IJMA

International Journal of Medical Arts

Volume 6, Issue 5, MAY 2024

P- ISSN: 2636-4174
E- ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Cardiothoracic Surgery]

Original Article

Surgical Management of Complicated Pleural Effusion

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Article information

Received: 02-09-2023

Accepted: 18-04-2024

DOI: 10.21608/IJMA.2024.233725.1799.

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Citation: Mohammed WA, Mohamed MR, Mohamed MA, Elshaer RE, Farag EM. Surgical Management of Complicated Pleural Effusion. IJMA 2024 May; 6 [5]: 4470-4477. doi: 10.21608/IJMA.2024.233725.1799.

ABSTRACT

Background: Management of complicated pleural effusion [CPE] with loculation aims to relieve symptoms while allowing the treatment of the associated disease.

Aim of the work: This study aimed to analyze the effect of different management strategies on early outcomes.

Patients and Methods: This prospective study was conducted during the period from December 2021 to February 2022. 48 patients suffering from CPE were enrolled in this study. Patients were subjected to drainage of the effusion; and were categorized as follows: Group I: Tube drainage [TD]; Group II: Surgery after TD failure.

Results: Out of the included patients, 37 [77.09%] patients were treated with TD, and 11 [22.91%] patients were treated with surgery after the failure of TD. A positive culture was reported in 11 [29.7%], compared to 11 [100%] patients in the surgery group [P <0.001]. The surgery group had a significantly [P <0.001] higher WBC count and ESR, compared to those treated with TD [P = 0.006]. Hospital and ICU stays were significantly [P <0.001] longer in the surgical group compared to the TD group. We found a significant association between hospital stay and surgery after TD failure [B=4.81; P <0.001] and COPD [B= 1.86; P = 0.008], while a significant association was found between ICU stay and surgery after TD failure [B=3.68; P <0.001], COPD [B=1.05; p=0.016], and albumin [B=-1.04; P = 0.04].

Conclusion: TD is an effective approach to managing early-stage CPE cases, and it was associated with significantly lower hospital and ICU stays. However, in case of TD failure, immediate surgery should be performed. Despite the increased length of hospital and ICU stay in the surgery group, the application of surgery is lifesaving.

Keywords: Complicated pleural effusion; Encysted effusion; Multiloculated effusion; Intercostal tube failure.

INTRODUCTION

The pleural space is normally filled with 5 to 10 mL of serous fluid, which is in a constant state of secretion and absorption. The imbalance between secretion and absorption leads to the accumulation of fluid in the pleural space [1]. Management aims to remove this accumulated fluid, and the first step in the management is to determine whether the fluid is complicated or not; this could be done by assessing the gross and biochemical picture of the fluid and whether it is free or loculated [2]. An exudative effusion is considered a complicated pleural effusion [CPE] according to Light's classification and requires drainage to allow the lung to re-expand [3, 4]. Hemothorax, empyema, malignant effusion, and a substantial volume of loculated effusion are also included under the umbrella of CPE [1].

A patient's prognosis is determined by the interaction of three factors: host factors [such as underlying conditions, physiological reserves, and immune responses], pleural space factors [such as loculation and organization stage, as well as fluid biochemistry], and therapeutic interferences [such as drainage, surgery, and the time of surgery] [5]. No management decision could predict the results for the majority of patients since the relationship between these factors and the outcome is unclear. However, the disease's progression may be influenced by the basic control of risk factors and the personalization of the management strategy [6].

Treatment of CPE includes thoracentesis, tube drainage [TD], pleurodesis, video assisted thoracoscopic surgery [VATS], and open thoracotomy decortication [TDC] [7]. Most CPE patients present with loculation and are in the progressive stage, where TD is ineffective. Therefore, regardless of the etiology, patient's general well-being, or effusion stage, the choice to decorticate must be made quickly in these situations [8]. While decortication is effective, there are certain risks associated with therapy, including bleeding and persistent air leaks that are correlated to the disease's stage. In order to reduce this risk as well as morbidity and mortality, TD should be made early [9].

There is insufficient evidence to determine the best time to operate; nonetheless, studies have indicated that early operations allow for satisfactory results. Patients' age, co-existing comorbidities, and post-operative physiotherapy all have a role in the risk of complications and mortality following surgery [10]. There is a lack of consensus on the best approach to management. In addition, several protocols have been established. The average duration of a hospital stay is between 12 and 21 days. Additionally, roughly 30% of CPE are not drained correctly due to procedural issues or patient/doctor preference [11].

In this study, we aimed to investigate the effect of different management strategies on early outcomes in patients with CPE.

PATIENTS AND METHODS

This was a multicenter prospective clinical study of 48 patients suffering from CPE [such as pyopneumothorax clubbed with CPE, encysted effusion, multiloculated effusion, etc.], who were managed from December 2021 to February 2022. It was conducted at three hospitals Egypt. Informed consent was obtained from all patients enrolled in the study. The institutional review boards of the centers approved the data collection for the registry. Approval from the research ethics committee of the Faculty of Medicine, Al-Azhar University, also was obtained**.**

Study Population: Patients of both sexes with ages ranging from 15 to 70-year, were included in the study. All cases had a unilateral CPE, defined as an effusion that includes a large amount of loculated effusion, empyema, malignant effusion, and hemothorax. We excluded patients with non-CPE, patients having tuberculosis, patients who refused to continue the study after the initial enrollment and the cases where VATS was provided as a primary treatment.

Study Procedure

All cases were managed with TD only; of them, 11 cases were managed by open surgical decortication secondary to TD failure. The indication for surgery was the failure of the lung to re-expand and the failure to drain the effusion using a tube, regardless the cause of effusion. All patients were subjected to the collection of demographic data, including age, sex, medical history, clinical picture, type of surgery, and comorbidities. The total hospital and ICU stays were assessed for all patients. Chest radiography in the form of plain x-ray and computed tomography [CT] was performed. The fluid was subjected to laboratory analysis.

The suspected diagnosis was made through clinical manifestations, blood analysis, and radiography of the chest. The diagnosis was then confirmed with an analysis of the fluid. It was considered CPE by one of the following criteria:

[1] The presence of bacteria in the fluid, as shown by the culture, [2] The presence of septations on ultrasound, or [3] Fluid biochemical criteria: glucose lower than 40 mg/dl, lactate dehydrogenase over 1400 UI, and pH lower than 7.2.

After the diagnosis was established, the use of empirical antibiotics was initiated. A chest tube was used to drain the fluid. A thoracic US or CT was performed if multiloculations were suspected. A corresponding TD was put in place when this indicated the existence of additional drainage sites. In difficult cases US or CT was used to confirm that the TD was positioned correctly [Figure 1]. Patients who did not improve with TD and who had radiographic evidence of pleural fibrosis and an entrapped lung underwent decortication. The effusion which was drained by the tube and the pleura which was taken after exploration was sent for cytological and histopathological diagnosis and there were no atypical cells in all the cases only reactive inflammatory cells with mesothelial cells [Figure 2].

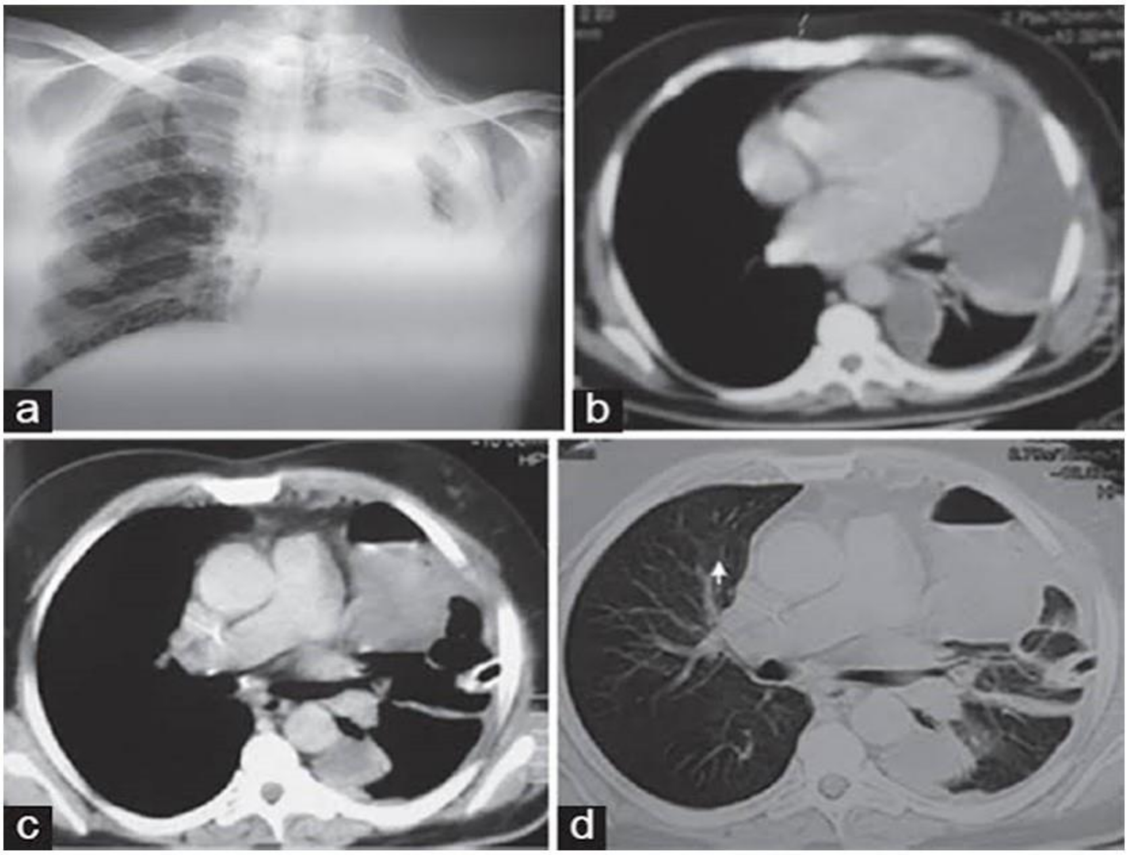

Figure [1]: Left side encysted pleural effusion before and after intercostal tube, which was inserted under CT-guidance

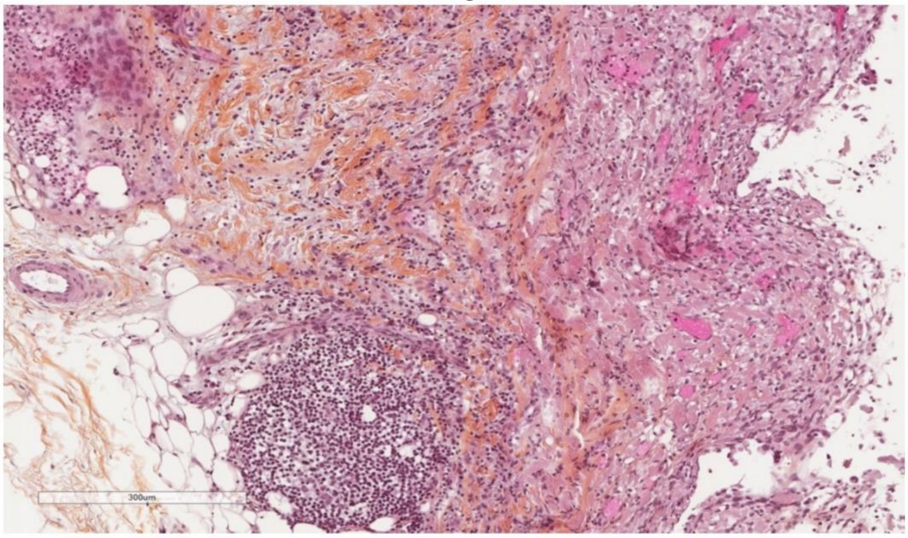

Figure [2]: Microscopic image of a mildly thickened pleura [adipose tissue at the left, pleural cavity at the right] showing some inflammation, with no atypical cells

Hospital stays, mortality rates, complications, and morbidity were all taken into account when concluding the effectiveness of various treatment modalities. Finally, we assessed the chest CT results and compared them with the initial findings. Complete fluid drainage and full lung expansion were considered signs of success, whereas signs of failure included the need for further treatment.

Statistical Analysis: Data were collected, coded, and entered into the Statistical Package for Social Science [SPSS] [IBM SPSS Statistics for Windows, Version 23.0, Armonk, New York: IBM Corporation]. The Chi-square test and Fisher exact test were used to assess qualitative data across groups after it had been presented as numbers and percentages. The Mann-Whitney U test and Kruskal-Wallis test were used to compare variables with non-normal distribution between the two groups, while independent T-test was used to compare normally distributed continuous data. The Spearman correlation test was used to evaluate the correlation between outcomes and other variables. A multi-variate linear regression analysis was performed to identify the factors associated with ICU and hospital stays duration. The P-value was considered significant at the level of <0.05.

RESULTS

Out of the included patients, 37 [77.09%] patients were treated with TD, and 11 [22.91%] patients were treated with surgery after the failure of TD, with an average time between TD and surgery of five days. When both groups were compared, there was no significant difference in terms of age [P = 0.489], gender [P = 0.977], diabetes [P = 0.246], renal failure [P = 1.00], obesity [P = 0.469], smoking [P = 0.720], addiction [P = 0.410], COPD [P = 0.661], neoplasm [Breast, Prostate, and Colon cancer] [P = 0.551], and corticosteroid [P = 0.661]. A positive culture was reported in 11 [29.7%], compared to 11 [100%] patients in the surgery group [p<0.001], as shown in Table 1.

Regarding the WBC count, it was found to be significantly [P <0.001] higher in the surgery group compared to the TD group in both serum and pleural samples. Similarly, patients who underwent surgery had a higher ESR compared to those treated with TD [P = 0.006]. Albumin level was comparable in both groups, whether it was taken from serum [P = 0.153] or pleura [P = 0.083], as shown in Table 2.

Among the patients who were treated with TD, 28-30 tube size was used in 6 patients, 32-34 in 16 patients, and 36-40 in 15 patients. In patients who underwent a surgical operation, 28-30 was used in 7 patients, 32-34 in 3 patients, and 36-40 in one patient [Table 3].

Regarding the outcomes, hospital stay was significantly [P <0.001] longer in the surgical group compared to the TD group [13.63 ± 1.12 vs. 8.75 ± 1.70 days]. Likewise, the ICU stay was substantially [P <0.001] longer in the surgical group compared to the TD group [5.36 ± 1.36 vs. 1.46 ± 0.90 days]. The complication rate was also higher in the surgical group than in the TD group [9.1% vs. 5.2%]; however, there was no statistically significant difference [P = 0.551]. Patients who were treated with 28-30 tube size were associated with significantly [P = 0.013] longer hospital stay than those who were treated with 32-34 [11.41 ± 2.20 vs. 8.94 ± 2.71 days]. Similarly, the ICU stay was longer in those who were treated with 28-30 tubes than those who were treated with 32-34 [3.00 ± 1.77 vs. 1.89 ± 1.85 days]; however, the difference was not statistically significant [P >0.05], as shown in Table 4.

We found a significant correlation between hospital stay and age [r = -0.295; P = 0.045], diabetes [r = -0.379; P = 0.009], pleural WBC [r = 0.342; P = 0.019], and serum WBC [r = 0.329; P = 0.024]. Similarly, a significant correlation was observed between ICU stay and pleural WBC [r = 0.459; P = 0.001] and serum WBC [r = 0.513; P <0.001]. The occurrence of complications was correlated with the presence of comorbidities such as COPD [r = 0.577; P <0.001], and the administration of corticosteroid [r = 0.577; P < 0.001]. A positive culture was significantly correlated with renal failure [r = 0.328; P = 0.023], pleural albumin [r = -0.426; P = 0.003], pleural WBC [r = 0.640; P <0.001], and serum WBC [r = 0.708; P < 0.001]. Chest tube size was correlated significantly with age [r = 0.432; P <0.001] as shown in Supplementary Table 1.

The multivariate regression analysis presented in Table 5 identified several predictors of ICU stay duration. The type of treatment, specifically surgery after TD failure compared to TD alone, was a significant predictor, with a regression coefficient [B] of 3.678 [P <0.001]. This indicates that patients who required surgery after TD failure had significantly longer ICU stays**.** Patients with renal failure had significantly shorter ICU stays [B=-2.3141, P = 0.009], while those with COPD had significantly longer stays [B=1.0468, P = 0.016]. Also, a higher albumin level was associated with shorter ICU stays [B=-1.0425, P = 0.04]. Other factors such as age, gender, presence of diabetes, obesity, smoking habit, addiction, and presence of a neoplasm were not found to significantly predict the length of ICU stay [P >0.05 for all].

Table 6 shows the results of the multivariate regression analysis for predictors of hospital stay duration. Notably, the necessity of surgery after TD failure was significantly associated with longer hospital stays [B=4.8104, P <0.001]. Patients with COPD also had significantly longer hospital stays [B=1.8573, P = 0.008].

Table [1]: Demographic and clinical characteristics of included patients

Variables		TD [n=37]	Surgery after TD failure [n=11]	P-value
Age	Mean ±SD	40.70±15.14	37.00±15.24	0.489$^{\beta}$
Gender	Male	20 [54.1%]	6 [54.5%]	0.977$^{\#}$
	Female	17 [45.9%]	5 [45.5%]	
DM	Yes	12 [32.4%]	1 [9.1%]	0.246$^{\#}$
	No	25 [67.6%]	10 [90.9%]	
Renal Failure	Yes	3 [8.1%]	1 [9.1%]	1.00$^{\alpha}$
	No	34 [91.9%]	10 [90.9%]	
Obesity	Yes	12 [32.4%]	2 [18.2%]	0.469$^{\#}$
	No	25 [67.6%]	9 [81.8%]	
Smoking	Yes	11 [29.7%]	4 [36.4%]	0.720$^{\#}$
	No	26 [70.3%]	7 [63.6%]	
Addiction	Yes	1 [2.7%]	1 [9.1%]	0.410 $^{\alpha}$
	No	36 [97.3%]	10 [90.9%]	
COPD	Yes	7 [18.9%]	1 [9.1%]	0.661$^{\#}$
	No	30 [81.1%]	10 [90.9%]	
Neoplasm	Yes	2 [5.4%]	1 [9.1%]	0.551 $^{\alpha}$
	No	35 [94.6%]	10 [90.9%]	
Corticosteroid	Yes	7 [18.9%]	1 [9.1%]	0.661$^{\#}$
	No	30 [81.1%]	10 [90.9%]	
Culture	Yes	11 [29.7%]	11 [100%]	<0.001*$^{\alpha}$
	No	26 [70.3%]	0 [0%]	

DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, TD: Tube drainage; *P-value indicates a statistically significant difference; $^{\#}$ Chi-square test; $^{\alpha}$ Fisher Exact test; $^{\beta}$ Mann-Whitney U test

Table [2]: Laboratory investigations

Parameter	TD [n=37]	Surgery after TD failure [n=11]	P-value
Plural Albumin	2.88±0.41	2.62±0.50	0.083$^{\alpha}$
Plural WBC	7784.86±2604.05	11376.36±1369.14	<0.001 $^{*\beta}$
WBC serum	7770.54±2081.03	11580.00±1431.95	<0.001$^{*\beta}$
ESR	20.92±18.91	41.27±26.17	0.006 $^{*\beta}$
Serum Albumin	3.059±0.55	2.77±0.66	0.153 $^{\alpha}$
PH	6.7±0.6	6.9± 0.3	<0.05$^{*\alpha}$
Glucose, mg/dLx	37 ± 0.2	31 ± 0.5	<0.001 $^{*\alpha}$

WBC: white blood cell, ESR: Erythrocyte Sedimentation Rate, TD: Tube drainage; *P-value indicates a statistically significant difference; $^{\alpha}$ Independent T-test; $^{\beta}$ Mann-Whitney U test

Table [3]: Operation Characteristics and Outcomes

Variable		TD [n= 37]	Surgery after TD failure [n=11]	P-value
Tube size		33±3	33±3	1.00 $^{\alpha}$
Hospital stays, days		8.75±1.70	13.63±1.12	<0.001*$^{\alpha}$
ICU stay, days		1.46±0.90	5.36±1.36	<0.001*$^{\alpha}$
Complications	Yes	2 [5.4%]	1 [9.1%]	0.551 $^{\beta}$
	No	35 [94.6%]	10 [90.9%]	

ICU: Intensive care unit, TD: Tube drainage; *P-value indicates a statistically significant difference; $^{\alpha}$ Independent T-test; $^{\beta}$ Fisher Exact Test

Table [4]: Relation between tube size and outcomes

Tube size	Hospital stays	ICU stay
28-30	11.41 ± 2.20 ^{a}	3.00 ± 1.77 ^{a}
32-34	8.94 ± 2.71 ^{b}	1.89 ± 1.85 ^{a}
36-40	9.87 ± 2.47 $^{a, b}$	2.37 ± 2.12 ^{a}

Means that carry different superscripts in each column are significantly different; ICU: Intensive care unit

Table [5]: Multivariate regression of the predictors of ICU stay

Predictor	B	95% Confidence Interval		p-value
		Lower	Upper	
Age	-0.029	-0.071	0.0129	0.168
Female vs. Male	0.5357	-0.4507	1.5221	0.278
Surgery after TD failure vs. TD	3.678	2.7851	4.5709	<0 .001*
DM [Yes vs. No]	0.2936	-0.6053	1.1924	0.512
Renal Failure [Yes vs. No]	-2.3141	-4.0125	-0.6158	0.009*
Obesity [Yes vs. No]	0.4966	-0.4414	1.4346	0.29
Smoking [Yes vs. No]	0.0467	-0.9217	1.0152	0.923
Addiction [Yes vs. No]	-0.3762	-1.9142	1.1618	0.623
COPD [Yes vs. No]	1.0468	0.2059	1.8877	0.016*
Neoplasm [Yes vs. No]	-0.4241	-1.8533	1.0052	0.551
Albumin	-1.0425	-2.0353	-0.0498	0.04*

DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease; TD: Tube drainage; *P-value indicates a statistically significant difference.

Table [6]: Multivariate regression of the predictors of hospital stay

Predictor	B	95% Confidence Interval		p-value
		Lower	Upper	
Age	-0.0327	-0.0971	0.0316	0.309
Female vs. Male	-0.119	-1.6062	1.3682	0.872
Surgery after TD failure vs. TD	4.8104	3.7146	5.9062	< 0.001*
DM [Yes vs. No]	-0.2298	-1.5973	1.1377	0.735
Renal Failure [Yes vs. No]	-1.3389	-3.862	1.1842	0.289
Obesity [Yes vs. No]	0.1296	-1.2817	1.5409	0.853
Smoking [Yes vs. No]	0.0648	-1.4009	1.5306	0.929
Addiction [Yes vs. No]	-0.0166	-2.3424	2.3092	0.989
COPD [Yes vs. No]	1.8573	0.5179	3.1967	0.008*
Neoplasm [Yes vs. No]	-1.9302	-4.0928	0.2324	0.079
Albumin	-0.4422	-1.9348	1.0504	0.551

DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease; TD: Tube drainage; *P-value indicates a statistically significant difference.

DISCUSSION

The management of CPE involves the treatment of the associated comorbidity, which might disturb the improvement of the clinical picture. When we looked at how comorbidities affected treatment outcomes, we found that managing comorbidities significantly reduced the need for surgical intervention. Determine the stage of CPE must be done before selecting the management strategy [12], which has been done in this study by radiological assessment via [chest radiograph, US, and/or CT]. Imaging-guided tube placements were advised and preferred over blind tube insertion since the majority of the patients had loculated effusion [13]. More than one tube may be required in situations with multiple loculations [14]. In the early stages, TD is the initial step in management; however, in later stages, open thoracotomy decortication is commonly required [15]. In 37 patients, CPE was successfully treated with TD alone in our study over a period of 9–13 days, with substantial reductions in the mean number of drainage days, hospital stays, and morbidity as compared to surgically treated cases.

The ideal tube diameter for CPE drainage is a subject of debate [16]. Large-diameter chest tubes were widely advised for drainage since several observational studies suggested that the use of small-diameter tubes might be challenging [17–19]. The surgeons prefer to use a large tube because TD failure often arises from chronic, loculated effusion rather than tube blockage, despite the radiologist reporting a successful outcome with small tubes [20]. In this study, we used large-bore tubes as advised by **Heffner *et al.*** [21].

Patients who do not have lung expansion after TD but still exhibit persistent symptoms of infection should consider surgery immediately [20]. According to **Wozniak *et al.*** [22], employing TD as a first treatment rather than surgery is a very reliable predictor of first treatment failure, which has an impact on patient mortality. In our study, we found that surgical management after the failure of TD was associated with significantly longer ICU and hospital stays. However, we believe that this difference was not attributed to the management approach, but to the patient's disease status, comorbidities, and other factors. We found a significant correlation between hospital stay and age, diabetes, pleural WBC, and serum WBC. Similarly, a significant correlation was observed between ICU stay and pleural WBC and serum WBC [23–27]. It was discovered that inefficient drainage, detection of microorganisms in CP, higher neutrophil fraction in blood, low hemoglobin levels and PaO2, and fever are all predictors of a longer hospital stay [28, 29]. Microbes found in the pleural effusion were another contributor to the patient's extended hospital stay. Isolating bacteria enables tailored antibiotic treatment [30], and this may also contribute to a shorter hospital stay. A positive culture was significantly correlated with renal failure, pleural albumin, pleural WBC, and serum WBC, highlighting the importance of investigating these parameters in each patient.

We admit that our study has some limitations, including the small sample size and the shorter duration of follow-up, which may affect the generalizability of our findings. Moreover, due to the small sample size, we could not perform a regression model to identify the predictors of hospital stay length.

Conclusion

In conclusion, the current study showed that the management of patient's comorbidities is critical for improving the outcomes of patients with CPE. TD is an effective approach to managing early-stage CPE cases, and it was associated with significantly lower hospital and ICU stays. However, in case of TD failure, immediate surgery should be performed. Despite the increased length of hospital and ICU stay in the surgery group, the application of surgery is lifesaving. Bacterial culture, serum, pleural WBC, and albumin should be assessed to evaluate the patient's condition and may contribute to the choice of proper management.

Conflict of interest: None.

Acknowledgment: None.

Funding Source: None.

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IJMA

International Journal of Medical Arts

Volume 6, Issue 5, MAY 2024

P- ISSN: 2636-4174
E- ISSN: 2682-3780