

Surgical management of childhood empyema: a clinical review

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Received: 29/01/2025

Accepted: 12/02/2025

Published: 10/04/2025

Cite this article: Külçe EC, Aldemir H, Çelik N, Küçük Külçe G. Surgical management of childhood empyema: a clinical review. *Surg Child*. 2025;2(2):41-47.

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ABSTRACT

Aims: In the treatment of childhood empyema, various therapeutic options are available, including tube thoracostomy followed by fibrinolytic therapy and thoracic surgical interventions. The use of fibrinolytics and video-assisted thoracoscopic surgery (VATS) has emerged as a significant innovation in managing these complications. While VATS is less invasive than thoracotomy and is considered the gold standard surgical method by some studies, there is no definitive consensus on its superiority. This study aimed to evaluate how treatment strategies evolve based on disease progression and to assess the impact of new therapeutic approaches in patients experiencing progressive stages of empyema.

Methods: This retrospective, single-center study evaluated patients under 18 years of age who underwent surgical interventions for empyema at an educational and research hospital between January 1, 2019, and January 1, 2023.

Results: A total of 20 patients with empyema in stage 2 (n=12) or stage 3 (n=8) were included in the study. These patients underwent fibrinolytic therapy and/or thoracic surgery. Patients were divided into three groups: group 1 included those treated with fibrinolytic therapy alone (n=6); group 2 included those receiving combined therapy (n=6); and group 3 consisted of those directly treated with VATS (n=8). Advanced statistical comparisons of hospital stay durations revealed significant differences between groups 1 and 2 and between groups 2 and 3 (p<0.05).

Conclusion: There is no definitive evidence to suggest the superiority of one treatment method over another for managing pleural empyema. Given the absence of standardized treatment protocols, a multidisciplinary approach involving timely and meticulous evaluation of each patient is crucial. Such an approach can improve prognosis and reduce hospitalization durations. Establishing a standardized protocol for empyema treatment could enhance response rates, shorten hospital stays, mitigate thoracic surgical risks, and facilitate earlier surgical decision-making for patients requiring thoracic intervention.

Keywords: Pleural empyema, pediatric, fibrinolytic, thoracic surgery

INTRODUCTION

Most community-acquired pneumonias resolve with medical treatment; however, approximately 0.6–2% of cases in the pediatric age group progress to empyema, with an incidence of 3.3 per 100,000 children.^{1,2} Empyema, which develops due to an imbalance in the hydrostatic and oncotic pressure in the pleural space, progresses through three stages. These stages are: stage 1 exudative, stage 2 fibrinopurulent, and stage 3 organized.^{1,3,5,6} Various treatment options are available for the management of empyema, including fibrinolytic therapy and thoracic surgical procedures following tube thoracostomy.⁷⁻¹⁰ The use of fibrinolytics and video-assisted thoracoscopic surgery (VATS) is considered an innovation in the treatment of these complications during childhood.² In stage 1 empyema, tube thoracostomy and antibiotic therapy are the first treatment options. In stage 2 empyema, favorable outcomes are achieved with fibrinolytic therapy following

tube thoracostomy. Some centers administer fibrinolytic therapy through the chest tube, while others place thinner catheters into the empyema cavity under imaging guidance. For patients who do not respond to this treatment, additional options include thoracotomy or less invasive procedures such as debridement and decortication performed with VATS. Although some studies suggest that VATS, being less invasive than thoracotomy, is the gold standard surgical method, there is no established consensus.^{7,11,12} In some patients, despite the sequential application of appropriate treatments in all stages, the empyema process persists, and progression through the stages is observed. A study was conducted on patients who experienced stage progression during empyema treatment to evaluate the parameters influencing the changes in treatment strategies according to this progression and to assess the impact of new treatment strategies.



METHODS

The study was conducted with the permission of Antalya Training and Research Hospital Clinical Researches Ethics Committee (Date: 25.05.2023, Decision No: 7/14). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In our retrospective single-center study, conducted with the approval of the ethics committee under protocol number 2023-127, patients under the age of 18 who underwent surgical intervention for empyema at Antalya Training and Research Hospital between January 1, 2019, and January 1, 2023, were evaluated. The patients' medical histories were reviewed, with a focus on past illnesses and particularly pulmonary pathologies. The presence of immunological deficiencies was also assessed. Additionally, it was determined whether the patients had received any treatment related to their existing complaints before reaching this stage. The days on which patients presented for treatment were recorded. The initial hospitalization laboratory tests were reviewed to determine whether there were any significant findings in blood biochemistry. Radiodiagnostic evaluations conducted prior to tube thoracostomy were assessed. Tube thoracostomy performed for fibrinolytic therapy was carried out routinely in accordance with the literature. The tube's localization was confirmed two hours post-procedure using a control X-ray. The characteristics of the collected fluid were analyzed, laboratory tests were performed, and the results were evaluated. On the second day, thoracic ultrasonography (USG) was used for further assessment. Patients whose treatment effectiveness remained uncertain were evaluated using high-resolution computed tomography (HRCT) of the thorax.

In the second stage, additional fibrinolytic therapy and/or thoracic surgery were planned for patients whose empyema did not resolve with tube thoracostomy. At our center, tissue plasminogen activator (t-PA) was used for fibrinolytic therapy. As per standard protocol, t-PA was administered via the previously placed chest tube at a dose of 0.1 mg/kg (maximum 6 mg/day) for three consecutive days, following guidelines in the literature.

Patients were clinically monitored, and their response to treatment was assessed using imaging methods. Fibrinolytic therapy was discontinued for all patients who showed significant improvement on X-rays and thoracic computed tomography (CT) scans, had fluid output from the chest tube of less than 5 ml/24 hours, and no longer exhibited pleural effusion.

To evaluate the impact of fibrinolytic therapy on laboratory results, hemogram and C-reactive protein (CRP) levels were recorded one day prior to the procedure, two days after the procedure, and one day before discharge.

In the third stage, thoracic surgery was directly planned for patients in whom parenchymal damage and empyema did not regress after tube thoracostomy or for those with parenchymal damage so extensive that they would not benefit from fibrinolytic therapy. This decision was made collaboratively by pediatric infectious disease and pediatric surgery clinicians, concluding that fibrinolytic therapy would not be effective. The procedure was performed under general anesthesia with the patient in the lateral decubitus position.

Using 5–10 mm trocars appropriate for the patient's age and body weight, a total of three trocars (one for the camera and two for surgical instruments) were inserted. Before concluding the procedure, chest tubes were replaced in a sterile manner through the same intercostal access (ICA), and surgical excision specimens were sent for pathological analysis. Body fluid samples were sent to microbiology, biochemistry, and pathology laboratories for further examination. For patients undergoing thoracic surgery, hemogram and CRP levels were recorded one day before the procedure, on the fifth day after the procedure, and one day before discharge. The patients' gender, age, presenting complaints, type of oxygen support, the side of the lung affected by empyema, the number of days after admission when the chest tube was removed, the presence of a bronchopulmonary fistula, the need for repeat thoracic surgery, the type and duration of antibiotic use, the presence of comorbid conditions, and the total duration of treatment were retrospectively reviewed using the hospital information system. Oxygen support was classified as follows: simple oxygen support if provided via a simple mask, nasal cannula, or reservoir mask; and advanced oxygen support if provided via high-flow oxygen or mechanical ventilation. Differences among these parameters during clinical follow-up were compared and discussed in light of the literature.

Statistical Analysis

In a 3x2 mixed design with an independent group factor (3 levels) and a repeated measurement factor (2 levels), the group*time interaction effect was set to $f = 0.90$. Using the F-test family and selecting ANOVA: repeated measures, within-between interaction, it was determined that a total of 18 patients would be required for a type I error rate (α) of 0.05 and a type II error rate (β) of 0.20. To statistically demonstrate the differences in procedures to be applied to the subjects for the research topic, account for potential data loss during the follow-up period, and achieve 80% study power, the sample size was determined to be 18 participants. The sample size was calculated using the G*power (v.3.9.1.7) software with the "as in SPSS" option activated in the options menu.

In the study, the normality of continuous variables was assessed both graphically and using the Shapiro-Wilk test. Descriptive statistics for the variables were presented as mean $\pm$ SD (standard deviation) and median (minimum-maximum) values. Cross-tables were created to compare categorical variables based on advanced treatment, with frequencies (n), percentages (%), and Chi-square test statistics reported. The Kruskal-Wallis non-parametric variance analysis was used to compare treatment methods with age, gender, and preoperative absolute neutrophil values. One-way ANOVA was employed to compare postoperative absolute neutrophil counts and length of hospital stay among treatment groups. Bonferroni correction was applied for pairwise comparisons, and the results were reported. To compare CRP levels between the group treated with fibrinolytics alone and the group treated with combined therapy, an Independent Samples t-test was used. Similarly, an independent Samples t-test was employed to compare CRP levels between the combined therapy group and the VATS-only group. To evaluate whether CRP and absolute neutrophil values showed differences at different measurement times (preoperative and postoperative), a paired samples t-test was applied for normally distributed parameters,



and the Wilcoxon signed rank test was used for non-normally distributed parameters. Statistical analyses and calculations were performed using IBM SPSS statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and MS Excel 2007. A p-value of <0.05 was considered statistically significant.

RESULTS

The demographic and clinical data of the patients are presented in **Table 1**. A total of 20 patients [stage 2 (n=12) or stage 3 (n=8)] with empyema were included in the study, for whom fibrinolytic therapy and/or thoracic surgery was planned. The patients were divided into three groups: group 1 (n=6), treated with fibrinolytic therapy alone; group 2 (n=6), treated with combined therapy; and group 3 (n=8), treated directly with

VATS. During and after thoracic surgery, none of the patients developed a bronchopulmonary fistula. One patient, despite resolution of the empyema following surgery, succumbed to sepsis. None of the patients required repeat thoracic surgery.

Cough was reported in 70% of the patients (n=14), difficulty in breathing in 65% (n=13), abdominal pain in 15% (n=3), and altered consciousness in 5% (n=1).

No statistically significant differences were found between the type of treatment applied and age, gender, the side of the lung affected by empyema, or the presence of comorbidities (p>0.05).

All patients who received fibrinolytic therapy alone (n=6) required only simple oxygen support. Among patients who underwent VATS at any stage of treatment, 42.9% (n=6) required simple oxygen support, while 57.1% (n=8) required

Table 1. Comparison of demographic and clinical characteristics based on advanced treatment methods

	Advanced treatment administered				Test statistical	P
	Fibrinolytic (n=6)	Fibrinolytic+VATS (n=6)	VATS (n=8)			
	n (%)	n (%)	n (%)			
Age						
Mean±SD	5.00±3.63	6.50±3.51	8.88±5.84	*χ²=2.022	0.364	
Median (min-max)	3.0 (3-12)	5.5 (3-12)	9.5 (1-15)			
Gender						
Male	3 (50.0)	3 (50.0)	5 (62.5)	χ²=0.479	0.999	
Female	3 (50.0)	3 (50.0)	3 (37.5)			
Location						
Right	3 (50.0)	3 (50.0)	1 (12.5)	χ²=4.040	0.325	
Left	3 (50.0)	3 (50.0)	6 (75.0)			
Bilateral	0 (0.0)	0 (0.0)	1 (12.5)			
Comorbidity						
None	5 (83.3)	4 (66.6)	2 (25.0)	χ²=8.767	0.099	
CP	0 (0.0)	1 (16.7)	0 (0.0)			
Multipl comorbidity	0 (0.0)	1 (16.7)	4 (50.09)			
Other	1 (16.7)	0 (0.0)	2 (25.0)			
Type of oxygen support						
Mask	4 (66.7)	1 (16.7)	1 (12.5)	χ²=13.323	0.028	
Nasal cannula	2 (33.3)	0 (0.0)	0 (0.0)			
Reservoir mask	0 (0.0)	3 (50.0)	1 (12.5)			
High flow oxygen	0 (0.0)	1 (16.7)	3 (37.5)			
MV	0 (0.0)	1 (16.7)	3 (3.75)			
Result						
Discharge	6 (100.0)	6 (100.0)	7 (87.5)	χ²=1.584	0.999	
Exitus	0 (0.0)	0 (0.0)	1 (12.5)			
Control examination						
Normal	6 (100.0)	4 (66.7)	7 (87.5)	χ²=4.936	0.158	
Expansion defect	0 (0.0)	2 (33.3)	0 (0.0)			
Exitus	0 (0.0)	0 (0.0)	1 (12.5)			
Echocardiography						
None	4 (66.7)	3 (50.0)	3 (37.5)	χ²=3.976	0.999	
Normal	2 (33.3)	3 (50.0)	3 (37.5)			
TD	0 (0.0)	0 (0.0)	1 (12.5)			
AD+TD	0 (0.0)	0 (0.0)	1 (12.5)			

* χ^2 : Kruskal-Wallis test, χ^2 : Ki kare test. VATS: Video-assisted thorascopic surgery, SD: Standard deviation, Min: Minimum, Max: Maximum

advanced oxygen support. A statistically significant difference was found in the type of oxygen support required based on the advanced treatment applied ($p=0.024$). However, in a multivariate logistic regression model investigating the effect of “type of oxygen support” on patients who underwent VATS, no statistically significant association was found for the need for advanced oxygen support ($p>0.05$).

No statistically significant difference was found between group 1 and group 2 in terms of pre-fibrinolytic and post-fibrinolytic CRP values ($p>0.05$). However, in group 1, a statistically significant difference was observed between the two time-dependent CRP measurements (pre-fibrinolytic and post-fibrinolytic) ($p=0.013$) (Table 2). Similarly, in group 2, a statistically significant difference was found between the time-dependent CRP measurements (pre-fibrinolytic and post-fibrinolytic) ($p=0.021$) (Figure 1).

No statistically significant difference was found between group 2 and group 3 in terms of preoperative and postoperative CRP values ($p>0.05$). However, in group 2, a statistically significant difference was observed between the two time-dependent CRP measurements (preoperative and postoperative) ($p=0.027$). Similarly, in group 3, a statistically significant difference was found between the time-dependent CRP measurements (preoperative and postoperative) ($p=0.015$) (Table 3, Figure 2).

No statistically significant difference was found in pre-procedure and post-procedure absolute neutrophil values among patients based on the type of treatment applied ($p>0.05$). However, in group 1, a statistically significant difference was observed between the two time-dependent absolute neutrophil measurements (pre-procedure and post-procedure) ($p=0.028$). Similarly, in group 2, a statistically significant difference was found between preoperative and postoperative absolute neutrophil values ($p=0.001$). In group 3, a statistically significant difference was also detected between preoperative and postoperative absolute neutrophil values ($p=0.003$) (Table 4, Figure 3).

The mean length of hospital stay was 21.50 ± 5.82 days for group 1, 37.83 ± 11.37 days for group 2, and 22.00 ± 12.06 days for group 3. A statistically significant difference was observed in the length of hospital stay among the treatment groups ($p=0.046$). Pairwise comparisons of the treatment groups revealed statistically significant differences in the length of hospital stay between group 1 and group 2, and between group 2 and group 3 ($p<0.05$).

DISCUSSION

In childhood pneumonia, the presence of comorbidities is considered one of the criteria for hospitalization, as it can negatively affect treatment success.¹³ In a study conducted by

Table 2. Time-dependent changes in CRP levels after fibrinolytic therapy between group 1 and group 2

	Group-1 (n=6)		Group-2 (n=6)		p (group)	
	Mean $\pm$ SD	Median (min-max)	Mean $\pm$ SD	Median (min-max)		
CRP						
Before fibrinolytic	216.5 $\pm$ 102.35	201.5 (117-333)	204.0 $\pm$ 101.64	172.0 (122-398)	t=0.212	0.836
End of the fibrinolytic	113.83 $\pm$ 54.49	126.0 (30-181)	101.67 $\pm$ 53.11	83.5 (48-181)	t=0.392	0.704
p (time)	t*=3.752; p=0.013		t*=3.313; p=0.021			

CRP: C-reactive protein, SD: Standard deviation, Min: Minimum, Max: Maximum

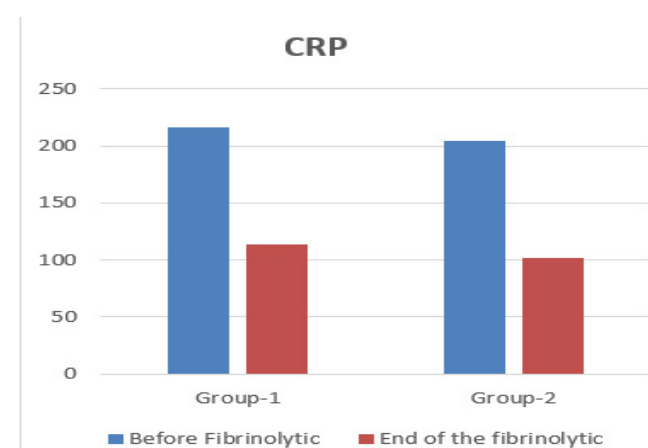


Figure 1. Distribution of CRP levels in group 1 and group 2

CRP: C-reactive protein

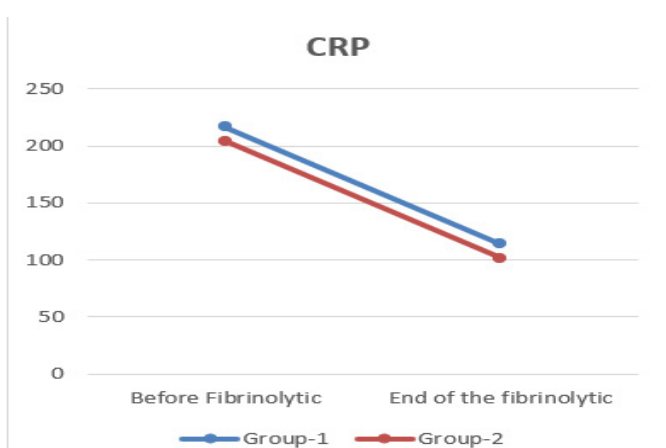


Table 3. Time-dependent changes in CRP levels after fibrinolytic application in group-2 and group-3 patient

	Group-2 (n=6)		Group-3 (n=8)		p (group)	
	Mean $\pm$ SD	Median (min-max)	Mean $\pm$ SD	Median (min-max)		
CRP						
Preop	66.00 $\pm$ 37.07	53.0 (21-126)	112.11 $\pm$ 85.38	87.5 (9.9-245)	t=1.366	0.202
Postop	48.50 $\pm$ 40.19	37.5 (12-110)	41.51 $\pm$ 37.60	30.0 (4.1-104)	t=0.334	0.744
p (time)	t*=3.085; p=0.027		t*=3.195; p=0.015			

CRP: C-reactive protein, SD: Standard deviation, Min: Minimum, Max: Maximum

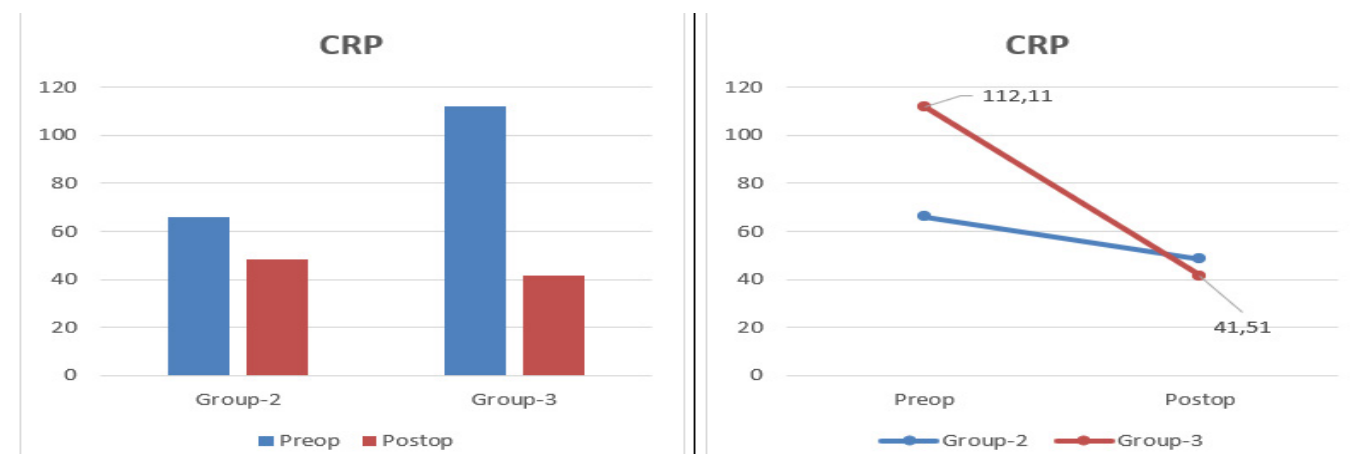


Figure 2. Group-2 and group-3 CRP distribution of values
CRP: C-reactive protein

Table 4. Time-dependent changes in absolute neutrophil values after treatment among groups

	Group-1 (n=6)	Group-2 (n=6)	Group-3 (n=8)		
	Mean±SD median (min-max)	Mean±SD median (min-max)	Mean±SD median (min-max)	p (day)	
NEU (%)					
Preop	71.83±15.85 76.5 (41-85)	68.67±20.17 77.0 (34-86)	74.94±10.82 78.5 (53-87.5)	$\chi^2=0.096$	0.953
Postop	46.67±18.82 49.5 (16-64)	48.50±23.68 53.5 (8-72)	53.00±15.27 46.0 (37-76)		
p (time)	p=0.028	p=0.001	p=0.003		

χ^2 : Kruskal-Wallis test, F: One-Way ANOVA test, SD: Standard deviation, Min: Minimum, Max: Maximum

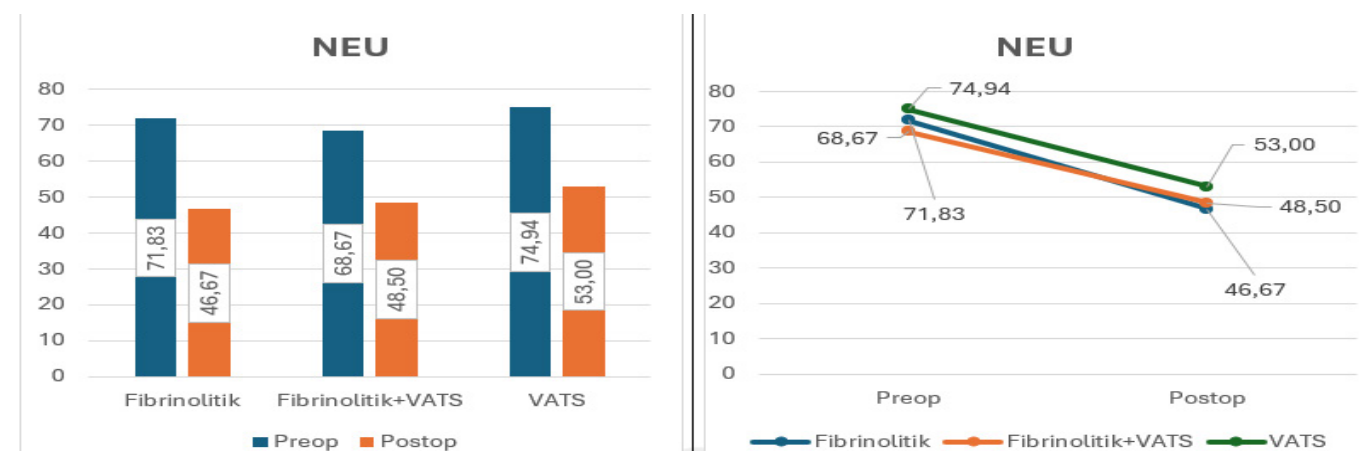


Figure 3. Distribution of absolute neutrophil values in treatment groups
VATS: Video-assisted thoracoscopic surgery

Çiftçi et al.⁷, it was observed that comorbidities in patients with empyema did not have an impact on the length of hospital stay. For patients with empyema who also have comorbidities, timely and meticulous treatment application may reduce the frequency of thoracic surgery. Conversely, in patients with empyema without comorbidities, delays in initial treatment or incorrect antibiotic choices may increase the need for thoracic surgery. Therefore, the treatment of such patients should be managed through a multidisciplinary approach.

De Benedictis et al.¹ highlighted that the World Health Organization (WHO) recommends initiating oxygen support when oxygen saturation falls below 90%, but noted existing disagreements. They argued that these disagreements stem from variations in the definition of hypoxia based on altitude. They emphasized the importance of advanced oxygen support to reduce the frequency of intubation in patients with acute respiratory distress.¹

More than half of the patients who underwent VATS at any stage of treatment required advanced oxygen support preoperatively. In contrast, patients treated with fibrinolytic therapy alone were able to maintain their oxygen saturation with simple oxygen support before the procedure, and a statistically significant relationship was found between these parameters. We believe that the completion of treatment in fibrinolytic therapy patients with simple oxygen support may indicate less lung damage compared to the other patient group, likely due to the correct treatment strategy.

There may be several reasons why patients require advanced oxygen support. One reason could be the lack of a standardized treatment protocol for childhood empyema, leading to delays or errors in treatment planning.^{7,11,12} Another possibility is the unexpected rapid clinical deterioration of the patient despite timely and appropriate treatment. We did not find any studies in the literature that specifically address these parameters.



Evaluating these parameters in studies with larger patient populations may provide more accurate results.

There is currently no established gold standard treatment strategy, either medical or surgical, for childhood empyema. In a comprehensive review, Buonsenso et al.¹⁴ noted the absence of a universally accepted treatment protocol for empyema and emphasized the importance of evaluating various surgical interventions in conjunction with appropriate antibiotic therapies. Elevated CRP levels in pneumonia patients despite treatment may indicate progression to pleural empyema.¹⁵ Studies have suggested that sequential measurements of acute phase reactants, as indicators of the inflammatory process, can be useful in assessing treatment response.^{1,12,16} Medeiros et al.¹⁷, in their study on sequential CRP measurements after surgical treatment of pleural empyema, evaluated CRP levels on the 2nd and 7th postoperative days. They observed a significant decrease in CRP by the 2nd postoperative day. While no significant difference in CRP reduction was found between patients treated with tube thoracostomy and VATS, they emphasized the utility of CRP changes in assessing hospital stay duration and treatment response.¹⁷

Ratta et al.², in their evaluation of treatment methods, found no superiority among methods in reducing laboratory parameters but highlighted that pleural debridement via VATS was significantly more effective. To evaluate surgical treatment response, we analyzed laboratory values one day before the procedure, on the 2nd postoperative day, and before discharge. In all cases, CRP and absolute neutrophil values showed significant decreases. By assessing the reduction in CRP and absolute neutrophil percentages at discharge and on the 14th day post-discharge, we concluded that all three treatment methods effectively reduced these parameters with no significant superiority among them.

Griffith et al.¹⁰ compared fibrinolytic therapy, VATS, and thoracotomy and found that VATS reduced both antibiotic use and hospital stay duration. Barglik et al.³, in their study comparing hospital stays of patients treated with fibrinolytic therapy versus direct VATS, concluded that patients who underwent direct VATS had shorter hospital stays. Studies on patients treated with direct VATS have emphasized shorter hospital stays, better empyema drainage, and a higher likelihood of improved lung volume.¹² In a review by Gates et al.¹⁸, it was noted that the shortest hospital stays were associated with thoracotomy, though VATS also resulted in very short stays. Considering the average duration of pleural empyema treatment to be 21 days, we observed that treatment durations in groups 1 and 3 were consistent with the literature, while the treatment duration in group 2 was significantly longer.¹⁹ In this group, the prolonged hospital stay was primarily due to the initial evaluation of the response to fibrinolytic therapy and the subsequent decision to proceed with VATS when no response was observed. We believe that this process is the main factor contributing to the extended hospital stay. Given the lack of significant differences in hospital stay duration, effects on laboratory parameters, complete recovery, and follow-up outcomes between groups 1 and 3, as well as the absence of a standard treatment protocol for pleural empyema, we recommend a multidisciplinary approach for careful evaluation of each patient. This approach can ensure dynamic contributions to the treatment process. If a standard treatment

protocol for the surgical management of empyema can be established, we believe that it would lead to faster treatment responses, shorter hospital stays, reduced thoracic surgery risks, and earlier decisions for patients requiring thoracic surgery.

Limitations

This study's retrospective, single-center design limits its generalizability. Multicenter studies with larger populations are necessary to obtain more accurate results.

CONCLUSION

There is no definitive evidence to suggest the superiority of one treatment method over another for managing pleural empyema. Given the absence of standardized treatment protocols, a multidisciplinary approach involving timely and meticulous evaluation of each patient is crucial. Such an approach can improve prognosis and reduce hospitalization durations. Establishing a standardized protocol for empyema treatment could enhance response rates, shorten hospital stays, mitigate thoracic surgical risks, and facilitate earlier surgical decision-making for patients requiring thoracic intervention.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of Antalya Training and Research Hospital Clinical Researches Ethics Committee (Date: 25.05.2023, Decision No: 7/14).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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