Original Article

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Surgical and Non-surgical Treatments in Pleural Empyema

Plevral Ampiyemde Cerrahi ve Cerrahi Olmayan Tedaviler

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ABSTRACT

Objective: Increasing number of patients are developing complicated pleural infection. We aimed at revealing the differences of treatment modalities performed in patients with empyema.

Methods: Patients those had been diagnosed and treated for empyema were assessed in a retrospective design. For the definitive diagnosis of empyema, thoracentesis was made. We categorized the patients in two groups as therapeutic drainage (group 1) and open surgery (group 2).

Results: A total of 360 patients, 57 of whom were women, were included. Tube drainage was applied to the patients in group 1, and therapeutic thoracentesis was applied to those not suitable for drainage. Patients who did not provide adequate drainage due to loculation were deloculated with fibrinolytic agent or video-assisted thoracoscopic surgery. In patients with advanced empyema with multiloculation and remarkable pleural thickening, which constituted group 2, decortication was performed by thoracotomy. Thoracoplasty was added in those who had insufficient lung volume. There were 292 (81.2%) patients in group-1 and 68 (18.8%) patients in group 2. In comparison of two groups, a significant difference was detected for lactate dehydrogenase ($p<0.001$) in pleural fluid and leukocyte count ($p=0.05$), hemoglobin ($p=0.01$), albumin ($p=0.002$), urea ($p=0.3$), and creatinine ($p=0.21$) levels in blood. The treatment results revealed no significant difference between three groups (recovered, sequelae changes, death), except for blood neutrophil count and antibiotic duration.

ÖZ

Amaç: Artan sayıda hastada komplike plevral enfeksiyon gelişmektedir. Biz ampiyemli hastalarda tedavi modaliteleri arasındaki farkları belirlemeyi hedefledik.

Yöntemler: Ampiyem teşhisi konulan ve tedavi edilen hastalar retrospektif bir tasarım ile değerlendirildi. Ampiyemin kesin teşhisi için torasentez yapıldı. Hastalar iki gruba ayrıldı; terapötik drenaj (grup 1) ve açık cerrahi (grup 2).

Bulgular: Çalışmada 57 kadın, toplam 360 hasta yer aldı. Grup 1'deki hastalara tüp drenaj ve tüp drenaj uygun olmayanlara terapötik torasentez uygulandı. Lokülasyon nedeniyle uygun drene edilemeyenlerde fibrinolitik ajanlar ya da video yardımlı torakoskopik cerrahi kullanıldı. Multilokülasyon ve belirgin plevral kalınlaşmaya sahip ileri ampiyemde (grup 2) torakotomi yoluyla dekortikasyon yapıldı. Yetersiz akciğer volümlü hastalarda torakoplasti uygulandı. Grup 1'de 292 hasta (%81,2) ve grup 2'de 68 hasta (%18,8) yer aldı. İki grup değişkenleri karşılaştırıldığında; plevral sıvıda laktat dehidrojenaz ($p<0,001$) ve kanda lökosit sayısı ($p=0,05$), hemoglobin ($p=0,01$), albumin ($p=0,002$), üre ($p=0,3$) ve kreatinin ($p=0,21$) düzeyleri açısından anlamlı farklılıklar izlendi. Tedavi sonuçları üç grup arasında (iyileşen, sekel gelişen, ölen) - kan nötrofil düzeyi ve antibiyotik süresi hariç - anlamlı farklılık göstermedi.

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ABSTRACT

Conclusion: Medical treatment plus therapeutic drainage therapy may be chosen as first treatment instead of open surgery in empyema.

Keywords: Thoracic empyema, surgery, video-assisted thoracic surgery, pleural fluid

ÖZ

Sonuç: Medikal tedavi ve terapötik drenaj tedavisi ampiyemde açık cerrahi yerine ilk tedavi yöntemi olarak tercih edilebilir.

Anahtar Sözcükler: Torasik ampiyem, cerrahi, video yardımlı torasik cerrahi, plevral sıvı

Introduction

Nearly 100 years ago, the management recommendations for empyema were early closed pleural drainage, avoidance of early open drainage, and sterilization of the empyema area. Though significant developments on antibiotherapy, radiology, intrapleural fibrinolytics, and minimally invasive surgery, these are still core principles. On the other hand, the morbidity, mortality, and burden of pleural infection remain high (1-3).

Patients with complicated pleural infection/empyema have been increasing, especially in children and older patients, requiring medical and surgical management. The optimal duration of therapy is not clearly defined. It is generally individualized based on the type of effusion, the adequacy of drainage, clinical and radiographic improvement and the immunity (4,5). Medical and surgical treatment both have complications. Also there are long-term complications of infection affecting pleural space including residual pleural thickening, and rarely, fibrothorax, bronchopleural fistula formation, empyema necessitatis and pleural calcification. The pleural involvement usually resolves over three to six months. Patients should be considered for decortication when they fail to improve and are symptomatic after six months. If an adequate and prompt therapy is administered, the long-term survival is good. Mortality is highest in those requiring open surgery or decortication. Comorbid conditions or surgical complications are usually the primary cause of death rather than empyema itself and is highest during the first 400 days (6,7).

Clinicians select type of antibiotic based on the site of acquisition, epidemiology, severity, individual risk factors for drug-resistant pathogens or infection with other specific organisms. Immunocompromised patients have higher hospitalization rates and mortality, and longer hospital stays. Pleural fluid biochemistry in the fibrinopurulent and organizing phases differ from those of the exudative phase requiring placement of a chest tube (4,5).

As empyema has poor prognosis, treatment should be started promptly at the time of diagnosis. Besides most patients recover, clinical outcomes remain poor with one in five patients requiring surgical intervention and 20% die within the first year of diagnosis (8).

The macroscopic appearance and smear/culture of pleural fluid may help to diagnose, while other biochemical and radiological characteristics are not specific. We aimed to reveal the role of blood/pleural fluid tests and patient-based properties as a prognostic marker in empyema. We aimed to reveal the consequences/differences of treatment modalities in empyema.

Methods

Design

The study was conducted in a retrospective design, which was approved by the institutional review board. Patients diagnosed as having empyema in clinic were included. Demographic characteristics of the patient population as well as routine blood test results, radiological imaging properties (thoracic ultrasonography and computed tomography) at the time of the first admission were retrieved from the hospital records. For the definitive diagnosis of empyema, the criteria for aspirating purulent fluid in thoracentesis with bacterial growth in the liquid sample taken and/or pH <7.20 and/or leukocytes >1,000/mm^3 was used.

Pulmonary function tests (PFTs) were performed using spirometry (Zan 500, Germany). Approval was obtained from the University of Health Sciences Türkiye, Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee (decision number: E.9801, date: 06.10.2017).

Definition of mortality: If a patient died any time from diagnosis to end of treatment, without any other reason, the result was evaluated as death.

The patients were evaluated as healed or sequelae according to the chest X-ray taken on 2nd week, 4th week and 3rd month control visits.

Thoracentesis: It was performed with a 16G branule from the region marked by thoracic ultrasonography under local anesthesia. Biochemical examinations, cytological examination and microbiological results of the aspirated fluid were evaluated. The number and duration of antibiotics given, and the surgical method applied were recorded.

Patients and Categorization

The patients were divided into two groups according to the treatment modalities, as therapeutic drainage (group 1) and open surgery (group 2). Tube drainage was applied to the patients in group 1, and therapeutic thoracentesis was applied to those not suitable for drainage. Patients who did not provide adequate drainage due to loculation were deloculated with fibrinolytic agent or video-assisted thoracoscopic surgery (VATS). In patients with advanced empyema with multiloculation and remarkable pleural thickening, which constituted group 2, decortication

was performed by thoracotomy. Addionally, thoracoplasty was added to patients who had insufficient lung volume. The RAPID score for pleural infection was used to predict mortality (9).

Statistical Analysis

The data were imported to a database formed by the Statistical Package for Social Sciences (SPSS) program V22 (IBM Corp, Armonk, New York, USA). Nominal variables were evaluated by their frequencies and percentages and compared by using cross tables. Continuous variables were used, and the normal distribution was examined by a normality test, graphical analysis, and by considering the sample size. Comparison of the variables was performed with parametric tests. One-Way ANOVA test was used for comparison of 3 groups. For all the statistical comparison tests, the probability of a type 1 error was α=0.05 and two sided. A p-value of <0.05 was considered statistically significant.

Results

A total of 360 patients, 57 of whom were women, were included. The mean age was 55.5±15.4 years; and 84.2% (n=303) was male. One hundred ninety-four (53.6%) patients had at least one comorbidity and 155 (61.5%) had smoking history. Most of the effusions were right sided (57.8%) while 43.3% of the effusions were free flowing. Most of the patients were treated with two or more antibiotics (n=248, 68.8%). Two hundred twenty-two (61.7%) patients were in the low-risk category of RAPID score, 17 patients (4.7%) were in high-risk group. There were 25 deaths (6.9%), and 143 patients (39.7%) were healed with sequelae.

Therapeutic drainage (therapeutic thoracentesis, VATS drainage, tube thoracostomy) was performed in 292 (81.2%, group 1) patients and open surgery (decortication with thoracotomy, thoracoplasty) was performed in 68 (18.8%, group 2) patients.

Group 1 and group 2 revealed no difference of outcome, as recovering with or without sequelae and death (p=0.36). But the patients in group 2 were mostly composed of low-risk patients according to the RAPID score (p=0.01). Pleural fluid lactate dehydrogenase (LDH) was significantly lower in patients of group 2 (median 2841 vs. 1670; p<0.001). Also, significant differences were present in blood leukocyteand neutrophil counts, hemoglobin, and albumin levels, all were higher in group 2 (respectively, p=0.05, p<0.001, p=0.01 and p=0.002). There was no difference in radiographic findings, PFTs, comorbidities, smoking history or antibiotherapy duration between the groups. Demographic characteristics of the study population and comparison of groups are presented in Table 1.

Study population was also categorized according to the treatment outcomes, as patients fully recovered without sequelae (n=192), patients with sequelae on radiography (n=143) and patients who died (n=25). Comparison of these groups revealed no difference in terms of age, gender, comorbidities, PFTs, pleural fluid analysis or RAPID score. Pleural fluid pH and albumin levels tended to be lower in patients with sequelae at the edge of significance

Table 1. The demography and comparison of group 1 (patients treated with therapeutic drainage) and group 2 (patients treated with open surgery)

Variables		Study population (n=360)	Group 1 (n=293)	Group 2 (n=67)	p-value
Age, years ± SD		55.5±15.4	57.1±15.1	48.6±1.8	<0.001
Gender, male		303 (84.2%)	243 (82.9%)	60 (89.6%)	0.2
Smoking history	Active	82 (32.5%)	64 (32.7%)	18 (32.1%)	0.69
	Ex-smoker	73 (29%)	59 (30.1%)	14 (25%)	
	Never smoker	97 (38.5%)	73 (37.2%)	24 (42.9%)	
Presence of comorbidities	None	167 (46.4%)	129 (44%)	38 (56.7%)	0.44
	1	155 (43.1%)	132 (45.1%)	23 (34.3%)	
	2 or more	38 (10.6%)	32 (10.9%)	6 (9%)	
Localization	Right	207 (57.8%)	169 (58.1%)	38 (56.7%)	0.25
	Left	137 (38.3%)	113 (38.8%)	24 (35.8%)	
	Bilateral	14 (3.9%)	9 (3.1%)	5 (7.5%)	
Radiographic appearance	Free	154 (43.3%)	125 (43.1%)	29 (43.9%)	0.99
	Loculated	137 (38.3%)	112 (38.6%)	25 (37.9%)	
	Multiloculated	65 (18.3%)	53 (18.3%)	12 (18.2%)	
Pulmonary function tests					
FEV1 (% ± SD)		57.0±17.6	56.4±17.7	58.5±17.3	0.49
FVC (% ± SD)		58.3±18.3	57.8±17.4	60.0±20.7	0.52
FEV1/FVC (n ± SD)		81.3±14.0	80.2±14.0	84.5±13.4	0.07

Table 1. Continued

Variables		Study population (n=360)	Group 1 (n=293)	Group 2 (n=67)	p-value
Laboratory parameters					
Pleural fluid					
pH		6.8±0.52	6.7±0.55	6.8±0.39	0.355
Glucose, mg/dL		5	5	2	0.751
Albumin, g/dL		1.7	1.7	1.9	0.559
LDH, u/L		2425	2841	1670	<0.001
Blood sample					
Leucocytes, /mm^3		12.400	12.000	14.000	0.05
Hemoglobin, gr/dL		11.4	11.4	11.8	0.01
Neutrophils, /mm^3		4.200	3.000	6.900	<0.001
CRP, mg/dL		14.7	15	12.8	0.4
LDH, u/L		185.5	182	187	0.61
Albumin, gr/dL		3.0	2.8	3.2	0.002
Protein, gr/dL		6.7	6.6	6.8	0.3
Urea, mg/dL		32	34	31	0.3
Creatinine, mg/dL		0.9	0.89	0.84	0.21
Polymicrobial growth		11	10	1	0.69
Number of antibiotics used	1	102	81	21	0.38
	2	183	154	29	
	3	52	40	12	
	4	13	9	4	
Treatment duration, months		1	1	1	0.35
RAPID score	0	48 (13.3%)	32 (10.9%)	16 (23.9%)	0.007
	1	81 (22.5%)	64 (21.8)	17 (25.4%)	
	2	93	75 (25.6%)	18 (26.9%)	
	3	74	61 (20.8%)	13 (19.4%)	
	4	47 (13.1%)	44 (15%)	3 (4.5%)	
	5	17 (4.7%)	17 (5.8%)	0	
RAPID risk category	Low-risk	222 (61.7%)	171 (58.4%)	51 (76.1%)	0.01
	Medium-risk	121 (33.6%)	105 (35.8%)	16 (23.9%)	
	High-risk	17 (4.7%)	17 (5.8%)	0	
Outcome	Recovered	192 (53.3%)	154 (52.6%)	38 (56.7%)	0.36
	Sequelae	143 (39.7%)	116 (39.6%)	27 (40.3%)	
	Death	25 (6.9%)	23 (7.8%)	2 (3%)	

FEV_1: Forced expiratory volume, FVC: Forced vital capacity, SD: Standard deviation

(respectively, p=0.09 and p=0.07). Among laboratory results, blood neutrophil count tended to be higher in patients who did not survive (p=0.03). Also, antibiotic duration was also shorter in this group of patients (p=0.03). Comparison of outcomes is presented in Table 2.

Discussion

When we compared the characteristics of patients treated with therapeutic drainage and patients who needed open surgery during the management of empyema, patients managed with open surgery were younger, with lower plural fluid LDH

Table 2. The outcomes of three groups: Recovered, sequelae changes, death

		Mean ± SD			
Variables		**Recovered (n=192)**	**Death (n=25)**	**Sequelae (n=143)**	**p-value**
Age (n)		55.9±15.3	55.7±15	55.2±15.5	0.951
Smoking, pack year (n)		38.4±28.8	39.5±31.4	39±23.8	0.991
FEV_1 (%)		60±15.3	56±14	56±19	0.576
FVC (%)		60±15	58±14	57±20	0.677
FEV_1/FVC (%)		82±14	80±13	81±14	0.885
Pleural fluid					
pH		6.8	6.9	6.8	0.09
Glucose (mg/dL)		7	6	2	0.42
Albumin (g/dL)		2.1	2.3	1.6	0.07
Lactate dehydrogenase (u/L)		1.848	2.876	3.167	0.37
Blood sample					
Leukocytes (x10^3/uL)		12.600	11.900	12.050	0.57
Hemoglobin (g/dL)		11.5	11.4	11.4	0.85
Neutrophile (x10^3/uL)		3.460	7.200	3.550	0.03
C-reactive protein (mg/dL)		13.7	12.4	16.2	0.79
Lactate dehydrogenase (u/L)		182	205	180	0.26
Albumin (g/dL)		2.9	2.6	2.9	0.25
Urea (mg/dL)		33	42.5	34.5	0.58
Creatinine (mg/dL)		0.87	1,04	0.89	0.36
Antibiotic duration (n)		1	0.85	1	0.03
RAPID score	Low risk	121 (63%)	12 (48%)	89 (62.2%)	0.26
	Medium risk	65 (33.9%)	10 (40%)	46 (32.2%)	
	High risk	6 (3.1%)	3 (12%)	8 (5.6%)	

FEV_1: Forced expiratory volume, FVC: Forced vital capacity, SD: Standard deviation

levels, and higher blood leukocyte and neutrophil counts, and hemoglobin and albumin levels. Also, their RAPID score was lower than patients treated with therapeutic drainage. There was not any difference of mortality among groups. No difference was found between groups of patients who died and who survived with or without sequelae, except blood neutrophil count and antibiotic treatment duration. The death rate was 6.9% in total, which is comparable to death rates in literature (10,11).

The decision to drain is based on the characteristics of the pleural fluid. The fluid should be drained immediately upon the appearance of pus. Biochemical properties of pleural fluid change in the presence of bacteria and inflammation. Pleural fluid pH, glucose and LDH levels are considered a priority in terms of drainage. In all patients with suspected (or diagnosed) empyema, initiation of antibiotics should be promptly and not be delayed for sampling or drainage procedures, etc. Prompt drainage of pleural fluid in addition to antibiotic therapy is also suggested. The initial procedure of choice is usually a single tube or catheter thoracostomy. Image-guided placement of a catheter(s) may be needed when pleural loculations prevent adequate drainage by a single tube (3,6,7,12,13). Simple surgical approach was performed in 81.4% and invasive surgical methods were performed in 18.6%. The average antibiotic duration was 1.77 months. In our patient population, patients who were treated with open surgery had comparatively better clinical condition with lower ages who comprised the patients suitable for major surgery. In addition, although higher mortality rates were reported in patients with empyema who were treated with pleural drainage with thoracoscopy alone (12-15), we observed no difference in mortality between treatment groups. The hospital mortality rate was lower in patients who underwent surgery than in those who underwent non-operative drainage (16). There are studies claiming otherwise. Although surgery was not possible because of poor clinical conditions in the non-survivor group, the mortality rate might have differed if surgery had been performed in anyone (17). It was also reported that the readmission and reintervention rates were higher in patients managed with chest tubes, suggesting a possible benefit from earlier surgical intervention (14,18).

In a serial of 71 patients, 11% died during treatment in hospital, where 89% underwent thoracic drainage; 70% were administered urokinase in the pleural cavity; and 11% underwent surgeries (17). The duration of antibiotic therapy and the length of hospital stay were 30 days and 23 days, respectively. Patients with poor performance score and patients with aspiration were significantly more common in the non-survivor group. Clinical condition, surgical intervention, and persistent pleural spaces were independent prognostic factors for empyema recurrence. In persistent pleural space, decortication and early thoracoplasty were advised (19).

Older age, high blood urea nitrogen (BUN) level, low serum albumin level, hospital-acquired infection, and the absence of purulence in RAPID scoring predicted poor prognosis at three months. High BUN level, an indicative of dehydration, is supposed to negatively affect prognosis (9,17). Although we found no difference in RAPID scores according to the patient outcomes, patients treated with open surgery tended to have lower RAPID scores which also reflected better clinical status of these patients.

There is a relation between albumin level, a plasma protein/marker of the nutritional status and infection. Importantly, polymicrobial etiology leads a poor prognosis for empyema (14,17,20). In categoric variables, gender, number of microorganisms isolated in culture, number of comorbidities, radiological location/appearance and number of antibiotics used were similar between two patient groups. Our culture results with polymicrobial growth were rare, so it was unavailable to retrieve robust data for these data.

Study Limitations

Being a monocentric retrospective study was a limitation. Although we had considerably high number of patients with real life data, it was impossible to eliminate selection bias.

On the other hand, we would like to point out that due to the retrospective design, surgery was performed as a necessity rather than an option for the patients included in the analysis. Indeed, various complications, sequelae and death were inevitable if good drainage was not provided. The similarity of these negative outcomes in treatment results was not an evidence of no need for surgery and drainage would be sufficient.

Conclusion

As a conclusion, it can be stated that medical treatment plus simple surgical intervention such as thoracentesis, tube thoracostomy, VATS, fibrinolytic therapy could be chosen as first treatment instead of more invasive intervention such as thoracoplasty, open surgery, decortication of the lung. More invasive techniques should be considered on individual cases, till more convincing evidence for better outcome are reported.

Ethics

Ethics Committee Approval: Approval was obtained from the University of Health Sciences Türkiye, Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee (decision number: E.9801, date: 06.10.2017).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Ç.Ç., A.E.E., A.Ü., Concept: S.D., N.A., Design: S.D., N.A., Data Collection or Processing: S.D., N.A., Ö.Ö., G.V.Ş., E.Ç.Ç., M.O.G., F.G., Analysis or Interpretation: S.D., N.A., Ö.Ö., G.V.Ş., M.O.G., F.G., A.E.E., Writing: S.D., A.E.E.

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