46 (0.20,0.72)	< 0.001	1.22 (0.79,1.64)	< 0.001	0.94 (0.51,1.36)	< 0.001
COPD	9.20 (4.87,13.53)	< 0.001	10.37 (6.23,14.46)	< 0.001	9.01 (1.48,16.54)	0.019	12.10 (5.37,18.84)	< 0.001
Stage	5.45 (1.25,9.65)	0.011	4.19 (0.19,8.18)	0.040	9.24 (2.15,16.34)	0.011	6.66 (0.09,13.23)	0.047

Table 6
Cultured microorganism from pleural effusion and tissue culture

Microorganism	All patients		Subphrenic origin	
	n	%	n	%
Aerobes	472	43.5	12	31.6
Streptococcus	221	20.3	3	7.9
Staphylococcus	108	9.9	6	15.8
Enterococcus	28	2.6	2	5.3
Escherichia coli	27	2.5	1	2.6
Pseudomonas aeruginosa	43	4	0	0
Mycobacterium tuberculosis	45	4.1	0	0
Anaerobes	209	19.2	3	7.9
Klebsiella	87	8	1	2.6
Fusobacterium	40	3.7	1	2.6
Bacteroides	12	1.1	1	2.6
Prevotella	45	4.1	0	0
Peptostreptococcus	7	0.6	0	0
Acinetobacter	18	1.7	0	0
Candida	25	2.3	1	2.6
Other	142	13.1	6	15.8
Not Identified	497	45.8	21	55.3

Figures

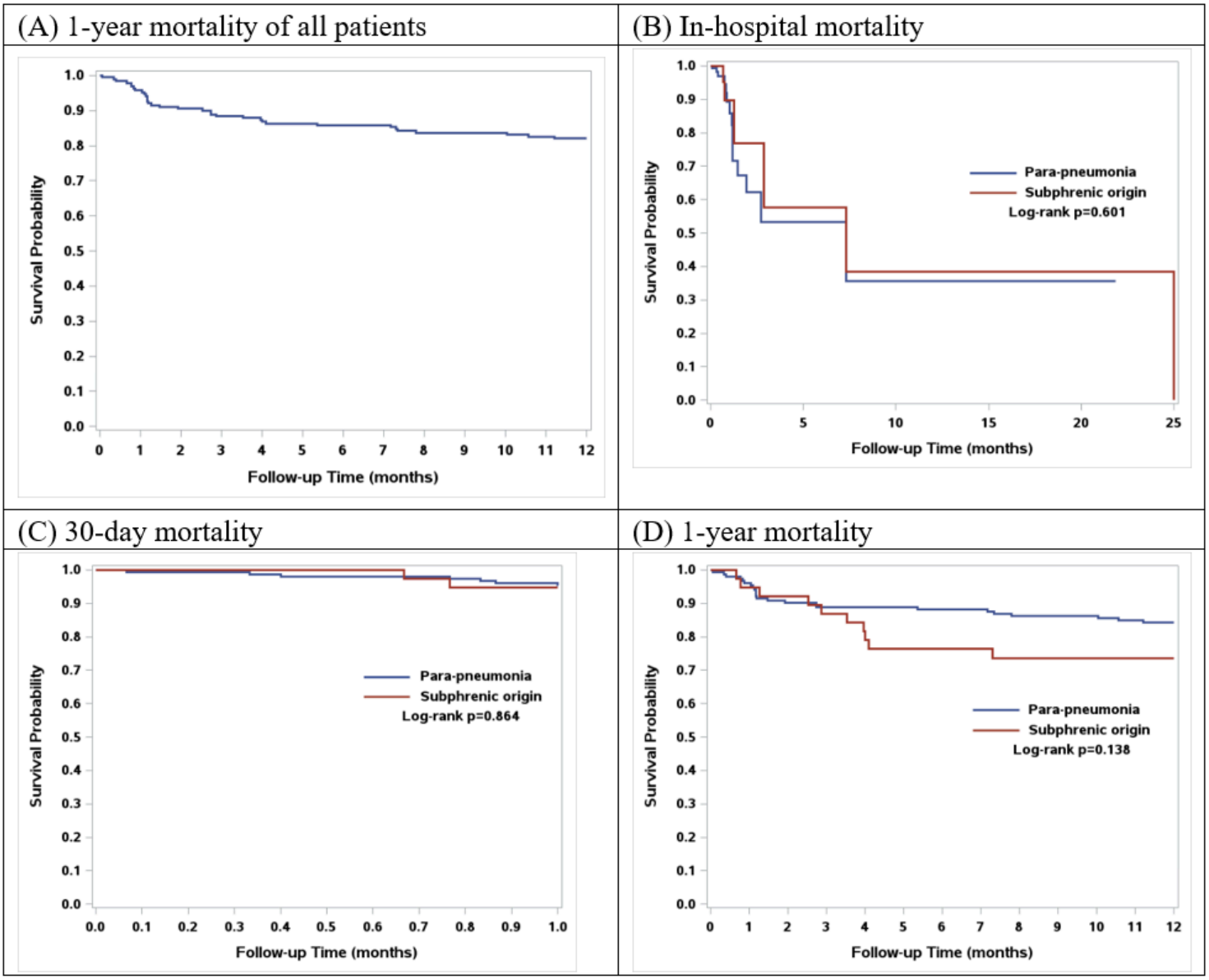


Figure 1

Kaplan-Meier curves for para-pneumonic and subphrenic origin patients

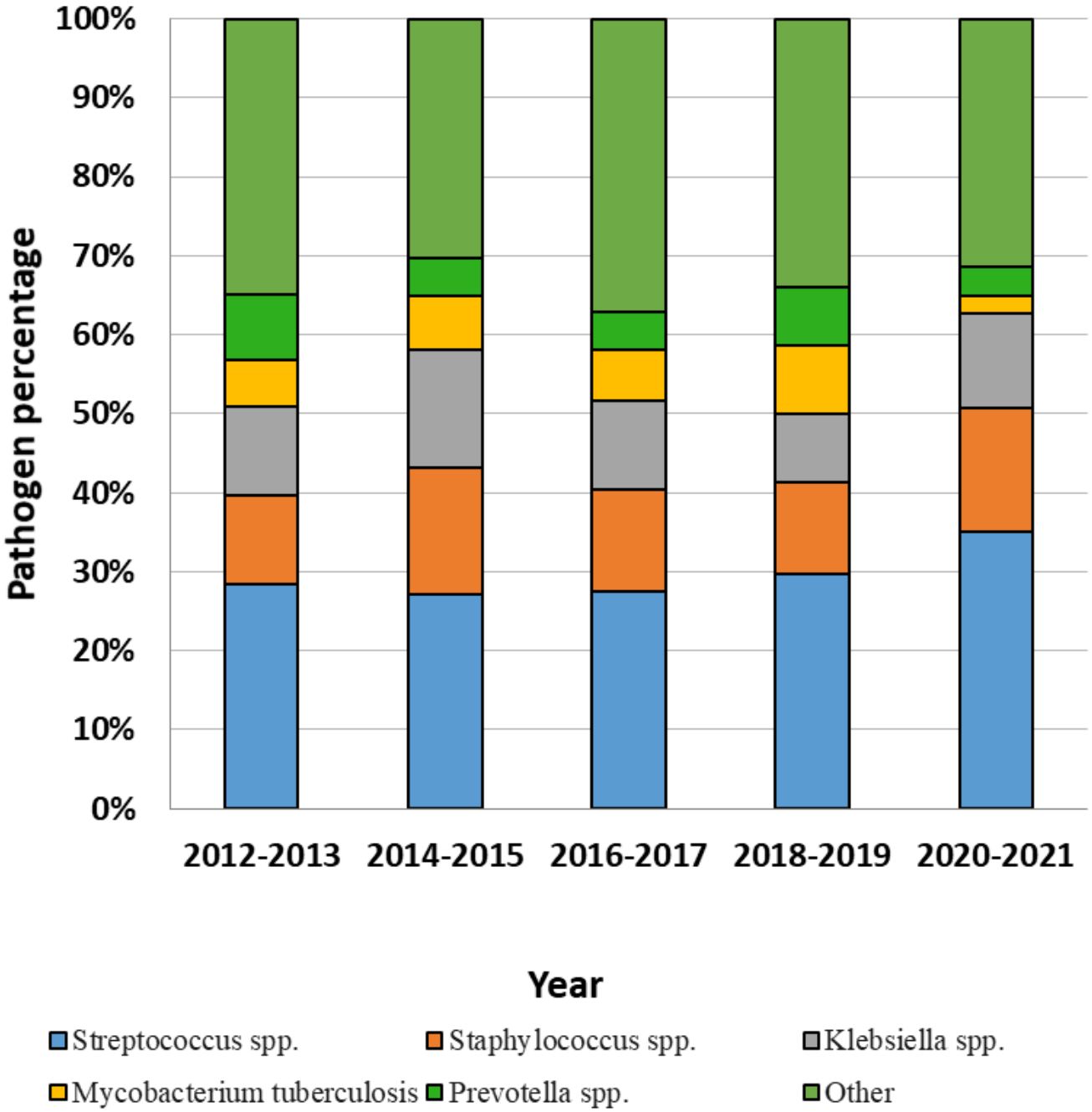


Figure 2

Distribution of microorganism according to the time frame