Introduction
Empyema is defined as the presence of purulent effusion in pleural space, and consists of three clinical stages. Pleural inflammation and increased capillary permeability results in the shift of pulmonary interstitial fluid to the pleural space [1], which is called an acute phase, featured with exudative purulent effusion with a low viscosity and low cell count [2], lasting for 1–5 days [3].

The transitional or fibrinopurulent stage usually develops during the first three weeks of infection [3]. In this grade, the bacterial invasion leads to the infection and loculation of pleural space [1], which is characterized by the accumulation of dense pus, and adherent fibrous bands and increased numbers of cells [2]. The chronic fibrosis phase, or organization stage, develops after three weeks [3]. Fibroblast proliferation and visceral plural fibrosis comes to restricted pulmonary function [4, 5]. Sedimentation of collagen on pleural wall may result in thickening of pleural space in almost 3 to 4 weeks, which is called ‘pleural peel’ [1, 5]. Incidence rate of empyema in all age groups has raised globally [6]. This increasing trend in the incidence of empyema has been confirmed by several studies. A review by Grijalva et al. showed that the hospital admission of empyema patients has doubled (3.04 per 100,000 in 1996 vs. 5.98 in 2008) [7]. Another study by Farjah et al. observed 4,424 patients with empyema and concluded an increased incidence of 2.8% annually (95% CI: 2.2%–3.4%) [8].

The most common cause of empyema is parapneumonic effusion, but postsurgical empyema is also frequently encountered [1]. Zejierska et al. conducted a survey to identify main etiologies of empyema: they indicated the pneumonia as the first (64%) and trauma and CRF as the next most important causes [9]. Empyema affects all age categories, but a higher prevalence is reported in seniors, disabled individuals and those with comorbidities. Major risk factors of empyema, according to previous studies, include age, male sex, debilitation, severe pneumonia, comorbid diseases (such as bronchiectasis, chronic obstructive pulmonary disease, alcoholism, diabetes, and gastroesophageal reflux disease) [4]. A review by Zablockis et al. on 120 patients with empyema showed that around 50% of patients had at least one risk factor or had immune suppressive status, such as neoplasms, taking immunosuppressive medications, or alcohol abuse [10]. Empyema...
mortality rate of 5-30% was reported, increasing to 40% among immunocompromised patients [4].

Antibiotic therapy, fibrinolytics, and pleural space drainage are considered the treatment choice in empyema at primary, early second, and second stage of the disease, respectively. Unsuccessful drainage cases are subjected to VATS. At the third stage (i.e., in the case of unexpandable lung, multiple loculations, and continued pleural sepsis), decortications would be indicated. Open drainage should be performed in patients who are too debilitated for VATS and thoracotomy [4].

This study was designed to compare the treatment outcomes of two methods of empyema treatment, chest tube vs. VATS, in order to determine whether VATS could be the first treatment choice.

Material and Methods
Participants
In this prospective analytical study, patients admitted to receive medical attention for empyema, between 2011-2012, were recruited. The inclusion criteria were patients aged over 18 years with diagnosis of empyema, who agreed to participate in the research; whereas, if the management method was changed for any reason and/or patients were unwilling to be assessed, then they were excluded from the study. A total of 60 patients, fulfilling the inclusion and exclusion criteria, were enrolled.

Intervention
Patients were explained about assessment, and written consent was obtained. They were divided among two groups of 30 patients in each. Thirty patients (50%), who were treated with chest tube, were classified as Group I, and 30 patients (50%) subjected for VATS were classified as Group II. Two techniques were evaluated and compared in terms of demographic information, length of hospital stay, patient satisfaction level, radiographic findings on postoperative day 7, discharge from the hospital with or without chest tube, need for second intervention, empyema pathogens, and treatment outcomes up to 3 months after the discharge. In order to determine the most common pathogen in two groups, the sample of pleural fluid was obtained after administration of chest tube in Group I and during VATS procedure in Group II. Both samples were submitted to laboratory to identify the involved pathogens.

Table 1. Comparison of quantitative variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>VATS</th>
<th>Chest tube</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>40±17.8</td>
<td>41±18.2</td>
<td>0.452</td>
</tr>
<tr>
<td>Length of hospital stay, days</td>
<td>6.8±2.3</td>
<td>9.8±4.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Patient satisfaction level, scores</td>
<td>8.4±3.3</td>
<td>6.7±2.4</td>
<td>0.031</td>
</tr>
</tbody>
</table>

Variables are reported as means ± standard deviation.

Table 2. Comparison of qualitative variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>VATS</th>
<th>Chest tube</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>5</td>
<td>5</td>
<td>0.365</td>
</tr>
<tr>
<td>Complete cure sensu radiography results on postoperative day 7</td>
<td>26</td>
<td>19</td>
<td>0.004</td>
</tr>
<tr>
<td>Discharge with chest tube</td>
<td>1</td>
<td>8</td>
<td>0.001</td>
</tr>
<tr>
<td>Need for secondary intervention</td>
<td>3</td>
<td>9</td>
<td>0.001</td>
</tr>
<tr>
<td>Length of hospital stay &gt; 10 days</td>
<td>2</td>
<td>8</td>
<td>0.002</td>
</tr>
<tr>
<td>Readmission 3 months after discharge (recurrence)</td>
<td>0</td>
<td>5</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Statistical analysis

Considering the type I error of 5%, power of 80%, and standard deviation (SD) of 1.7, according to previous studies, the sample size of 60 was identified, divided into two subgroups of 30 patients in each. For analyses of quantitative and qualitative variables, we used mean ± SD and frequency, respectively. Data was statistically analyzed by SPSS software, version 19. Then, the one-sample Kolmogorov–Smirnov test confirmed the normal distribution of data, and the independent samples t-test was performed. We also used chi-squared test to compare the qualitative ratios. The statistical significance was considered at the values of p<0.05.

Results

We recruited 60 patients diagnosed with empyema and divided them into two groups, 30 patients in each. Group I included patients treated by chest tube, while Group II subjected to VATS. Quantitative data (including age, patient satisfaction level, and length of hospital stay) were compared between two groups. There was no statistically significant difference between groups in mean age (p=0.452), but the difference in the patient satisfaction level was reported as statistically significant in Group II (p=0.001). In addition, results showed a significant reduction in length of hospital stay in Group II vs. Group I (p=0.001) (Table 1).

Qualitative ratios included radiographic outcomes on postoperative day 7, discharge with or without chest tube, need for second intervention, and condition of a patient during 3 months after therapy. The ratios were statistically compared. Both groups were similar in terms of sex ratios.

Based on the radiographic findings 7 days after the intervention, patients undergoing VATS had a higher rate of lung expansion, compared with Group I (p=0.004). In Group II, fewer patients had chest tube at discharge time (p<0.001), and the need for second intervention was reported lower than in Group I (p<0.001).

In Group I, 9 patients were hospitalized again to undergo the second intervention for empyema: 2 cases of chest tube placement, 4 cases of thoracotomy, and 3 cases subjected to VATS treatment. Length of hospital stay and need for second admission in those treated with VATS were significantly lower than in chest tube treatment (p=0.002, p=0.001) (Table 2).

Pneumococcus was detected as the most common pathogen of pleural effusion in both groups and among patients who did not need the thoracic surgery. In addition, the similar combination therapy, including Ceftriaxone and Clindamycin, was administrated in both groups.

Discussion

Despite the administration of effective antibiotics, the mortality and morbidity rate of empyema still remains high [11]. Treatment of choice in empyema depends on various factors, including underlying disease, type of pleural effusion and stage of the disease [5], but generally involves two options: surgical and nonsurgical therapy. Nonsurgical and surgical intervention (open thoracotomy decortications or VATS) is considered for managing the first and second stage of the disease, respectively. The third stage and any treatment method failures are managed with open thoracotomy decortication. The appropriate candidate for VATS are patients in multiloculated and early second stage, before the formation of peel, while after the development of peel, the

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optimal therapy is thoracotomy [3]. While VATS is considered an effective and safe treatment of empyema in some studies, other authors described the chest tube as a relevant therapy [12, 13]. Pneumothorax (with an incidence rate of 2-6%), hemothorax (with an incidence rate of 1%), re-expansion pulmonary edema (rare), and organ laceration (rare) are considered main complications of thoracentesis [5]. A review by Rodriguez et al. illustrated that besides possible complications, chest tube is a safe and relevant treatment method of empyema [14]. Hemothorax was defined as one of critical complications of chest tube in the study by Karmy-Jones et al. in 2008 [15]. Some previous reviews also analyzed the efficacy of chest tube and VATS. Cobanoglu et al., in 2011, prospectively evaluated 60 patients with empyema in terms of treatment duration, length of a hospital stay, treatment success, duration of recovery, mortality and morbidity rate. The result revealed that the length of hospital stay and morbidity rate with chest tube drainage was significantly higher than with VATS. Besides, direct observation of lesion in VATS results in accurate diagnosis and expelling the blood clot, preventing the complications, which results in a shortened period of a hospital stay and fewer complications, compared with chest tube [16]. A review article by Zahid et al. also compared the effectiveness of two techniques, concluding that VATS was more effective and faster treatment procedure, compared with chest tube [17]. Another comparison by Scarci et al. indicated that VATS, compared with chest tube, had shorter treatment period and hospital stay, along with fewer procedural complications, second admissions, and repeated operations. There were not statistically significant differences in the duration of antibiotic therapy, treatment cost, admission and imaging examination between two groups [18]. An analysis by Chambers et al. also confirmed the superior outcomes of VATS via reduced duration of chest tube drainage, hospital stay (both postoperative stay and total number of hospital days), postoperative pain and complications such as air leak, sepsis, atelectasis and 30-day mortality. The need for surgery depends on the stage of empyema, but generally, in VATS group, it is lower than in chest tube group [19].

Conclusion
According to the results of this study, reduced hospital stay in VATS group, and consequently, duration of chest tube drainage and time to return to work were less in these patients, which can be evaluated statistically in further assessments. Additionally, to our knowledge, this was the first study analyzing the patient satisfaction level, clinical condition at discharge time, which were remarkably improved in those treated with VATS. Due to the accurate diagnosis in VATS, a lower rate of recurrence (readmission) and need for second intervention was detected. Concurrent with previous studies, results of our research highlighted the VATS as a technique associated with fewer complications and favorable outcome in treatment of empyema patients. Although all related studies revealed a better outcome of VATS [20, 21], further studies are needed to introduce the VATS as an optimal treatment into the guidelines. Our study provided an essential benchmark to design further investigations to define the first-line therapy in empyema.

Limitations
There are some advantages of this study, such as assessing patient satisfaction level and accurate data collection. Nonetheless, relatively small sample sizes limited the extrapolation of the results of this research. Further studies with larger sample sizes are required to introduce the VATS as an optimal treatment option for empyema.

Conflict of interest
No potential conflict of interest was reported by any of the authors.

Ethical approval
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee of Shahid Beheshti University of Medical Sciences and with the 1964 Declaration of Helsinki.

References


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