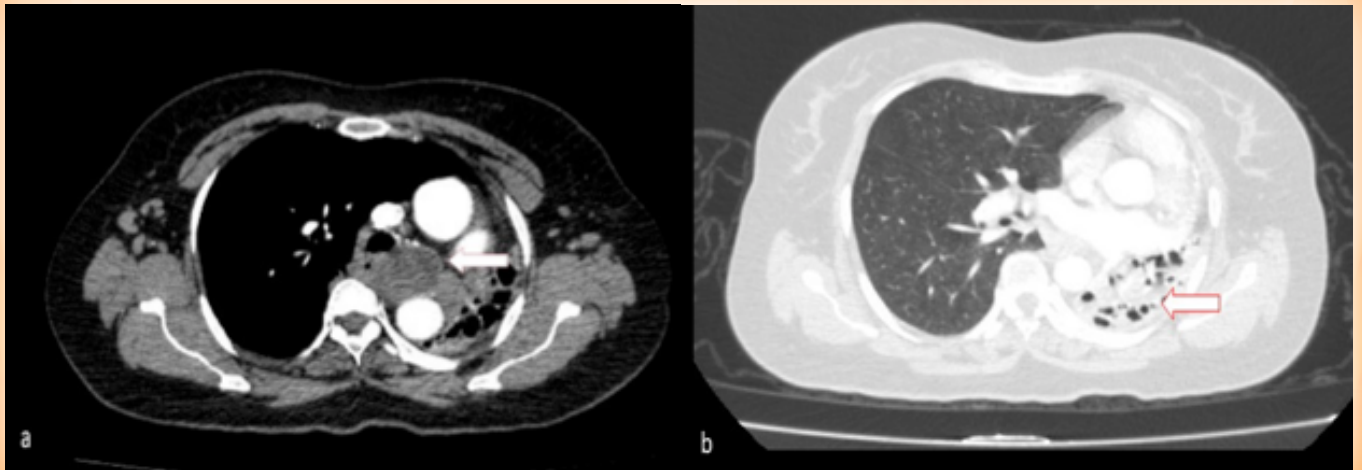


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Official e-Publication of:

Turkish Society of Thoracic Surgery (TSTS)

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To cite this article: Çelik B, Pirzirenli MG, Bilgin Büyükkarabacak Y, Yılmaz V, Gürz S, Taslak Şengül A, Başoğlu A. Clinical and radiological characteristics of patients treated with the diagnosis of spontaneous pneumomediastinum. Curr Thorac Surg 2021 Jan 15; 6(1): 1-6.

Original Article

Clinical and radiological characteristics of patients treated with the diagnosis of spontaneous pneumomediastinum

 Burçin Çelik*,  Mehmet Gökhan Pirzirenli,  Yasemin Bilgin Büyükkarabacak,  Volkan Yılmaz,  Selçuk Gürz,  Ayşen Taslak Şengül,  Ahmet Başoğlu

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ABSTRACT

Background: Pneumomediastinum is defined as the presence of air in the mediastinal region. It is associated with events or diseases leading to a sudden increase in alveolar pressure. The air in the mediastinum may originate in the pharynx, the tracheobronchial tree or the esophagus. This study aimed to assess the clinical and radiological characteristics of patients who were diagnosed with spontaneous pneumomediastinum and received treatment at our clinic.

Materials and Methods: A total of 23 patients who had spontaneous pneumomediastinum and were treated at our clinic between 2007 and 2019 were retrospectively assessed for their age, etiological factors, clinical and radiological characteristics; treatment and outcomes. Chest radiography and computed tomography of the thorax were used for diagnosis in all patients.

Results: Of the patients, 15 were males and eight females and their mean age was 33.91 (15-82) years. The most common symptom on admission was shortness of breath (n = 12) and chest pain (n = 11). The etiological factors were excessive vomiting in six patients and excessive cough in five. Radiologically, the most common findings besides pneumomediastinum were subcutaneous emphysema (n = 6) and pneumothorax (n = 4). Of the patients, seven required esophagoscopy, four required bronchoscopy and no pathology was observed. All patients were fully recovered when they were discharged.

Conclusions: The underlying etiological factor is crucial in pneumomediastinum. Conservative treatment methods are often sufficient in spontaneous pneumomediastinum patients with no pathology in endoscopic evaluation.

Keywords: pneumomediastinum, radiology, spontaneous, conservative treatment

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Doi: 10.26663/cts.2021.0001

Received 13.05.2020 accepted 30.09.2020

Presented as a poster presentation at the 7th National Congress of Lung Cancer (24-27 November 2016, Antalya).

Introduction

Pneumomediastinum (mediastinal emphysema) is defined as the presence of air in the mediastinum observed on chest radiography or computed tomography (CT) of the thorax. Spontaneous pneumomediastinum (SPM), a very rare clinical condition, is defined as nontraumatic pneumomediastinum without surgical or endoscopic interventions, thoracic trauma or mechanical ventilation support [1-3]. SPM was first reported by Hamman in 1939, with an incidence range from 1:7000 to 1:45000 in all hospital admissions [4-6].

In many patients, pneumomediastinum is associated with events or diseases causing a sudden increase in the alveolar pressure. It causes alveolar rupture through an increase in alveolar pressure and bronchial obstruction of the check-valve type. Due to this alveolar rupture, the air in the lung parenchyma proceeds towards the interstitial region around the vessel and the bronchus, then towards the lung hilus and the mediastinum. The air goes through the mediastinum, anterior chest wall and between the large vessels in the neck, which leads to subcutaneous emphysema. It may also go inside the visceral pleura through the peribronchial and vascular structures and cause pneumothorax if the visceral pleura is ruptured [2,3].

Many factors are involved in the etiology of spontaneous pneumomediastinum. Deep breathing maneuvers such as forced vital capacity or excessive exercise, Valsalva maneuvers such as giving birth or weight-lifting, closed chest trauma, especially in patients with obstructive pulmonary disease and who receive positive end-expiratory pressure therapy and the sudden atmospheric pressure drops such as in a rapid descent by a diver or pilot are among the known etiological causes. Of the cases, 30% present with no etiological cause [5-7].

In this study, we aimed to retrospectively assess the clinical and radiological characteristics of patients who had spontaneous pneumomediastinum and were treated at our clinic.

Materials and Methods

Twenty-three patients treated with the diagnosis of SPM in our clinic between the years 2007-2019 were assessed retrospectively. The patients were evaluated according to their age, gender, etiological factors, smoking habits, clinical and radiological characteristics and treatment outcomes. After the diagnosis of SPM, oral intake was

discontinued for 24 hours, and nasal oxygen therapy, bed rest, prophylactic antibiotics (cefazolin sodium 1000 mg, 2x1 iv.) and pain relief treatment (diclofenac 75 mg/3 mL, im.) were provided when necessary. Oral intake was re-initiated and prophylactic antibiotics were discontinued in patients with no pathology (pneumothorax, pleural fluid, mediastinal enlargement and parenchymal infiltration) in their chest radiography at the 24th and 48th hours of hospitalization and with normal laboratory values (Hb, Hct and leukocyte). Patients with normal radiological and clinical findings were discharged on the following day. The study was approved by the institutional review board (No: 2020/654) and conducted in accordance with the principles of the Declaration of Helsinki.

Results

Of the 23 patients diagnosed with spontaneous pneumomediastinum, 15 were males and eight females. Their mean age was 33.91 (15-82) years. Symptoms on admission were shortness of breath in 12 patients, chest pain in 11, difficulty swallowing in five and swelling in the neck and face in five. Of them, 10 had accompanying diseases (COPD in five, malignancy in three) and 14 (61%) had a history of smoking (Table 1).

Considering the underlying etiologies of our patients, six (26%) had excessive retching or vomiting and five (21%) had an excessive cough. All cases underwent CT of the thorax and six of them had subcutaneous emphysema, four had pneumothorax and three had neck emphysema. The CT findings of two patients raised suspicion of esophageal rupture, but no rupture was detected in rigid esophagoscopy for diagnostic purposes.

Esophagoscopy was performed as an invasive procedure in seven patients, especially in four of them with excessive vomiting, and bronchoscopy was done in four. No esophageal or bronchial injury was detected in any of these endoscopic interventions. Two patients required VATS wedge resection for treatment purposes. All the cases had SPM and all were fully recovered when they were discharged. Morbidity was observed in two cases, one due to pneumonia caused by excessive vomiting and one due to prolonged air leakage following VATS bullous wedge resection. Mean duration of hospitalization was 4.43 (2-14) days and no problems were observed in any of our patients in their outpatient follow-ups. Figure 1 shows the algorithm for the diagnosis and treatment of spontaneous pneumomediastinum, created in accordance with our results.

Table 1. Clinical and radiological characteristics of the patients.

	Age/ Sex	Symptom	Accompanying diseases	Etiological factors	Smoke (p/y)	Radiological features	Invasive procedure	Hospital stay (day)
1	73/M	Chest pain, shortness of breath	Emphysema	Bullea	30	Pneumomediastinum + right pneumothorax	VATS wedge resection	7
2	28/F	Swelling of the face	Pregnancy	-	-	Pneumomediastinum + left pneumothorax	-	2
3	21/M	Chest and left arm pain	-	-	-	Pneumomediastinum + air density in the neck	-	5
4	35/F	Shortness of breath	Hypothyroidism	-	-	Pneumomediastinum + air density in the neck	-	5
5	16/M	Chest pain	-	Excessive alcohol intake and vomiting	5	Pneumomediastinum + subcutaneous emphysema	Rigid esophagoscopy	3
6	64/M	Shortness of breath	Tuberculosis	Bullea	30	Pneumomediastinum + right pneumothorax + bilateral apical bullea	-	5
7	33/F	Difficulty swallowing chest pain	-	Esophageal stenosis, pneumonia	-	Pneumomediastinum + air density around the esophagus + pneumonia in the right lower lobe	Rigid esophagoscopy	4
8	23/M	Retching	-	Excessive vomiting	5	Pneumomediastinum + subcutaneous emphysema	Rigid esophagoscopy + rigid bronchoscopy	5
9	54/M	Shortness of breath	Renal cell ca	-	-	Pneumomediastinum + subcutaneous emphysema	-	3
10	82/M	Chest pain, shortness of breath	Asthma	Bullea	40	Pneumomediastinum + subcutaneous emphysema + right apical bullea	VATS wedge resection	14
11	71/F	Swelling in the neck	Lung cancer COPD	Bullea	45	Pneumomediastinum + subcutaneous emphysema + left apical bullea	-	3
12	15/M	Chest pain, difficulty swallowing	-	-	-	Pneumomediastinum	-	2
13	22/M	Shortness of breath, difficulty swallowing	-	Excessive vomiting	3	Pneumomediastinum + subcutaneous emphysema	-	3
14	27/F	Shortness of breath, cough	Pregnancy	Bullea	4	Pneumomediastinum + right apical bullea	-	2
15	18/M	Shortness of breath, difficulty swallowing	-	-	5	Pneumomediastinum	-	2
16	19/F	Chest pain, shortness of breath	-	Excessive cough	4	Pneumomediastinum + esophageal rupture?	-	3
17	18/F	Chest pain, syncope	Mental retardation	Excessive vomiting, retching	3	Pneumomediastinum + bilateral pneumothorax	Rigid esophagoscopy	13
18	31/M	Cough, chest pain	Testicular cancer	Excessive cough	-	Pneumomediastinum + left pleural thickening + pneumonia in the left lower lobe	-	6
19	41/F	Shortness of breath, swelling in the neck	Migraine, depression	Excessive cough	-	Pneumomediastinum	Flexible bronchoscopy	4
20	27/M	Chest pain	-	-	5	Pneumomediastinum + widespread air density around the esophagus	Rigid esophagoscopy	3
21	18/M	Swelling in the neck and chest	Asthma, septoplasty	Cough, retching	-	Pneumomediastinum	Rigid esophagoscopy	3
22	19/M	Chest pain, shortness of breath	-	-	5	Pneumomediastinum	-	2
23	25/M	Shortness of breath, swelling in the neck, difficulty swallowing	-	Cough, vomiting	10	Pneumomediastinum	Rigid esophagoscopy + rigid bronchoscopy	3

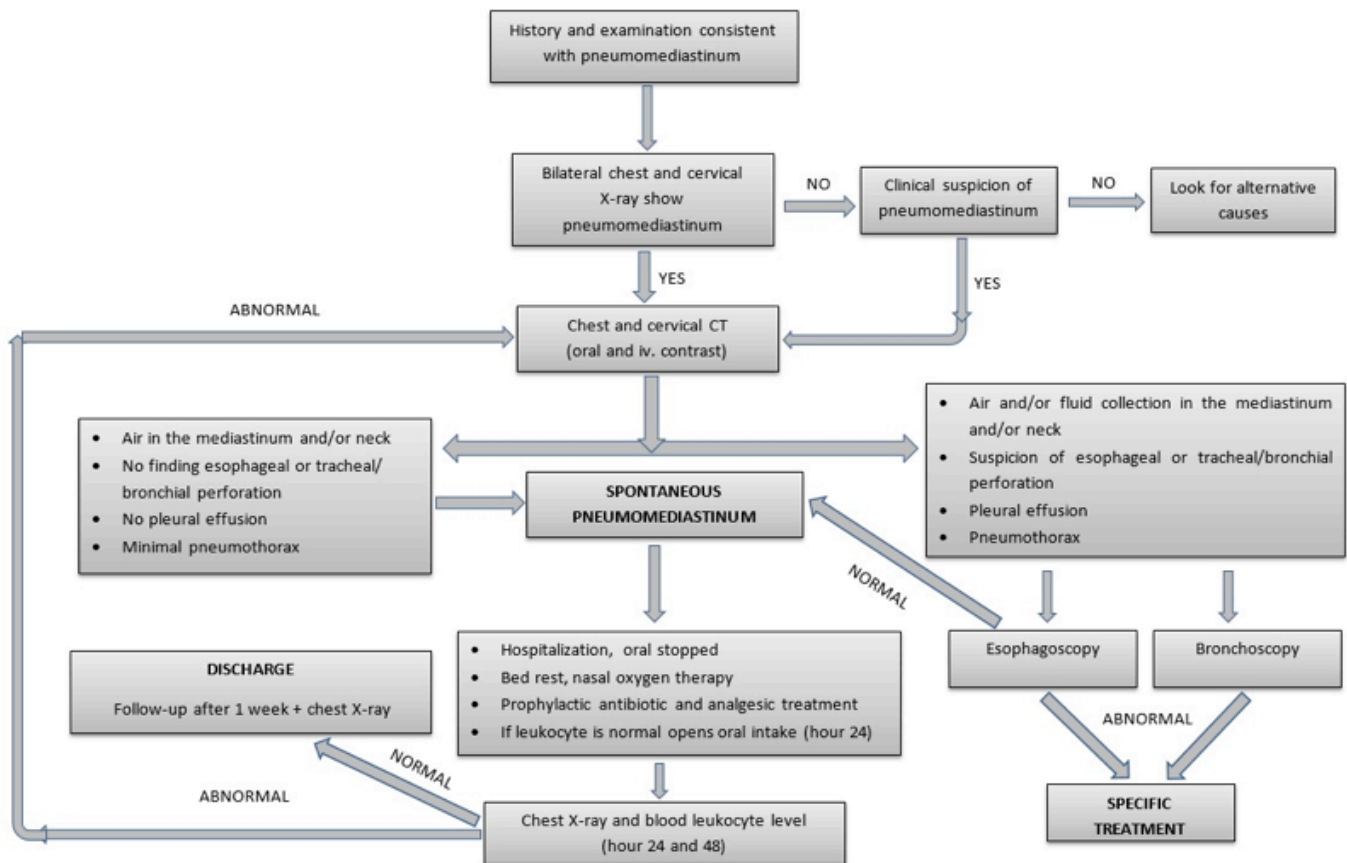


Figure 1. Algorithm for management of spontaneous pneumomediastinum.

Discussion

Spontaneous pneumomediastinum is a rare clinical condition, which is often observed in tall young men and usually heals spontaneously. Bronchial asthma is the most common etiological factor accompanying SPM (also known as nontraumatic pneumomediastinum) [8]. Pneumomediastinum has an incidence of 1:7000 to 1:45000 per year among all hospital admissions in adults and of 2.5/1000 per year in all live births [4-6]. SPM was detected in 23 (0.48%) of nearly 4710 patients consulted to our clinic in the emergency department during the study period.

Spontaneous pneumomediastinum develops after physical activities that increase intrathoracic pressure such as excessive cough, intense exercise, Valsalva maneuvers; an excessive strain of the esophagus and vaginal delivery. Moreover, barotrauma, the snorting of cocaine and other drugs can increase alveolar and intrabronchial pressure and lead to pneumomediastinum and subcutaneous emphysema. There have also been rare cases reported in the literature including pulmonary function testing, playing wind instruments, inflat-

ing balloons and convulsion [1-3]. A severe cough in children caused by pertussis, diphtheria, bronchiolitis or acute bronchitis can also cause pneumomediastinum [9,10]. Mihos et al. reported some causes of pneumomediastinum to be doing sports, scuba diving and playing basketball and football [11]. Of the cases, 39% to 100% present with a precipitating factor [3,8]. In accordance with the literature, 65% our patients had an underlying precipitating factor and the most common of them were vomiting and excessive cough.

Of the SPM cases, 32% are active smokers and 14% to 18% have bronchial asthma or emphysema [3,7,8]. We found that 60.8% of our patients were active smokers and 22% had bronchial asthma or emphysema as an accompanying disease.

In pneumomediastinum, if the mediastinum pressure rises suddenly or decompression fails to be sufficient, the mediastinal pleura ruptures and causes pneumothorax which can be observed in around 10-18% of the SPM cases [2,3]. The tension pneumomediastinum is the more severe clinical form of pneumomediastinum which mimics cardiac tamponade [7]. Pneumothorax

was detected in four (17.4%) of our patients, while none had tension pneumomediastinum. None of the patients diagnosed with pneumothorax required tube thoracotomy and all the patients were recovered by nasal oxygen therapy.

The clinical presentation involves sudden chest pain accompanying shortness of breath, cyanosis, fullness in the neck veins; feeling of something being stuck in the throat, dysphagia, dysphonia and neck and subcutaneous emphysema. The signs and symptoms depend largely on the amount of air in the mediastinal space and the presence of a concomitant infection [1,7]. In the clinic, localized retrosternal chest pain is the most common symptom. The pain starts suddenly and increases with deep breaths and coughs [3]. In our patients, the most common symptoms were shortness of breath at 52% and chest pain at 48%, followed by difficult swallowing. In fact, the amount of air in the mediastinum is the only cause of all these findings and the symptoms of a rupture of the mediastinal pleura due to the amount of air in the mediastinum determine the patient's clinic.

Physical examination often indicates the presence of air in the subcutaneous tissues in the neck and chest wall [7,8]. The typical physical finding of SPM is a cracking sound (Hamman's Sign) at auscultation in the anterior chest, synchronous with peak heart rate. Hamman's Sign is a typical finding for physical examination, although it's detected only in 10-20% of the patients [1-3]. The most common finding of physical examination was subcutaneous and neck emphysema in our patients and Hamman's Sign was detected in none.

PA chest radiography and thorax CT have an important role in the diagnosis of SPM. On PA chest radiography, accumulation of air may be detected surrounding the mediastinal pleura, esophagus or the main bronchi. Thorax CT is the most sensitive method to diagnose pneumomediastinum and should be preferred, particularly in cases with no determined underlying etiological factor. Observing an air density in the mediastinum on thorax CT confirms the diagnosis [7,8,12]. We use thorax CT in the radiological diagnosis of SPM at our clinic and demand a CT with oral and intravenous contrast if there is suspicion of esophageal perforation in the patient's history. The most common radiological findings on thorax CT were subcutaneous or neck emphysema and pneumothorax in our patients. Two of them were suspected for esophageal perforation on radiology,

however, no pathology was observed in the procedure for endoscopic diagnosis.

The differential diagnosis of spontaneous pneumomediastinum includes acute coronary syndrome, pericarditis, pneumothorax; pulmonary embolism, tracheobronchial rupture and Boerhaave Syndrome [1-3]. Following the diagnosis of pneumomediastinum, bronchoscopy and esophagoscopy should be performed if the patient is suspected for rupture of the airways or the esophagus. The patient's clinic and thorax CT findings are key in guiding the endoscopy decision. Esophagoscopy was performed in seven of our patients and bronchoscopy in four and no pathology was detected.

The treatment approach should mostly be conservative (bed rest, pain relief, prophylactic antibiotics and nasal oxygen therapy) if there is no injury in the main bronchus or the esophagus in the treatment of pneumomediastinum and no large source of air leakage can be detected from lung tissue (such as bulla or bleb). Nasal oxygen support and bed rest are the most important elements in treatment and antibiotics are recommended for mediastinitis prophylaxis [2,3].

The aim is to make sure not to overlook a serious underlying cause leading to this condition in the management of pneumomediastinum. These patients should be followed-up for at least 24-36 hours. This clinical condition often regresses spontaneously within 48 hours. Oral administration is initiated and the patients are discharged with follow-up including chest radiography and complete blood count. Mihos et al. reported a mean hospital stay of 3.8 days in their 25 cases with pneumomediastinum due to sports injuries [11]. Our patients had a mean follow-up period of 4.4 days. The recurrence rate of untreated spontaneous pneumomediastinum is quite rare. Abolnik et al. reported recurrence in two of 25 patients over a two-year period [13]. We observed no recurrence in our patients.

SPM is often a benign and restricting clinical condition with no mortality. Mortality rates reach up to 40% in secondary pneumomediastinum while this rate is 0% in spontaneous pneumomediastinum [7,8]. Morbidity was observed in two patients, however, mortality was observed in none in our series.

To conclude, spontaneous pneumomediastinum is a benign clinical condition which needs to be followed-up by conservative treatment methods. If an injury of

the airways or esophagus is considered in the etiology, endoscopic intervention with cause-based treatment should be performed. Although it is rarely observed in healthy adolescents and young adults, spontaneous pneumomediastinum should be considered in the differential diagnosis when sudden chest pain and shortness of breath are present.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

Ethics approval

The study was approved by the Ethics Committee of Ondokuz Mayıs University (No: 2020/654).

Authors' contributions

BC; Conceived and designed the analysis, collected the data, contributed data/analysis tools, performed the analysis, co-wrote the paper MGP; Conceived and designed the analysis, performed the analysis, VY; Collected the data, SG; Collected the data, co-wrote the paper, YBB; Contributed data/analysis tools, ATŞ, AB; co-wrote the paper.

References

1. Takada K, Matsumoto S, Hiramatsu T, Kojima E, Shizu M, Okachi S et al. Spontaneous pneumomediastinum: an algorithm for diagnosis and management. *Ther Adv Respir Dis* 2009; 3: 301-7.
2. Kim KS, Jeon HW, Moon Y, Kim YD, Ahn MI, Park JK et al. Clinical experience of spontaneous pneumomediastinum: diagnosis and treatment. *J Thorac Dis* 2015; 7: 1817-24.
3. Sahni S, Verma S, Grullon J, Esquire A, Patel P, Talwar A. Spontaneous pneumomediastinum: time for consensus. *N Am J Med Sci* 2013; 5: 460-4.
4. Hamman L. Spontaneous mediastinal emphysema. *Bull Johns Hopkins Hosp* 1939; 64: 1-21.
5. Macia I, Moya J, Ramos R, Morera R, Escobar I, Saumench J et al. Spontaneous pneumomediastinum: 41 cases. *Eur J Cardiothorac Surg* 2007; 31: 1110-4.
6. Iyer VN, Joshi AY, Ryu JH. Spontaneous pneumomediastinum: analysis of 62 consecutive adult patients. *Mayo Clin Proc* 2009; 84: 417-21.
7. Caceres M, Ali SZ, Braud R, Weiman D, Garrett HE. Spontaneous pneumomediastinum: a comparative study and review of the literature. *Ann Thorac Surg* 2008; 86: 962-6.
8. Dajer-Fadel WL, Arguero-Sanchez R, Ibarra-Perez C, Navarro-Reynoso FP. Systematic review of spontaneous pneumomediastinum: A survey of 22 years' data. *Asian Cardiovasc Thorac Ann* 2014; 22: 997-1002.
9. Gasser CR, Pellaton R, Rochat CP. Pediatric Spontaneous Pneumomediastinum: Narrative Literature Review. *Pediatr Emerg Care* 2017; 33: 370-4.
10. Chalumeau M, Le Clainche L, Sayeg N, Sannier N, Michel JL, Marianowski R et al. Spontaneous pneumomediastinum in children. *Pediatr Pulmonol* 2001; 31: 67-75.
11. Mihos P, Potaris K, Gakidis I, Mazaris E, Sarraes E, Kontos Z. Sports-related spontaneous pneumomediastinum. *Ann Thorac Surg* 2004; 78: 983-6.
12. Zylak CM, Standen JR, Barnes GR, Zylak CJ. Pneumomediastinum revisited. *Radiographics* 2000; 20: 1043-57.
13. Abolnik I, Lossos IS, Breuer R. Spontaneous pneumomediastinum. A report of 25 cases. *Chest* 1991; 100: 93-5.

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To cite this article: Aker C, Sezen CB, Ceritoglu A, Dogru MV, Aksoy Y, Kalafat CE, Erdogan V, Cansever L, Metin M. Prognostic value of Glasgow Prognostic Score in patients with non-small cell lung cancers undergoing pN2 pneumonectomy. Curr Thorac Surg 2021 Jan 15; 6(1): 7-13.

Original Article

Prognostic value of Glasgow Prognostic Score in patients with non-small cell lung cancers undergoing pN2 pneumonectomy

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ABSTRACT

Background: The aim of this study was to assess the relationship between Glasgow Prognosis Score (GPS) and survival in patients who underwent pneumonectomy due to pN2 non-small cell lung cancer (NSCLC).

Materials and Methods: A total of 45 patients who were determined to have pN2 disease after pneumonectomy between 2007 and 2016 were retrospectively analyzed. The patients were assigned a GPS between 0 and 2 as follows: elevated CRP level (>1.0 mg/dL) and hypoalbuminemia (<35 mg/dL) was classified as GPS 2, elevated CRP but albumin >35 mg/dL was classified as GPS 1, and CRP <1.0 mg/dL and albumin >35 mg/dL were classified as GPS 0.

Results: Of the 45 patients included in the study, 42 (93.3%) were male and 3 (6.7%) were female. Eighteen (40%) of the patients had adenocarcinoma and 27 (60%) had squamous cell carcinoma. Skip pN2 (pN0N2) was detected in 10 patients. Mean follow-up time was 28 months. The 5-year survival rate was 40.2%. The main prognostic factors associated with survival were GPS and adjuvant therapy ($p = 0.023$, $p = 0.001$).

Conclusions: In this study, there was no relationship between N1 status and survival in pneumonectomy patients with pN2 NSCLC, whereas GPS score and adjuvant therapy were found to be prognostically significant in terms of survival.

Keywords: lung carcinoma, pneumonectomy, Glasgow Prognostic Score, survival, prognosis, prognostic scores

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Doi: 10.26663/cts.2021.0002

Received 13.06.2020 accepted 14.07.2020

Introduction

Lung cancers are currently the leading cause of cancer-related deaths. Early detection of non-small cell lung cancer (NSCLC) is crucial for the success of surgical treatment [1]. Pathologic N2 (pN2) status is a negative prognostic factor in NSCLC. In the literature, the 5-year survival rate for patients with N2 disease varies from 20 to 35%. The International Association for the Study of Lung Cancer (IASLC) argues that N2 disease must be evaluated together with N1 lymph nodes and that N1 disease also impacts survival [2]. Another important factor affecting cancer prognosis is inflammation [3]. Inflammation-based prognostic scoring systems are used to determine the prognosis of cancer patients. The Glasgow Prognostic Score (GPS) is a scoring system that enables the prediction of tumor behavior and patient prognosis based on albumin and C-reactive protein (CRP) levels [3]. There are few studies in the literature related to GPS and survival outcomes in NSCLC. Previous studies showed that GPS was the most important prognostic factor for survival in adenocarcinoma patients [4]. However, there are no published studies on the relationship between GPS and survival in N2 disease.

The aim of the present study was to investigate the factors affecting survival in pneumonectomy patients found to have N2 disease and to evaluate the relationship between GPS and survival in NSCLC.

Materials and Methods

The study was approved by the institutional review board (No:20189/1525) and conducted in accordance with the principles of the Declaration of Helsinki. We retrospectively evaluated the records of patients who underwent pneumonectomy in our hospital between June 2007 and December 2016 due to NSCLC and were determined to have pN2 disease. A total of 3370 patients with NSCLC underwent surgery during the study period, 395 of whom had pneumonectomy. Patients who received neoadjuvant therapy and those who were lost to follow-up were excluded. As a result, a total of 45 pN2 (8.8%) patients who underwent pneumonectomy were included in the study. The study flow chart is shown in Figure 1.

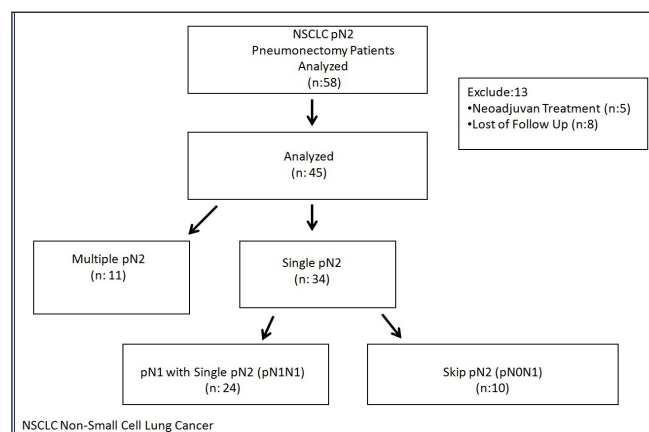


Figure 1. Study flow chart.

Patients found to have single station pN2 were divided into two groups:

- Patients with single station pN2 skip metastasis (pN0N2)
- Patients with single pN1 and single pN2 involvement (pN1N2)

Preoperative Assessment

All patients underwent thoracic computed tomography (CT), positron emission tomography (PET-CT), and cranial magnetic resonance imaging (MRI) during preoperative assessment. Respiratory function tests and electrocardiogram were performed to evaluate pulmonary and cardiac reserve. Carbon monoxide diffusion test and lung perfusion scintigraphy were also done for patients with forced expiratory volume in the first second (FEV1) less than or equal to 40% of the predicted value. Patients with a history of cardiac disease and those aged 60 years or older were evaluated with echocardiogram by a cardiologist. In addition, all patients were examined preoperatively by fiberoptic bronchoscopy. Invasive mediastinal staging was performed by EBUS or mediastinoscopy in all patients with findings of pathological mediastinal lymph node in radiological imaging. The IASLC 2009 lymph node map was used for mediastinal lymph node classification [5].

GPS was determined based on serum CRP and albumin levels before and after surgical treatment. Patients with both high CRP (>1.0 mg/dL) and low albumin (<35 mg/dL) were classified as GPS 2, patients with high CRP but albumin >35 mg/dL were classified as GPS 1, and patients with CRP <1.0 mg/dL and albumin >35 mg/dL were classified as GPS 0.

Postoperative Follow-up

Early mortality was defined as deaths that occurred in hospital or within the first postoperative month. Follow-up information was obtained from all patients through office visits or telephone interviews either with the patient, a relative, or their primary physicians. The patients were followed up by oncologists with thoracic CT and physical examination every 3 months for the first 2 years, every 6 months between 2 and 5 years, and once a year thereafter.

Statistical Analysis

The differences in proportions between groups were compared by using Chi-Square test. Difference between two groups for continuous variables was evaluated by Student's test. Mann-Whitney U test was used to test the difference between two groups in terms of ordinal or non-normally distributed continuous variables. Survival analysis was conducted using the Kaplan–Meier method and curves were compared using the log-rank test. The level of statistical significance was accepted as $p < 0.05$ for all analyses.

Results

Of the 45 patients included in the study, 42 (93.3%) were male, 3 (6.7%) were female, and the mean age was 59.4 ± 7.14 years (47-84 years). The patients had a mean smoking history of 35.9 ± 17.8 pack-years. Preoperative CRP and albumin levels were 35.07 ± 44.3 mg/dL and 3.92 ± 0.52 g/dL, respectively. Thirteen patients (28.9%) underwent right-side resection and 32 patients (71.1%) underwent left-side resection. The mean tumor diameter was 5.55 ± 3.21 cm and the mean bronchial resection margin was 2.55 ± 1.98 cm. Eighteen patients (40%) had adenocarcinoma and 27 (60%) had squamous cell carcinoma. Twenty-seven patients (60%) had stage 3A disease and 18 (40%) were stage 3B. The mean number of resected lymph nodes was 19.4 ± 8.26 (8-47). Skip pN2 (pN0N2) was detected in 10 patients. Tumor diameter was significantly larger in patients with GPS 1-2 compared to those with GPS 0 ($p = 0.009$). There were no statistical differences in GPS according to demographic and histopathological characteristics of the patients (Table 1).

Table 1. Comparison of demographic and clinical characteristics of the patients.

Variables		GPS 0		GPS 1-2		p-value
		(n)	(%)	(n)	(%)	
Gender	Male	17	94.4	25	92.6	0.807
	Female	1	5.6	2	7.4	
Age (years)		57.9 ± 6.18		60.5 ± 7.6		0.390
Age (years)	<65	15	83.3	18	66.7	0.215
	>65	3	16.7	9	33.3	
Smoking (pack-years)		32.6 ± 19.3		38.2 ± 16.7		0.237
FEV1 (%)		75.5 ± 16.2		76.8 ± 15.6		0.835
FEV1 (L)		2.24 ± 0.52		2.26 ± 0.55		0.826
Side of Resection	Right	14	77.8	18	66.7	0.420
	Left	4	22.2	9	33.3	
Resection	Standard	15	83.3	22	81.5	0.874
	Extended	3	16.7	5	18.5	
Tumor diameter (cm)		4.05 ± 1.25		6.55 ± 3.71		0.009
Stage	3A	15	83.3	12	44.4	0.009
	3B	3	16.7	15	55.6	
Histopathology	AdenoCa	9	50	9	33.3	0.264
	SqCC	9	50	18	66.7	
pN2	Single	14	77.8	20	74.1	0.777
	Multiple	4	22.2	7	25.9	
Adjuvant treatment	No	1	5.6	7	28	0.111
	Yes	17	94.4	18	72	

Abbrev.: AdenoCA; Adenocarcinoma, SqCC; Squamous Cell Carcinoma, GPS; Glasgow Prognostic Score

Table 2. Factors associated with survival in pN2 NSCLC patients after pneumonectomy.

Variables		2-Year Survival (%)	5-Year Survival (%)	Median Survival (Months)	95% CI	p value
Gender	Male	57.1	39	42	28-57	0.641
	Female	66.7	---	31	7-54	
Histopathology	AdenoCa	55.6	34.7	28	9-46	0.805
	SqCC	59.3	43.3	32	10-53	
N status	pN0N2	60	36	31	16-45	0.673
	pN2	57.1	41	32	2-61	
Single station pN2	pN0N2	60	36	31	16-45	0.651
	pN1N2	54.2	44.3	28	0-64	
Stage	3A	55.6	38.5	28	9-46	0.783
	3B	61.1	41.9	33	15-50	
GPS	0	76.5	62.6	62	30-93	0.023
		46.4	27.1	11	0-26	
Single station pN2	Aorticopulmonary (5-6)	45.5	34.1	22	2-41	0.736
	Inferior mediastinal (7-8-9)	65	47.7	42	9-74	
	Superior mediastinal (2-3-4)	33.3	---	17	0-42	
Adjuvant treatment	No	0	0	2	2-5	0.001
	Yes	74.3	51.7	62	27-96	

Abbrev.: GPS; Glasgow Prognostic Score, AdenoCa; Adenocarcinoma, SqCC; Squamous Cell Carcinoma

Two patients died within the first postoperative month. No statistically significant association was detected between GPS and early mortality ($p = 0.509$). Eight patients (17.8%) did not receive adjuvant therapy postoperatively due to unstable general condition or refusal of medical treatment.

Mean follow-up time was 28 ± 24.76 months. The 5-year survival rate was 40.2% (median 32 months). The main prognostic factors associated with survival were found to be GPS and adjuvant therapy ($p = 0.023$, $p = 0.001$). Prognostic factors associated with survival are shown in Table 2 (Figure 2).

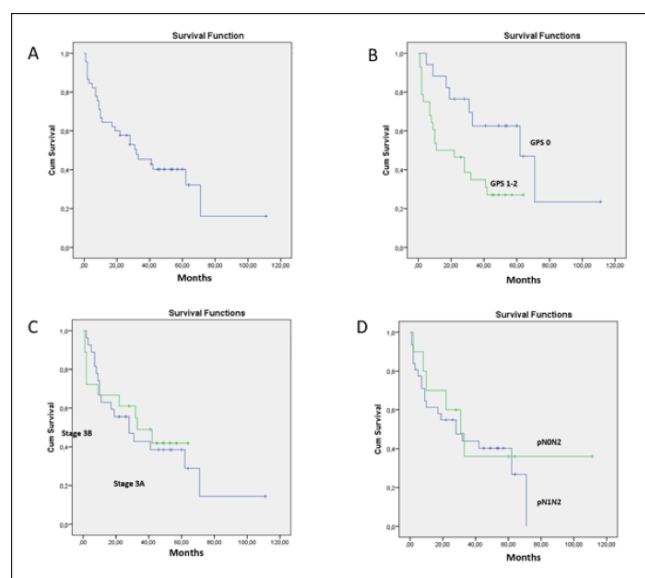


Figure 2. (A) Kaplan–Meier survival curves for overall survival, (B) according to GPS value, (C) Cancer stage, (D) pN2 status.

Discussion

Inflammation in the tumor microenvironment is thought to significantly impact tumor proliferation, angiogenesis, invasion, metastasis, and survival in NSCLC. Systemic inflammatory markers are used to predict prognosis [6]. CRP is a nonspecific inflammatory acute phase protein, and elevated serum CRP levels are observed to adversely affect prognosis [7]. Chronic inflammation may lead to DNA damage, increased cell proliferation, and the development of cancer [8]. CRP is secreted by hepatocytes and is a marker of local inflammation [9]. Albumin is an indicator of nutritional status in cancer patients, and malnutrition has been associated with low survival [10]. In recent years, the GPS has been used to predict cancer behavior and prognosis in patients with colorectal carcinoma in particular. While there are publications before 2015 on the correlation between GPS and pancreatic cancer, hepatocellular carcinoma, trauma, and intensive care unit admission, the number of publications on GPS in NSCLC are limited [4,11,12].

In our study, we found that low GPS was among the factors associated with longer survival in pN2 patients who underwent pneumonectomy. The 5-year survival rate was 62.6% for GPS 0 patients versus 27.1% for patients with GPS 1–2 ($p = 0.023$). In their study on 272 patients with colorectal carcinoma, Nozoe et al. found that survival was significantly worse in GPS 1 patients compared to GPS 0 patients ($p = 0.009$) and in GPS 2 patients compared to GPS 1 patients ($p < 0.0001$). Similarly, survival was significantly worse in modified Glasgow Prognostic Score (mGPS) 1 patients compared to mGPS 0 patients ($p = 0.009$) and in mGPS 2 patients compared to mGPS 1 patients ($p = 0.006$) [13]. In a meta-analysis by Jin et al. [12] evaluating 5369 NSCLC patients treated with surgery and/or chemotherapy, it was found that elevated CRP levels were associated with shorter survival time (HR = 2.058; 95% CI: 1.51–2.80; $p < 0.05$). In the same study, survival rate was lower with GPS ≥ 1 compared to GPS 0 ($p < 0.001$). Minami et al. [14] reported that mGPS was not associated with survival in stage 3B and 4 squamous cell carcinoma patients who received first-line cytotoxic chemotherapy after curative surgery or radiotherapy ($p = 0.61$).

National Comprehensive Cancer Network (NCCN)

guidelines recommend adjuvant chemotherapy for patients determined to have N1 and N2 disease following NSCLC surgery [15]. In their study of patients who received adjuvant therapy after curative resection, Park et al. [16] reported longer disease-free survival after full-dose chemotherapy. In the literature, it can be seen that survival rates are significantly lower among patients who do not receive adjuvant therapy. Speggiari et al. [17] found that the 5-year survival rate in potential N2 patients who received chemotherapy after surgery was 18%, while the survival rate in patients who received chemotherapy alone or chemoradiotherapy alone was 8% ($p = 0.02$). In our study, postoperative adjuvant therapy was associated with higher survival rate after pneumonectomy in pN2 patients when compared with patients who did not receive adjuvant therapy ($p < 0.001$).

Skip N2 is observed in 17.2–42.3% of pN2 NSCLC patients [18]. There is still no clear consensus on whether skip N2 has a better prognosis than non-skip N2 [19,20]. This is primarily due to the heterogeneity of pN2 disease. In our study, patients with pN0N2 disease had better 5-year survival than patients with pN1N2. Although these results are similar to those in the literature, there have been some publications indicating otherwise [21]. Legras et al. [22] reported a 5-year survival rate of 25% in patients with N2 disease. Survival was worse in pure N2 patients who were also pN1 (5-year overall survival rate 21% vs. 34%, HR = 2.09, $p < 0.001$). Similarly, Yazgan et al. [23] also reported much better survival in pure N2 disease compared to pN1N2.

The main limitations of this study are the small patient group and its retrospective design. Furthermore, although it was a single-center study, the surgeries were performed by different surgeons.

In conclusion, based on the findings of this study, N1 status did not affect survival in N2 patients who underwent pneumonectomy due to NSCLC, whereas GPS and adjuvant therapy were significant prognostic factors. Therefore, we believe that assessment with GPS may be beneficial for patients planned to undergo resection in order to determine postoperative prognosis.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

Ethics approval

The study was approved by the Ethics Committee of Health of Science University (No: 20189/1525).

Authors' contributions

CA; Performed the analysis, co-wrote the paper, contributed data/analysis tools, CBS; performed the analysis, co-wrote the paper, AC, MVD; co-wrote the paper, YA, CEK,VE; Collected the data, LC, MM; Contributed data, co-wrote the paper.

References

1. Metin M, Citak N, Sayar A, Pekcolaklar A, Melek H, Kök A et al. The role of extended cervical mediastinoscopy in staging of non-small cell lung cancer of the left lung and a comparison with integrated positron emission tomography and computed tomography: does integrated positron emission tomography and computed tomogr. *J Thorac Oncol* 2011; 6: 1713-9.
2. Rami-Porta R, Goldstraw P. 25 – The Eighth Edition of the Tumor, Node, and Metastasis Classification of Lung Cancer. Second Edi. Elsevier Inc.; 2018. doi:10.1016/B978-0-323-52357-8.00025-1.
3. Al Murri AM, Bartlett JMS, Canney PA, Doughty JC, Wilson C, McMillan DC. Evaluation of an inflammation-based prognostic score (GPS) in patients with metastatic breast cancer. *Br J Cancer* 2006; 94: 227.
4. Machida Y, Sagawa M, Tanaka M, Motono N, Matsui T, Usuda K et al. Postoperative survival according to the glasgow prognostic score in patients with resected lung adenocarcinoma. *Asian Pacific J Cancer Prev* 2016; 17: 4677-80.
5. Rusch VW, Asamura H, Watanabe H, Giroux DJ, Rami-Porta R, Goldstraw P. The IASLC lung cancer staging project: a proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. *J Thorac Oncol* 2009; 4: 568-77.
6. Peebles KA, Lee JM, Mao JT, Hazra S, Reckamp KL, Krysan K et al. Inflammation and lung carcinogenesis: applying findings in prevention and treatment. *Expert Rev Anticancer Ther* 2007; 7: 1405-21.
7. Jing X, Huang C, Zhou H, Li C, Fan L, Chen J et al. Association between serum C-reactive protein value and prognosis of patients with non-small cell lung cancer: a meta-analysis. *Int J Clin Exp Med* 2015; 8: 10633.
8. Sayar I, Isik A, Akbas EM, Eken H, Demirtas L. Bone marrow metaplasia in multinodular goiter with primary hyperparathyroidism. *Am J Med Sci* 2014; 348: 530-1.
9. Morris-Stiff G, Gomez D, Prasad KR. C-reactive protein in liver cancer surgery. *Eur J Surg Oncol* 2008; 34: 727-9.
10. Alifano M, Mansuet-Lupo A, Lococo F, Roche N, Bobbio A, Canny E et al. Systemic inflammation, nutritional status and tumor immune microenvironment determine outcome of resected non-small cell lung cancer. *PLoS One* 2014; 9: e106914.
11. Forrest LM, McMillan DC, McArdle CS, Angerson WJ, Dunlop DJ. Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. *Br J Cancer* 2003; 89: 1028.
12. Jin J, Hu K, Zhou Y, Li W. Prognostic value of the Glasgow prognostic score in lung cancer: evidence from 10 studies. *Int J Biol Markers* 2018; 33: 201-7.
13. Nozoe T, Matono R, Ijichi H, Ohga T, Ezaki T. Glasgow Prognostic Score (GPS) can be a useful indicator to determine prognosis of patients with colorectal carcinoma. *Int Surg* 2014; 99: 512-7.
14. Minami S, Ihara S, Komuta K. Pretreatment lymphocyte to monocyte ratio as a prognostic marker for advanced pulmonary squamous cell carcinoma treated with chemotherapy. *J Clin Med Res* 2018; 10: 657.
15. National Comprehensive Cancer Network. Non-small cell lung cancer (version 6.2018). 2018. Available from: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
16. Park H, Oh D, Ahn YC, Pyo H, Noh JM, Sun J et al. Role of Adjuvant Thoracic Radiation Therapy and Full Dose Chemotherapy in pN2 Non-small Cell Lung Cancer : Elucidation Based on Single Institute Experience 2017; 49: 880-9.
17. Spaggiari L, Casiraghi M, Guarize J, Brambilla D, Petrella F, Maisonneuve P et al. Outcome of Patients With pN2 “Potentially Resectable” Nonsmall Cell Lung Cancer Who Underwent Surgery After Induction Chemotherapy. *Semin. Thorac. Cardiovasc. Surg.*, vol. 28, Elsevier; 2016, p. 593-602.

18. Gorai A, Sakao Y, Kuroda H, Uehara H, Mun M, Ishikawa Y et al. The clinicopathological features associated with skip N2 metastases in patients with clinical stage IA non-small-cell lung cancer. *Eur J Cardiothorac Surg* 2014; 47: 653-8.
19. Nakagiri T, Sawabata N, Funaki S, Inoue M, Kadota Y, Shintani Y et al. Validation of pN2 sub-classifications in patients with pathological stage IIIA N2 non-small cell lung cancer. *Interact Cardiovasc Thorac Surg* 2011; 12: 733-8.
20. Sonobe M, Date H, Wada H, Okubo K, Hamakawa H, Teramukai S et al. Prognostic factors after complete resection of pN2 non-small cell lung cancer. *J Thorac Cardiovasc Surg* 2013; 146: 788-95.
21. Hanagiri T, Takenaka M, Oka S, Shigematsu Y, Nagata Y, Shimokawa H et al. Clinical significance in the number of involved lymph nodes in patients that underwent surgery for pathological stage III-N2 non-small cell lung cancer. *J Cardiothorac Surg* 2011; 6: 1-8.
22. Legras A, Mordant P, Arame A. Long-Term Survival of Patients With pN2 Lung Cancer According to the Pattern of 2014; 97: 1156-62.
23. Yazgan S, Ucvet A, Gursay S, Samancilar O, Yagci T. Single-station skip-N2 disease: good prognosis in resected non-small-cell lung cancer (long-term results in skip-N2 disease). *Interact Cardiovasc Thorac Surg* 2018; 28: 247-52.

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To cite this article: Seyrek Y, Cansever L, Bedirhan MA. Which factors significantly reduce long-term survival after pulmonary metastasectomy? Curr Thorac Surg 2021 Jan 15; 6(1): 14-20.

Original Article

Which factors significantly reduce long-term survival after pulmonary metastasectomy?

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ABSTRACT

Background: In this study, a survival analysis was performed of patients who underwent pulmonary metastasectomy over the past 10 years in our clinic. We aimed to elucidate the factors that significantly affected overall survival and identify subgroups of patients who may not benefit from pulmonary metastasectomy.

Materials and Methods: We retrospectively reviewed 68 patients with a history of extra-thoracic malignancy who underwent pulmonary metastasectomy between January 2009 and December 2018. The overall survival rate was analyzed according to age, sex, histological type of the primary tumor, metastatic side, surgical approach type, pulmonary resection type, number of nodules resected, disease-free interval, and nodal status.

Results: The actuarial survival rate after pulmonary metastasectomy was 78% (95% confidence interval [CI]: 71-84) at 2 years and 48% (95% CI: 41-52) at 5 years. Patients with disease free interval < 12 months had a far worse survival rate ($p = 0.001$). Patients with sarcoma had a significantly worse prognosis than those with epithelial tumors or melanoma ($p = 0.001$). Patients with negative nodal status had a significantly better prognosis ($p = 0.001$), while patients with metastatic hilar lymph nodes also had significantly better survival compared to patients with metastatic mediastinal lymph nodes (N2) ($p = 0.001$).

Conclusions: Tumor histology is the main determinant of overall survival and prognosis after pulmonary metastasectomy. The presence of multiple metastases in different unilateral lobes and N2 disease appeared to be the worst prognostic factors. Patients with either of these two significant negative prognostic factors should be evaluated carefully via a multidisciplinary approach and pulmonary metastasectomy should be performed only in selected patients.

Keywords: metastasectomy, pulmonary, negative prognostic factors, long term survival

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Doi: 10.26663/cts.2021.0003

Received 22.06.2020 accepted 20.07.2020

Introduction

Debate regarding the efficacy of pulmonary metastasectomy (PM) began 35 years ago. A complete PM improves the survival of patients with controlled primary tumor sites. Removing as little healthy lung tissue as possible while obtaining clear margins is the main goal of PM. Although the impact of lymph node dissection on survival remains unclear, it is recommended to ensure correct staging for further oncological treatment. Histological confirmation of metastasis is necessary to increase the cure rate [1]. Lung metastases are rarely symptomatic, where metastases that do cause symptoms generally fall outside the criteria for PM, which are typically based on the opinion of a multidisciplinary team.

In this study, a survival analysis was performed of patients who underwent PM over the past 10 years in our clinic. We aimed to elucidate the factors that significantly affected overall survival and identify subgroups of patients who may not benefit from PM.

Material and Methods

We retrospectively reviewed 117 patients with a history of extra-thoracic malignancy who underwent complete curative resection of pulmonary nodules between January 2009 and December 2018. Of these patients, 58% presented with pulmonary metastases ($n = 68$), 28% were newly diagnosed with non-small-cell lung cancer (secondary primary/metachronous lung cancer; $n = 32$), and 14% had benign lesions ($n = 17$). The study was approved by the institutional review board (No: 20-35 / 9.5.2020) and conducted in accordance with the principles of the Declaration of Helsinki.

All patients were evaluated by a multidisciplinary team, including a surgeon, oncologist, and radio-oncologist, and received chemotherapy before PM. Thin-slice computed tomography (CT) scans were performed no later than 30 days after surgery and 18F-Fluorodeoxyglucose positron emission tomography/CT was used to rule out extrathoracic metastases and assess the degree of lymph node involvement [2].

All of the patients included in this study had their primary tumors controlled, no extrapulmonary metastases, and a limited number of pulmonary lesions that could all be removed; moreover, it was confirmed that the patients could tolerate resection of all lesions. Pa-

tients with primary lung carcinoma, an unresectable primary tumor, possible extrathoracic metastasis, preoperatively detected pleural carcinomatosis, predicted incomplete metastasectomy, or benign lesions were excluded from the study. Moreover, putative clinical prognostic factors, such as the number of metastases, lymph node involvement, and the disease-free interval (DFI) were evaluated before surgery, although we did not exclude patients with a short DFI, suspected mediastinal lymph node metastasis, or high number of metastases (where these factors were presumed to be relative contraindications in some previous studies) [3,4].

The DFI was defined as the time between the treatment of the primary tumor and diagnosis of metastases. An age analysis was performed by dividing the patients into three groups: young adults (<35 years), adults (35–55 years), and seniors (>55 years). The DFI was classified as <12 months, 12–36 months, or >36 months.

Non-anatomic wedge resection with safe margins was performed if metastases were located in the lung periphery; anatomic pulmonary resection were performed if the metastasis was centrally located, there were multiple lesions in the same segment or lobe, and a wedge resection was not anatomically feasible to remove all metastases. In addition, if a preoperative histological analysis suggested possible primary lung cancer, the patient underwent pulmonary anatomic resection and lymphadenectomy.

The mediastinal lymph nodes were sampled or dissected in all PM patients. The lymph nodes were sampled mostly during the earlier part of our study, and were dissected during PMs for the last 5 years. The regional lymph node classification of Mountain and Dresler was used [5]. Mediastinal lymph node metastases were referred to as N2 disease, hilar lymph node metastases as N1 disease, and the absence of lymph node metastasis as N0 disease.

No patient had a germ cell tumor, and primary tumors were classified as one of three histological types: epithelial tumor, sarcoma, or melanoma. Epithelial tumors included colorectal carcinoma, head and neck carcinoma, breast carcinoma, renal cell carcinoma, hepatocellular carcinoma, prostate carcinoma, and uterine carcinoma. Sarcomas included soft tissue sarcoma, osteosarcoma, synovial sarcoma, and uterine leiomyosarcoma.

All patients were reviewed retrospectively. The overall survival rate was analyzed according to age, sex, histological type of the primary tumor, metastatic side (right vs. left), surgical approach type (video-assisted thoracic surgery [VATS] vs. open thoracotomy), pulmonary resection type (wedge vs. anatomical resection), number of nodules resected (solitary vs. multiple), DFI, and nodal status (N0–N2).

Statistical Analysis

Survival estimates were calculated with the Kaplan–Meier method and compared with the log-rank test. Overall survival was defined as the time between the first metastasectomy and last follow-up or death. Data are presented as a mean $\pm$ standard error of the mean. IBM SPSS Statistics for Windows software (version 22.0; IBM Corp., Armonk, NY, USA) was used for the statistical analyses. A p -value < 0.05 was considered significant.

Results

Sixty-eight patients who underwent complete PM were included in the study. There were 37 males (54.4%) and 31 females (45.6%). The mean age was 51 years (range: 16–76 years). Young adults comprised 13% of the cohort ($n = 9$), while adults comprised 47% ($n = 32$) and seniors 40% ($n = 27$). Twenty-three patients (34%) had a DFI of 0–12 months, 38 (56%) had a DFI of 12–36 months, and 7 (10%) had a DFI of ≥ 36 months. Eleven patients had preoperative symptoms (16%); one had hemoptysis, four had shortness of breath, three had chest pain, and three had persistent cough. Postoperative complications were reported in 10 patients (15%); atrial fibrillation, $n = 5$; prolonged air leak, $n = 3$ [all sarcoma patients], pneumonia, $n = 1$; and chylothorax, $n = 1$). No postoperative deaths were recorded. The mean hospital stay after surgery was 5.2 days (range: 2–28 days).

Metastasectomy was performed by videothoracoscopy in 29 cases (43%), and by open thoracotomy in 39 cases (57%). In total, 45 (66%) wedge resections and 23 (34%) anatomical pulmonary resections, including 16 (23.5%) lobectomies, 6 (9%) segmentectomies, and 1 (1.5%) pneumonectomy, were performed. In addition to pulmonary resection, one patient needed a chest wall resection, and diaphragmatic resection was performed in another case. Unilateral recurrent PM was performed in three patients and bilateral consecutive PM was performed in two others. Thirty-three patients (48%) had a

solitary metastasis, and thirty-five (52%) had multiple metastases. A solitary metastasis was detected in 48% of epithelial tumors ($n = 25$), 46% of sarcomas ($n = 6$), and 66% of melanomas ($n = 2$). The histopathology report revealed 52 epithelial tumor metastases (76%), 13 sarcoma metastases (19%), and 3 melanoma (5%) metastases. Epithelial tumor metastases ($n = 52$) included 2 uterine carcinomas (1 endometrium carcinoma and 1 cervix carcinoma), 2 hepatocellular carcinomas, 30 colorectal carcinomas (23 colon carcinomas and 7 rectal carcinomas), six breast carcinoma, 6 head and neck carcinomas (3 laryngeal carcinomas, 2 nasopharyngeal carcinomas, and 1 parotid gland tumor), 4 renal cell carcinomas, and 2 prostate carcinomas. Sarcoma metastases ($n = 13$) included five osteosarcomas, one soft tissue sarcoma, three synovial sarcomas, and four uterine leiomyosarcomas (Table 1). Mediastinal lymph node metastases (N2) were detected in 9 cases (13%); (21%) hilar lymph nodes (N1) were positive in 14 cases, and 45 patients (66%) had N0 disease. Three patients with sarcoma, 3 patients with colorectal carcinoma, 2 patients with head and neck and 1 patient with uterine carcinoma metastases had N2 disease.

Table 1. Patient characteristics.

Variables	Number of patients ($n=68$)	Percent (%)
Male	37	54.4%
Female	31	45.6%
Young adults	9	13%
Adults	32	47%
Seniors	27	40%
DFI < 12 months	23	34%
DFI 12–36 months	38	56%
DFI > 36 months	7	10%
VATS	29	43%
Thoracotomy	39	57%
Wedge resection	45	66%
Anatomical resection	23	34%
N2 disease	9	13%
N1 disease	14	21%
N0	45	66%
Solitary metastasis	33	48%
Multiple metastases	35	52%
Epithelial tumors	52	76%
Sarcoma	13	19%
Melanoma	3	5%

Abbrev.: DFI; disease-free interval

Table 2. Patients survival rates according to analyzed variables.

Variable	2-year survival rate (%)	5-year survival rate (%)	p
Male	75±4%	32±2%	0.001
Female	92±3%	68±3%	
Young adults	100%	65±3%	
Adults	80±3%	52±2%	0.349
Seniors	56±2%	38±2%	
DFI <12 months	42±2%	10±2%	0.001
DFI 12-36 months	92±2%	64±2%	
DFI >36 months	100%	86±2%	
VATS	75±5%	38±2%	0.653
Thoracotomy	75±3%	58±2%	
Wedge resection	82±3%	70±2%	
Anatomical resection	82±2%	38±2%	0.007
N2 disease	0%	0%	0.001
N1 disease	38±2%	0%	
N0	100%	72±5%	
Solitary metastasis	68±2%	50±5%	0.826
Multiple metastases	84±2%	50±3%	
Multiple metastases within same lobe	80±5%	63±2%	
Multiple metastases in different unilateral lobes	88±2%	0%	0.027
Epithelial Tumors	82±5%	52±3%	0.001
Sarcoma	82±3%	38±2%	
Melanoma	65±5%	60±2%	

Abbrev.: DFI; disease-free interval

After a mean follow-up of 39.65 ± 12.3 months, 33 patients (48.5%) had died. The mean survival time after PM was 61 ± 5.5 months. The actuarial survival rate after PM was 78% at 2 years and 48% at 5 years. The 2- and 5-year actuarial survival rates according to age, sex, DFI, nodal status, histology, number of metastases, surgery type, surgical approach, and metastasis side are shown in Table 2. Overall, patients with sarcoma had a significantly worse prognosis than those with epithelial tumors or melanoma ($p = 0.001$). Patients with breast carcinoma in the epithelial tumor group had a better prognosis ($p = 0.001$). Patients with DFI < 12 months had a far worse survival rate ($p = 0.001$). Female patients had significantly better overall survival compared to male patients ($p = 0.038$). N0 patients had a significantly better prognosis compared to N1 and N2 patients ($p = 0.001$), while N1 patients had

significantly better survival compared to N2 patients ($p = 0.001$). Lastly, we performed a subgroup analysis, dividing the patients with multiple metastases into “multiple metastases within the same lobe” and “multiple metastases in different lobes” groups: the former group had a significantly better 5-year overall survival compared to the latter group (67.7 ± 7.6 vs. 37 ± 3.3 months; 63% vs. 0%, $p = 0.027$). Age, number of metastases, surgery type, metastasis side, and surgical approach did not affect long-term survival.

Discussion

The lung is the one of the most common sites of metastases, and PM is widely considered an effective treatment for patients with oligometastases, which is characterized by limited systemic tumor metastasis [6]. The main objectives of PM are to confirm the metastatic nature of the disease and increase survival. In addition, a personalized approach to treatment has redefined the role of PM, as a method for obtaining metastatic samples to identify changes in biomarkers or resistance patterns, so that on-cological treatment can improve patient outcomes [7].

Complete PM refers to the removal of all detectable metastases with a negative margin, although the evolution of millimetric lung metastases left behind is also interesting [8]. Pulmonary metastases occur when primary cancer cells detach after local growth, migrate through the systemic circulation, and lodge in the lungs. They receive their blood supply from the pulmonary arteries (84%) or bronchial arteries (16%) [9]. Thin-slice multi-detector row CT scanning, which we routinely perform before PM, can be used to evaluate the lungs in 1-mm sections within 5 seconds, for a detection sensitivity comparable to intraoperative bimanual palpation during thoracotomy [10]; however, its sensitivity for proven pulmonary metastases is only approximately 80% [11]. Even though impalpable or undetected metastases cannot be removed, that does not mean that they do not exist. Even if we assume that the patient has undergone a complete PM, there may be still some viable millimetric metastases. Moreover, circulating tumor cells, which are presumed to be dormant before implantation and become active after implantation, have been detected by reverse transcription-polymerase chain reaction and immunocytochemical methods [12,13]. Thus, “complete” might only be a relative term for metastasectomy procedures. Many retrospective studies have reported that PM increased survival [14,15]. In our study, we aimed

to identify factors that significantly influence the overall survival of patients after PM based on our 10-year clinical experience.

The overall 5-year survival rate after PM ranges from 30% to 40% [16,17]. However, the 5-year survival rate was higher, at 48%, in our study. Several negative prognostic factors are known to be responsible for the large difference in survival rate among populations of patients undergoing PM. Prognostic factors for poor survival include a short DFI, multiple lung metastases, and thoracic mediastinal/hilar lymph node involvement [18].

A shorter DFI is associated with a poorer prognosis in patients with a history of malignancy [18]. In our study, patients with a short DFI (<12 months) had a significantly lower 5-year overall survival rate (9%, 23.6 ± 3.8 months) compared to the other patients, as expected ($p = 0.001$).

Although there seems to be a consensus that a solitary pulmonary metastasis is a better prognostic factor for 5-year overall survival than multiple metastases; we did not detect any difference between the solitary and multiple metastasis groups in our study [19,20]. Thus, the presence of “multiple metastases” did not appear to be an important variable, whereas the presence of “metastases in different lobes” was a significant negative prognostic factor. However, we did not spot any related similar results on this matter in literature; but we know that different lung segments have their own unique lymphatic drainage pathways to the mediastinal nodes so we can speculate that separate metastases in different lobes may induce greater lymph node metastasis which eventually reduces survival [2,21].

The reported rate of nodal involvement ranges from 12% to 32%; the 5-year survival of PM patients is highest when there is no lymph node invasion, and poorest when there is lymph node invasion [22,23]. Ercan et al. [22] reported a rate of lymph node involvement of 28.6% in metastatic lung carcinoma, with poor survival observed in patients with lymph node metastases. Pfannschmidt et al. [23] detected lymph node metastases in 29% of patients; the 3-year survival rate for patients with negative lymph node status was 69%, compared to 38% in the presence of lymph node metastasis. In our study, the rate of nodal involvement was 34%, and the 5-year survival rate of the N0 patients (69%) was significantly better than that of the N1 (9%) and N2 (0%) patients ($p = 0.001$). All of our patients with

N2 disease ($n = 9$) died within 1 year after PM. Furthermore, the N1 patients had a significantly better survival rate than the N2 patients ($p = 0.001$). A more obvious difference was seen between the 2-year survival rates of the N1 and N2 subgroups (37% vs. 0%). Thus, N1 and N2 should not be considered together in terms of prognosis, although we found no study that emphasized the prognostic superiority of N1 over N2.

The histology and genotype of the primary tumor are among the most important factors in prognosis and survival after PM. The mechanism of metastasis varies depending on the histological type of the tumor: colorectal metastases have a high rate of pleural invasion, and of interstitial and aerogenous spread of floating cancer cells, which are in turn associated with a high rate of local recurrence [24]. Melanoma does not show pleural invasion, but is associated with a higher probability of perivascular growth and an increased incidence of lymphangitic spread [25]. Compared to other tumors, our patients with pulmonary metastatic sarcoma (38%) had the lowest overall survival following PM ($p = 0.001$), as expected because sarcomas are fast-growing tumors with relatively short doubling-times). Most studies have reported that patients with sarcoma have a worse prognosis compared to those with other malignancies, with 5-year survival rates after PM reported at 25–40% [26,27]. Regarding our patients with epithelial tumors, the breast cancer patients had a significantly higher overall survival (90%) than all other epithelial tumor subgroups. This also explained why females had a significantly better survival rate than males. However, this finding was not consistent with the literature; Staren et al. reported a 5-year survival rate of 36%, while Tanaka et al. reported a rate of 30% for breast cancer patients after PM [28,29]. Unexpectedly, patients with head and neck carcinoma had the second highest survival rate (67%) among the epithelial tumor subgroups; previous studies reported 5-year survival rates of up to 40% [30]. Surprisingly, we observed high overall survival in patients with melanoma ($n = 3$, 67.3 ± 34 months; 64%) compared to the previously reported rate (27%) [31]. However, the limited number of cases with melanoma prevented us from establishing any firm hypothesis.

If a tumor is aggressive and has a short doubling time, tumor debris may transition to full-grown metastasis, thus leading to a poor prognosis (as typically observed in patients with sarcoma). Aggressive tumors

are likely to be associated with multiple metastases, short DFI, or nodal metastases and, consequently, poor survival. The prognosis is favorable for less aggressive tumors with a moderate doubling time.

The main limitations of this study are the small patient group and its single-center retrospective design. Moreover, the carcinoembryonic antigen level, which is a putative negative prognostic factor, was not analyzed, and genotype analysis was not performed. Moreover, no patient had a germ cell tumor, and only a small number of patients had melanoma; thus, the patient group showed a relative lack of diversity.

In conclusion, tumor histology is the main determinant of overall survival and prognosis after PM. In our study, significant negative prognostic factors included multiple metastases in different unilateral lobes, a short DFI (< 12 months), both mediastinal and hilar lymph node involvement, and sarcoma metastasis. The presence of multiple metastases in different unilateral lobes and N2 disease appeared to be the worst prognostic factors. Thus, preoperatively, patients with either of these two significant negative prognostic factors should be evaluated carefully via a multidisciplinary approach, and PM should be performed only in selected patients.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

Ethics approval

The study was approved by the Ethics Committee of Health Sciences University (No: 20-35/9.5.2020).

Authors' contributions

YS; Co-wrote the paper, conceived and designed analysis, collected data, LC; co-wrote the paper, contributed data, performed analysis, MAB; designed the analysis.

References

1. Gonzalez M, Zellweger M, Nardini M, Migliore M. Precision surgery in lung metastasectomy. *Future Oncol* 2020; 16: 7-13.

2. Detterbeck FC, Grodzki T, Gleeson F, Robert JH. Imaging requirements in the practice of pulmonary metastasectomy. *J Thorac Oncol* 2010; 5: S134-9.
3. Yano T, Shoji F, Maehara Y. Current status of pulmonary metastasectomy from primary epithelial tumors. *Surg Today* 2009; 39: 91-7.
4. Internullo E, Cassivi SD, Van Raemdonck D, Friedel G, Treasure T. ESTS Pulmonary Metastasectomy Working Group. Pulmonary metastasectomy: a survey of current practice amongst members of the European Society of Thoracic Surgeons. *J Thorac Oncol* 2008; 3: 1257-66.
5. Mountain CF, Dresler CM. Regional lymph node classification for lung cancer staging. *Chest* 1997; 111: 1718-23.
6. Hellman S, Weichselbaum RR. Oligometastases. *J Clin Oncol* 1995; 13: 8-10.
7. Moorcraft SY, Jones T, Walker BA, Ladas G, Kalaitzaki E, Yuan L et al. Molecular profiling of colorectal pulmonary metastases and primary tumours: implications for targeted treatment. *Oncotarget* 2017; 8: 64999-5008.
8. Perentes JY, Krueger T, Lovis A, Ris HB, Gonzalez M. Thoracoscopic resection of pulmonary metastasis: current practice and results. *Crit Rev Oncol Hematol* 2015; 95: 105-13.
9. Brooks SA, Lomax-Browne HJ, Carter TM, Kinch CE, Hall DM. Molecular interactions in cancer cell metastasis. *Acta Histochemica* 2010; 112: 3-25.
10. Kang MC, Kang CH, Lee HJ, Goo JM, Kim YT, Kim JH. Accuracy of 16-channel multi-detector row chest computed tomography with thin sections in the detection of metastatic pulmonary nodules. *Eur J Cardiothorac Surg* 2008; 33: 473-9.
11. Parsons AM, Ennis EK, Yankaskas BC, Parker LA Jr, Hyslop WB, Detterbeck FC. Helical computed tomography inaccuracy in the detection of pulmonary metastases: can it be improved? *Ann Thorac Surg* 2007; 84: 1830-6.
12. Smith B, Selby P, Southgate J, Pittman K, Bradley C, Blair GE. Detection of melanoma cells in peripheral blood by means of reverse transcriptase and polymerase chain reaction. *Lancet* 1991; 338: 1227-9.
13. Molnar B, Ladanyi A, Tanko L, Sréter L, Tulassay Z. Circulating tumor cell clusters in the peripheral blood of colorectal cancer patients. *Clin Cancer Res* 2001; 7: 4080-5.

14. Perentes JY, Zellweger M, Gonzalez M. Personalized surgery for the management of pulmonary metastasis. *J Thorac Dis* 2018; 10: 52-5.
15. Erhunmwunsee L, D'amico TA. Surgical management of pulmonary metastases. *Ann Thorac Surg* 2009; 88: 2052-60.
16. Mountain CF, McMurtrey MJ, Hermes KE. Surgery for pulmonary metastasis: a 20-year experience. *Ann Thorac Surg* 1984; 38: 323-30.
17. Pastorino U, Buyse M, Friedel G, Ginsberg RJ, Girard P, Goldstraw P et al. Long-term results of lung metastasectomy: prognostic analyses based on 5206 cases. *J Thorac Cardiovasc Surg* 1997; 113: 37-49.
18. Gonzalez M, Gervaz P. Risk factors for survival after lung metastasectomy in colorectal cancer patients: systematic review and meta-analysis. *Future Oncol* 2015; 11: 31-3.
19. Zellweger M, Abdelnour-Berchtold E, Krueger T, Ris HB, Perentes JY, Gonzalez M. Surgical treatment of pulmonary metastasis in colorectal cancer patients: Current practice and results. *Crit Rev Oncol Hematol* 2018; 127: 105-16.
20. Renaud S, Alifano M, Falcoz PE, Magdeleinat P, Santelmo N, Pages O et al. Does nodal status influence survival? Results of a 19-year systematic lymphadenectomy experience during lung metastasectomy of colorectal cancer. *Interact Cardiovasc Thorac Surg* 2014; 18: 482-7.
21. Riquet M, Hidden G, Debesse B. Direct lymphatic drainage of lung segments to the mediastinal nodes. An anatomic study on 260 adults. *J Thorac Cardiovasc Surg* 1989; 97: 623-32.
22. Ercan S, Nichols FC 3rd, Trastek VF, Deschamps C, Allen MS, Miller DL et al. Prognostic significance of lymph node metastasis found during pulmonary metastasectomy for extrapulmonary carcinoma. *Ann Thorac Surg* 2004; 77: 1786-91.
23. Pfannschmidt J, Klode J, Muley T, Dienemann H, Hoffmann H. Nodal involvement at the time of pulmonary metastasectomy: experiences in 245 patients. *Ann Thorac Surg* 2006; 81: 448-54.
24. Renaud S, Seitlinger J, Lawati YA, Guerrero F, Falcoz PE, Massard G et al. Anatomical Resections Improve Survival Following Lung Metastasectomy of Colorectal Cancer Harboring KRAS Mutations. *Ann Surg* 2019; 270: 1170-7.
25. Balch CM, Soong SJ, Murad TM, Smith JW, Maddox WA, Durrant JR. A multifactorial analysis of melanoma. IV. Prognostic factors in 200 melanoma patients with distant metastases (stage III). *J Clin Oncol* 1983; 1: 126-34.
26. Saleh W, AlShammari A, Sarraj J, AlAshgar O, Ahmed MH, AlKattan K. Surgical treatment of pulmonary metastasis: report from a tertiary care center. *Asian Cardiovasc Thorac Ann* 2018; 26: 296-301.
27. Tsuchiya H, Kanazawa Y, Abdel-Wanis ME, Asada N, Abe S, Isu K et al. Effect of timing of pulmonary metastases identification on prognosis of patients with osteosarcoma: the Japanese Musculoskeletal Oncology Group study. *J Clin Oncol* 2002; 20: 3470-7.
28. Staren ED, Salerno C, Rongione A, Witt TR, Faber LP. Pulmonary resection for metastatic breast cancer. *Arch Surg* 1992; 127: 1282-4.
29. Tanaka F, Li M, Hanaoka N, Bando T, Fukuse T, Hasegawa S et al. Surgery for pulmonary nodules in breast cancer patients. *Ann Thorac Surg* 2005; 79: 1711-5.
30. Liu D, Labow DM, Dang N, Martini N, Bains M, Burt M et al. Pulmonary metastasectomy for head and neck cancers. *Ann Surg Oncol* 1999; 6: 572-578.
31. Dalrymple-Hay MJ, Rome PD, Kennedy C, Fulham M, McCaughan BC. Pulmonary metastatic melanoma -the survival benefit associated with positron emission tomography scanning. *Eur J Cardiothorac Surg* 2002; 21: 611-5.

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Original Article

Postoperative complications and follow up after Abramson surgery

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ABSTRACT

Background: Abramson technique is a worldwide technique used for minimally invasive treatment of pectus carinatum. We have performed this surgery since 2012. This article presents our experience about Abramson surgery.

Materials and Methods: Between June 2012 and December 2019 64 patients with pectus carinatum underwent minimally invasive surgery.

Results: Mean age of the patients were 14.4 years (range 8-25 years). 47 were male, 17 were female. All patients referred to our clinic with cosmetic complaints. 14 (21.8%) patients also had clinical symptoms in preoperative period. Mean duration of operation was 61 minutes. Mean blood loss was 30 ml and death wasn't seen in any patient. Complication was seen in 15 (10.7%) patients in postoperative period. Splitting of cables was seen in 7 (10.9%) patients as the most common complication in the long term follow-up. Duration of hospitalization ranged from 3 to 15 days (average 5.1 ± 2.9 days). Reoperation was performed in 17 (26.5%) patients.

Conclusions: Minimally invasive surgery is successful for the treatment of pectus carinatum.

Keywords: chest, pectus, deformity, congenital, thoracic, minimally invasive surgery, follow up study

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Doi: 10.26663/cts.2021.0004

Received 24.06.2020 accepted 03.12.2020

Introduction

Pectus carinatum (PC) is the second most common morphological disorder of the chest wall [1]. PC is generally noticed in childhood, but becomes more severe during puberty. There are two types of PC. The chondrogladiolar type presents with protrusion of the gladiolus and inferior costal cartilages along the most prominent area of the sternum; kinetic, orthotic and surgical treatments are available [2]. The first surgical technique was reported by Mark Ravitch in 1952. However, this technique involves both resection of cartilaginous rib regions and sternal osteotomy. Postoperative scarring is extensive, despite the basic aim of aesthetic improvement [2]. Nuss developed minimally invasive surgery for patients with pectus excavatum. The widespread acceptance of this technique encouraged minimally invasive repair of PC, initially introduced by Abramson in 2005 [3,4]. In this approach, the chest wall is not opened. A metal bar of defined composition is used to depress the sternum to an appropriate position, in accordance with the Nuss method. Importantly, this approach is effective [4].

Here, we describe the clinical features and outcomes of 64 patients treated with the Abramson technique from 2012 to 2019.

Materials and Methods

Sixty-four patients (47 male patients, 17 female patients; mean age, 14.4 years [range, 8-25 years]) underwent Abramson surgery in our Thoracic Surgery Clinic between June 2012 and December 2019. Their data were retrospectively analysed in this study. Written informed consent was obtained from all adult patients and the parents of young patients. Our institutional ethics committee approved the study (No: 19/2020).

All patients were referred to our clinic because of cosmetic complaints. Fourteen (21.8%) patients exhibited preoperative clinical symptoms: 11 (17.1%) had chest pain and three (4.6%) had dyspnea on exertion. Six (9.2%) patients had comorbidities. Three had asthma, two had atrial septal defects, and one had scoliosis (Table 1).

All patients exhibited chondrogladiolar deformities, which were symmetric in 20 patients and asymmetric in 44. Sternal compression tests were performed and sternal flexibility was checked while patients stood with their backs to a wall.

Patients were hospitalized 1 day preoperatively; a complete blood count, a chest X-ray, and routine bio-

chemical tests were performed before surgery. All patients underwent computed tomography, as well as preoperative cardiac and pulmonary tests.

Surgical technique

The chest was measured preoperatively and appropriately sized bars were chosen. Surgery was performed with all patients under general anesthesia. All operations were performed by the same surgical team. The bars reached both midaxillary lines and were compatible with the chest wall. Three-centimeter-long incisions were created on both sides of the chest wall in the midaxillary line, at the level of the highest sternal protrusion evident in the supine position. A Kelly clamp (an introducer) was used to enter the chest wall. The introducer was inserted horizontally over the sternum to reach the contralateral side of the chest wall. A submuscular tunnel was created in the region over the highest sternal protrusion. One bar and two stabilizers were placed in accordance with the method described by Abramson. The bars were made of surgical steel, they were 13 mm wide and 2 mm thick (Hipokrat, Izmir, Turkey). The bars extended from the right side of the chest wall, with the concavities facing anteriorly. They were confined to the tunnel formed in the submuscular area. As the tip of a bar emerged from the presternal tunnel, it was directed to the left side of the chest wall. Two adjacent ribs lying under the midaxillary line incision were rotated through 90° and sternal cables were then placed (Pioneer Surgical, Marquette, MI, USA). The cables were passed through the holes of the stabilizers. The bars were thus bilaterally applied to the chest wall as shown in Figure 1 and 2 [5-6]. We didn't bend the pectus bar after putting it through stabilizers while performing Nuss procedure, because in some cases we encountered with bending of the bar in the medial aspect during bar removal.

Table 1. Clinical data of the pectus carinatum patients before surgery.

Characters	n (%)
Gender	64
Male	47
Female	17
Age	14.4±7.8 years (8-25 years)
With clinical symptoms	14 (21.8%)
Chest pain	11 (17.1%)
Dyspnea on effort	3 (4.6%)
Comorbidity	6 (9.2%)
Asthma	3
Atrial septal defect	2
Scoliosis	1

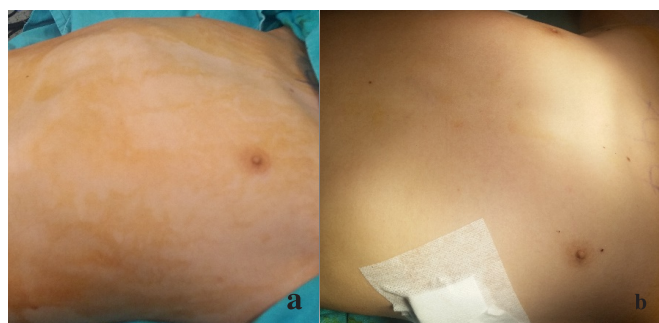


Figure 1. Preoperative (a), postoperative (b) view of a 11 year-old male patient with asymmetric pectus carinatum.

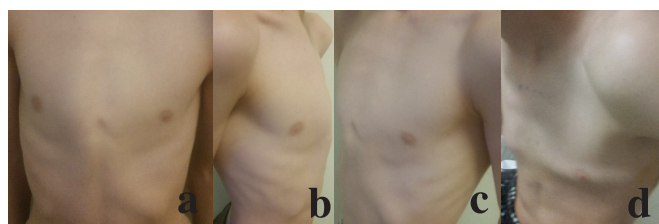


Figure 2. Preoperative posteroanterior (a), right lateral (b), left lateral (c), postoperative (d) view of a 14 year-old male patient with asymmetric pectus carinatum.

Results

Bar length ranged from 11 to 40.6 cm and stabilizers were placed on both bar ends. The mean operation duration was 61 minutes. The mean blood loss was 30 mL. A chest radiograph was obtained for each patient in the early postoperative period. Systemic analgesia and antibiotics were prescribed.

All patients achieved their desired aesthetic outcomes. The duration of hospitalization ranged from 3 to 15 days (mean: 5.1 ± 2.9 days). Patients were advised to return to normal activities in 2-3 weeks.

Complications developed in 15 (10.7%) patients (Table 2). Early complications included pneumothorax ($n = 3$), wound infection ($n = 2$), and hematoma ($n = 1$). Cable splitting was the most common long-term complication; it developed in seven (10.9%) patients. Other long-term complications included allergy-induced bar exposure ($n = 3$), bar dislocation ($n = 3$), and costal fracture ($n = 1$). Recurrences developed in two (3.1%) patients. Re-operations were required in 17 (26.5%) patients (Table 3); split cables were repaired in seven (10.9%) patients, while dislocated bars were replaced in three (4.6%). Bars were replaced in two (3.1%) patients

with recurrent disorder. The bar was removed because of dyspnea in one (1.5%) patient; the bar was replaced with a short bar in one (1.5%) patient because of severe pain. The Nuss operation was performed during bar extraction in two patients who exhibited overcorrection. There were no mortalities.

The mean follow-up time was 34.2 months after the first operation. The last Abramson operation was performed in December 2019. Bars were removed from 93.7% of patients. The mean follow-up time after removal was 37.4 months in 60 patients, with one bar per patient. All results were satisfactory after bar removal.

Table 2. Clinical data of surgery and complications.

Characters	n (%)
Surgery duration	Mean: 62.1 ± 21 min. (30-150 min)
Blood loss during surgery	30
Hospital stay	Mean: $5.1 \text{ days} \pm 2.9 \text{ days}$ (3-15 days)
Death	0
Complications	15(10.7%)
Splitting of cables	7(10.9%)
Bar exposure due to bar allergy	3(4.6%)
Pneumothorax	3(4.6%)
Bar dislocation	3(4.6%)
Recurrence	2(3.1%)
Wound infection	2(3.1%)
Hematoma	1(1.5%)
Costa fracture	1(1.5%)
Follow-up period in patients with removed bars	37.4 month

Table 3. Clinical data of reoperations.

Characters	n (%)
Reoperation	17(26.5%)
Repair of splitted wires	7(10.9%)
Replacement of dislocated bar	3(4.6%)
Replacement of the bar for recurrence	2(3.1%)
Pectoralis flap for infection	2(3.1%)
Pulling off the bar	1(1.5%)
Replacement with a short bar	1(1.5%)
Nuss for overcorrection	2(3%)

Discussion

PC is a deformity caused by abnormal growth of cartilaginous rib regions. Chondrogladiolar type patients exhibit protruding upper sternum. Chondromanubrial type patients exhibit protrusion of the entire sternum. Ravitch developed the classical surgical technique in 1952 and it was used worldwide for decades [7]. Sternal osteotomy and resection of costal cartilages is performed in some patients, while other patients require sternal and subperichondrial resection, or sternal osteotomy and subperichondrial resection of deformed cartilage. However, the classical surgical technique is very invasive and painful, scarring is extensive and aesthetic issues occur. Surgery is lengthy, as is postoperative hospitalization. The recurrence rates are higher than those of patients treated using the Abramson technique. Notably, the Abramson technique is less invasive and incisions are small. Sternal osteotomy and resection are not required [5]. The chondromanubrial type chest wall is overly rigid to allow bar placement and open surgery is indicated. However, chondrogladiolar type PC can be treated using the Abramson technique. Abramson et al. reported that, it is preferable to operate during puberty. However, the procedure can be performed at any age. In the present study, we did not consider age when treating our patients. The youngest patient was 8 years of age, while the oldest was 25 years of age. We performed a preoperative sternum compression test. Each patient stood with their back to a wall and received manual compression of the sternum. If this compression temporarily corrected the deformity, surgery was scheduled [4].

All patients exhibited chondrogladiolar type deformities. Those with chondromanubrial type deformities were excluded as their chest wall rigidity did not allow presternal bar insertion. Patients with asymmetry were treated by application of compressive pressure to the sternum and this transferred the protruding chondrosternal junctions to the vertebrae [8]. The chest wall must be flexible if this minimally invasive technique is used i.e. patient age is important. Yuksel et al. reported that, 12-18 years of age was optimal because the chest wall is more flexible in puberty. In our present study, 10 patients were 18-25 years of age. The sternum compression test and surgical results were successful in these patients [4].

Non-surgical methods are also available. Bracing is the most common, non-surgical, external compression method. Surgical methods may be preferred if braces

do not provide conformity. Lee et al. reported that pain, discomfort, and distress led to poor conformity [9]. We surgically treated patients who were not indicated for bracing and for whom bracing was unsuccessful.

The most common, early postoperative complications were pneumothorax and allergy-induced bar exposure. All instances of pneumothorax resolved spontaneously and there was no need for tube thoracostomy. Yuksel et al. and Ozkaya et al. also reported that pneumothorax was the most common, early postoperative complication [8,10,11]. Abramson et al. reported bar allergies in 2% and 4% of patients in two different series [11]. Implant removal was not required for those patients, as they responded to medical treatment. Yuksel et al. reported bar allergy in five of 172 patients [8]. In this study the bar allergy rate was 4.6% and surgical revision was performed for these patients.

Abramson et al. and Yuksel et al. attached stabilizers to the tips of the bars and placed screws within holes in the tips. These bars were then bilaterally secured using four cables [11-12]. Here, we used bar and stabilizer system, as well as four sternal cables, to supply the rigidity of the chest wall. Lee et al. reported that the cables split in all of their patients [9]. In our study, the cables split in seven (10.9%) patients, which constituted the most common, late follow-up complication; we repaired the split cables. Yuksel et al. reported cable breakdown in six of 172 patients [8]. Because the reoperation rate was high, we preferred to avoid excessive cable tightening during surgery.

Our hypothesis is that, ratio of cable breakdown can be decreased with refrainment from tightening the cables so much during surgery. Furthermore, a preoperative skin test for bar allergy should be routine, to reduce the need for re-operations caused by bar allergy. In the 2005 study by Abramson et al. (40 patients), the most common complication was adherence of skin to the bar in the first eight patients because of subcutaneous placement. Subpectoral bar placement eliminated this complication [2].

We prefer to maintain the bar on the chest wall for 3 years. An early bar removal may increase the possibility of recurrence. Yuksel et al. also preferred to maintain the bar in place for at least 2 years [11]. In our study, bars were removed from 15 patients after a mean duration of 23.5 ± 6.4 months (range, 19-27 months). Ozkaya et al. reported bar removal from 44 of 101 patients

after a median of 24.8 ± 4.5 months [10]. We removed bars early from nine adults because of poor bar compliance caused by chest wall rigidity. Sliding bars were removed early from four patients. Furthermore, pectus excavatum developed in two patients from whom bars were removed early.

The limitations of this study included its single-centre design and lack of a control group.

In conclusion, the Abramson technique is a rapid and simple treatment of chondromanubrial type PC. The incisions are small, surgery is brief, blood loss is minimal, hospitalization time is short, and pain is minimal. The technique should be preferred to open surgery, because of minimal complications and better cosmetic results.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

Ethics approval

The study was approved by the Ethics Committee of Health Sciences University (No: 19/2020).

Authors' contributions

TA, MA; Conceived and designed the analysis, collected the data, contributed data and analysis tools, performed the analysis, co-wrote the paper.

References

1. Suh J, Joo S, Lee GD, Haam SJ, Lee S. Minimally Invasive Repair of Pectus Carinatum in Patients Unsited to Bracing Therapy. *Korean J Thorac Cardiovasc Surg* 2016; 49: 92-8.
2. Özkaya M, Bilgin M. Minimally invasive repair of pectus carinatum by modification of the Abramson technique. *Wideochirurgia Tec M* 2018; 13: 383-7.
3. Kálmán A. Initial results with minimally invasive repair of pectus carinatum. *J Thorac Cardiovasc Surg* 2009; 138: 434-8.
4. Bilgin M, Oral A. Early results of minimal invasive surgery in patients with pectus carinatum. *Türk Gogus Kalp Dama* 2012; 20: 307-11.
5. Abramson H, D'Agostino J, Wuscovi S. A 5-year experience with a minimally invasive technique for pectus carinatum repair. *J Pediatr Surg* 2009; 44: 118-23.
6. Yuksel M, Bostanci K, Evman S. Minimally invasive repair of pectus carinatum using a newly designed bar and stabilizer: a single-institution experience. *Eur J Cardiothorac Surg* 2011; 40: 339-42.
7. Katrancioglu Ö, Akkas Y, Karadayi S, Sahin E, Kaptanoğlu M. Is the Abramson technique effective in pectus carinatum repair? *Asian J Surg* 2018; 41: 73-6.
8. Yuksel M, Lacin T, Ermerak NO, Sirzai EY, Sayan B. Minimally Invasive Repair of Pectus Carinatum. *Ann Thorac Surg* 2018; 105: 915-23.
9. Lee SY, Song IH, Lee SJ. Minimal invasive extrathoracic presternal compression using a metal bar for correction of pectus carinatum. *Pediatr Surg Int* 2014; 30: 25-30.
10. Özkaya M, Bilgin M. Minimally invasive repair of pectus carinatum: a retrospective analysis based on a single surgeon's 10 years of experience. *Gen Thorac Cardiovasc Surg* 2018; 66: 653-7.
11. toraks.org [Internet]. Minimal İnvaziv pektus karinatum düzeltme ameliyatı: Teknik ve uygulama, Marmara deneyimi; c2011 [cited 2011 June]. Available from <https://www.toraks.org/uploadFiles/book/file/1992011103239-196203.pdf>.
12. Abramson H, Aragon X, Blanco JB, Ciano A, Abramson L. Minimally invasive repair of pectus carinatum and how to deal with complications. *J Vis Surg* 2016; 2: 64.

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To cite this article: Pekçolaklar A, Nalbant M, Metin M. The factors affecting morbidity, mortality and survival in patients who underwent intrapericardial resections due to non-small cell lung cancer. Curr Thorac Surg 2021 Feb; 6 (1): 26-32.

Original Article

The factors affecting morbidity, mortality and survival in patients who underwent intrapericardial resections due to non-small cell lung cancer

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ABSTRACT

Background: Complete surgical resection has been the gold standard in the treatment of lung cancer. Intrapericardial approach may be required to resect the advanced stage tumors completely. This study aims to compare the morbidity and mortality rates of intrapericardial and standard pneumonectomies.

Materials and Methods: The records of patients operated on due to non-small cell cancer between the years 2001 and 2008 were evaluated retrospectively. The data including age, sex, respiratory function tests, tumor site, cell type, stage, resection type, complications, mortality and survival rates were recorded. The morbidity, mortality and survival rates of intrapericardial and standard pneumonectomies were compared.

Results: The study included 126 cases with pneumonectomy (90 standard, 36 intrapericardial) with mean age of 56.6 ± 8.42 years. Major morbidity rates of intrapericardial and standard groups were 30.6% and 21.1% respectively, and the difference was not significant ($p = 0.233$). Mortality rates of intrapericardial and standard groups were 8.3% and 8.9% respectively, and the difference was not significant ($p = 0.533$). The mean survival of all patients was 24.13 ± 3.13 months. The survival rate was significantly in the intrapericardial group compared to standard group (23 months vs 32 months, $p = 0.03$).

Conclusions: Intrapericardial approach is a safe method in the treatment of locally advanced lung cancer without increasing morbidity or mortality.

Keywords: pneumonectomy, lung cancer, mortality

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Doi: 10.26663/cts.2021.0005

Received 17.06.2020 accepted 13.10.2020

Introduction

Despite developing technology and struggle lung cancer has kept still its rank as one of the deadliest cancers [1]. The stage of the disease and the physical characteristics of the patient determine the strategy of the treatment. A complete surgical resection is superior to both chemotherapy and radiotherapy. Inoperability has decreased to acceptable rates by the improvements in staging and imaging modalities.

The surgical dissection especially is difficult in centrally located tumors, tumors invading pulmonary artery or veins, in the presence of lymph nodes attacking the hilar structures, hilar fibrosis or previous dissections. Opening the pericardium may usually be necessary in these situations to control the hilar vessels [2,3]. It also helps to access the proximal pulmonary artery and superior vena cava (SVC) when the centrally located tumor invade the pericardium.

The aim of the current study is to analyze the morbidity and mortality in patients who underwent pneumonectomy between 2001 and 2008 due to non-small cell lung cancer (NSCLC) by comparing the results of patients with standard pneumonectomy to pneumonectomy performed through the intrapericardial approach.

Material and Methods

The medical records of all patients with resections due to non-small cell lung cancer between 2001 and 2008 were evaluated retrospectively. The age, sex, pulmonary function tests (vital capacity and forced expiratory volume in the first second), location, histopathology and stage of the tumor, type of resection, morbidity, mortality, and survival of the cases were noted. Patients with incomplete resections, completion pneumonectomies, N2 disease detected by mediastinoscopy and cases with incomplete data were excluded from the study.

A thorough physical examination, routine biochemical tests, pulmonary function tests, arterial blood gas analysis, and fiberoptic bronchoscopic examination were performed in all cases. Computed thoracic tomography (CT) was performed in all cases to better localize the tumor and evaluate the mediastinal lymph nodes. The histopathological diagnosis was reached by either transbronchial or trans-thoracic needle biopsy. A positron emission tomography (PET/CT) was performed to exclude a distant metastasis and detect mediastinal lymph node invasion since 2003. In centrally located

tumors and patients with tumors over 3 cm a cranial magnetic resonance imaging (MRI) was performed.

Before surgery, all patients underwent pulmonary function tests to calculate the FEV1 and a perfusion scintigraphy was performed in patients with FEV1 less than 800 mL. A pO₂ over 60 mmHg and pCO₂ less than 45 mmHg were the limits of arterial blood gas analysis for performing the surgical resection. Patients with a history of heart disease, active chest pain, dysrhythmia, or age over 70 were referred to a cardiologist assess the cardiac risk. The cardiac risk was assessed by the consultant cardiologists according to the ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery. To detect the situation of the mediastinal lymph node standard or extended mediastinoscopy was performed in all cases. Patients with N2 disease were referred to oncology for neoadjuvant therapy, and with N3 disease for definitive chemotherapy. The pathology reports were examined, and patients were re-staged according to 8th TNM staging system reported by the international association of the study of lung cancer (IASLC) [4].

Standard posterolateral thoracotomy was performed in all cases after rigid bronchoscopy and double lumen endotracheal intubation under general anesthesia. Pulmonary vessels were stapled in the standard group while they were sutured with non-absorbable sutures in the intrapericardial group. Bronchi were closed with stapler in all cases. A prolene mesh was used when necessary to restore the pericardial defects. The opening of the pericardium was not routine. However, in cases where either pulmonary veins or artery was invaded intrapericardially, or presence of invasion of the superior vena cava or atrium then the pericardium was opened. Furthermore, when the hilar dissection was not possible due to fibrotic lymph nodes or dense adhesion the pericardium was opened. Chest wall resection was added to the planned procedure in cases with tumors invading the chest wall.

After the operation, all cases were monitored in the intensive care unit for at least 24 hours and patient-controlled analgesia was provided. Patients were seen at the outpatient unit after discharge every 3 months for the first 2 years and every 6 months then on to detect any possible recurrences. All minor and major complications were noted. Arrhythmias of any kind that deteriorated the general condition of the patient and required medical treatment were accepted as major complication.

Exitus in the first 30 days and 90 days was accepted early and late mortality rates, respectively. Survival data were provided from either outpatient records or phone calls to the patients or their relatives. The study was approved by the institutional review board (No: 2020-31) and was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Categorical variables were depicted as percentages and frequencies while continuous variables as means and standard deviation. Chi square test was used to compare the categorical data and Student's t-test was for comparing the means of the groups. To calculate the survival Kaplan-Meier survival analysis and for comparing the groups log-rank test were performed. Because the statistical calculations were based on the data of all cases included in the study period, the power analysis was not performed. IBM SPSS (version 15.0, SPSS Inc. Chicago, Illinois, United States) was used to perform all calcu-

lations and $p < 0.05$ was accepted as statistical analysis.

Results

During the study period a total of 393 patients underwent pulmonary resection, and 126 out of these were pneumonectomy. The remaining cases were lobectomy (201), segmentectomy (18), completion pneumonectomy (6), incomplete resection (12), N2 or N3 patients (57), and lost follow-up (23) and not included in the statistical analyses. Out of 126 pneumonectomy cases 36 were performed through the intrapericardial approach. This group was compared to remaining 90 cases with standard pneumonectomy with respect to morbidity, mortality, and survival.

Forty-two of the cases were male and the mean age of all cases was 56.6 ± 8.42 (Table 1). The rate of patients with neoadjuvant therapy was higher in the intrapericardial group but the difference did not reach statistical significance. Moreover, the tumor stage was more advanced in the intrapericardial group than the standard group.

Table 1. Clinical characteristics of the patients.

	Standard pneumonectomy (n=90)	Intrapericardial pneumonectomy (n=36)	P
Years	56.7±8.71 (39-76)	56.5±8.37 (35-72)	0.860
Sex (Male, Female)	M: 81 (90%) F: 9 (10%)	M: 32 (%88) F: 4 (%12)	0.540
Tumor Location (Right-Left)	R: 33 (36%) L: 57 (64%)	R: 23 (63%) L: 13 (37%)	0.009
FEV1 (L)	1.97±0.75	1.89±0.53	0.530
Co-morbidity	56 (62%)	24 (66%)	0.680
Neoadjuvant Therapy	5 (5.5%)	6 (16%)	0.070
Histopathology (Adenocarcinoma-SCC)	Adenocarcinoma: 39 (43%) SCC: 51 (57%)	Adenocarcinoma: 14 (39%) SCC: 22 (61%)	0.690
TNM Stage	Stage II: 34 (38%) Stage IIIa: 50 (57%) Stage IIIb: 6 (5%)	Stage II: 4 (12%) Stage IIIa: 30 (82%) Stage IIIb: 2 (6%)	0.020
Indications for intrapericardial pneumonectomy		SPV invasion: 15 (42%) IPV invasion: 5 (14%) Atrium invasion: 6 (16%) PA invasion: 3 (8%) SVC invasion: 3 (8%) Difficult hilar dissection: 2 (6%) Anatomic variation: 2 (6%)	

Abbrev.: SPV; superior pulmonary vein, IPV; inferior pulmonary vein, PA; pulmonary artery, SVC; superior vena cava, SCC; Squamous Cell Carcinoma

Table 2. The distribution of the complications.

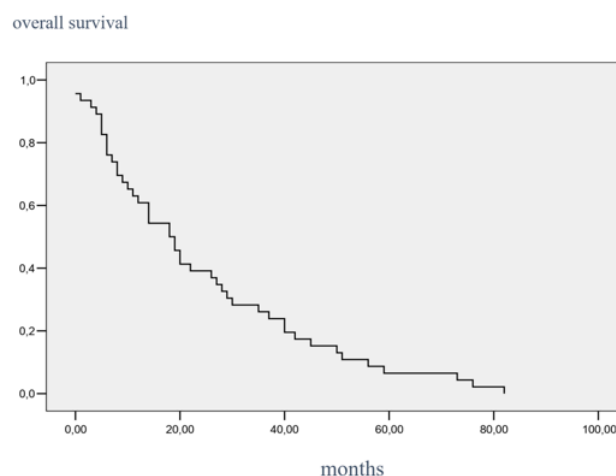
	Standard pneumonectomy n=19 (21.1%)	Intrapericardial pneumonectomy n=11 (30.6%)	P
Arrhythmia	23 (26%)	11 (31%)	0.650
Bronchopleural fistula	11 (12%)	6 (16%)	0.520
Hemorrhage	5 (6%)	2 (5%)	0.640
Pneumonia	6 (7%)	3 (8%)	0.710
Hoarseness	2 (2%)	1 (3%)	0.630
Empyema	4 (4%)	1 (3%)	0.550
Pulmonary emboli	1 (1%)	1 (3%)	0.490
Vena cava superior thrombus	-	1 (3%)	-
Cerebral emboli	-	1 (3%)	-
Myocardial infarction	2 (2%)	-	-

Arrhythmias were the most frequent symptom in both groups whereas bronchopleural fistula was the most mortal complication (Table 2). Major morbidity rate was calculated in the intrapericardial group and the standard group 30.6% (11 cases) and 21.1% (19 cases), respectively, but the difference did not reach statistical significance ($p = 0.263$). The treatment of arrhythmias was provided by the consultant cardiologist of the hospital. A total of seven cases developed postoperative hemorrhage and all required thoracotomy to control the source of bleeding. The most demanding complication was bronchopleural fistula experienced in 17 cases. The initial intervention was tube thoracostomy and appropriate antibiotics in all cases. The fistula was minor and responded to the treatment in seven cases. Two out of 10 remaining cases underwent omentoplasty in the early postoperative period. Thoracostoma was performed in the remaining eight cases. After serial debridement of the cavity omentoplasty was added in the cases. Two cases were not eligible for omentoplasty and followed at outpatient debridement and wound dressing. In cases with pneumonia appropriate antibiotics were given and pulmonary physiotherapy was also added. Mechanical ventilation was added to the treatment when the patient developed respiratory failure.

Three cases (8.3%) in the intrapericardial group died during the first month of operation. One of the two cases who had right pneumonectomy and partial vena cava superior resection died from thrombus development in the SVC, and the other died from cerebral emboli. The last patient with left pneumonectomy in this group died from pulmonary embolism. In the standard group the rate mortality in the first 30 days was 8.9% (8 cases).

Six cases died from pneumonia and respiratory failure because of bronchopleural fistula development and the remaining 2 died from myocardial infarction. The difference between the mortality rates of the groups was not statistically significant ($p = 0.533$). Univariate analysis showed that right pneumonectomy affected both morbidity and mortality when compared to left pneumonectomy ($p = 0.002$).

The mean survival of all cases was 24.13 ± 3.13 months (Figure 1). Intrapericardial and standard groups had 23 ± 6.37 months and 32 ± 5.53 months of mean survival times, respectively, and the difference was found statistically significant ($p = 0.030$). In survival analysis age (over 60, 21 months vs younger 60, 37 months) and advanced tumor stage (stage 3, 22 months vs stage 2, 39 months) were found to significantly affect the survival adversely ($p = 0.001$).

**Figure 1.** Overall survival of all patients

Discussion

Complete resection is sine qua non in the treatment of lung cancer surgery. To reach this goal extended resections are required when necessary [5,6]. These extended resections carry more morbidity and mortality when compared to standard procedures [7,8]. Hilar dissection is especially difficult in the presence of centrally located tumors invading pulmonary artery or veins, attacked and fixed lymph nodes preventing the vascular dissection, and previous hilar dissection. These situations require intrapericardial approach to control the vascular structures to make complete resection possible [9]. Allison reported that intrapericardial approach was especially safer and faster in the treatment of tumors invading the pericardium in 1946 [10]. Later, in 1948 Brock reported intrapericardial approach (Block dissection pneumonectomy) as more curative operation [11].

In this series the most frequent indication for opening the pericardium was the invasion of the pulmonary veins like many series in the literature [9,12,13]. In contrast, Dartavelle et al. reported on 30 cases of T4 tumors invading the superior vena cava [14]. In the recent decades some advanced staging techniques, transesophageal echocardiography (TEE), and videopericardioscopy (VPC), have been used to better delineate the intrapericardial invasion and to prevent futile thoracotomies and incomplete resections [15-17]. During the study period TEE was unavailable and videopericardioscopy was rarely performed. The superior vena cava invasion ranked the 5th place and a graft was used to restore the continuity.

The morbidity and mortality rates of pneumonectomies performed due to lung cancer has been reported as low as 24% to 59% and from 3% to 12% respectively [7,18,19]. Although right pneumonectomies have higher morbidity and mortality rates it was rarely reported that intrapericardial pneumonectomies carried higher rates compared to standard approach. Intrapericardial pneumonectomies had acceptable morbidity and mortality rates despite of higher supraventricular arrhythmia rates. Krowka et al reported that the reason for post-operative arrhythmias were pericardial irritation, intrapericardial ligation of the pulmonary vessels, extended resections, longer operation time, and atrial injury [20]. In a large series with 259 cases Foroulis et al reported that right pneumonectomy over left and intrapleural pneumonectomy over standard pneumonectomy had higher arrhythmia risk [21]. The overall

morbidity rate in this series was around 24% and was at the lower edge of the literature. The possible reason could be the definition and classification of the complications were not uniform. Whereas the overall mortality of the study was 8.7% and was close to the upper limit of the study. The advanced tumor stage and high rate of right pneumonectomy could explain the relatively high rate of mortality.

The most challenging complication after pneumonectomy is the development of bronchopleural fistula. The risk of BPF has been reported between 2.1% and 8%, and intrapericardial ligation of the vessels did not increase the risk [22]. In this study the rate of BPF was higher than the literature, and, the risk was found higher in the intrapericardial group besides. Existence of more advanced tumor stage and higher number of right pneumonectomy in this group might explain this discrepancy. Furthermore the study was performed in a teaching hospital. The operations were performed by various surgeons and fellows with different experiences.

Pricopi et al reported on that the right side, advanced age, and advanced tumor stage increased the mortality whereas the extent of the resection did not change it in a series with 2064 cases [19]. Similarly, Park et al pointed out that pneumonectomy had higher mortality rates when compared to lesser resections, but he also reported that intrapericardial approach did not affect the mortality rate significantly [23].

The five-year survival of non-small cell lung cancer was reported between 21% and 31% in the literature [24,25]. In a series consisting of 55 pneumonectomies with stage IIIA overall survival was found 29%, and interestingly 42% of the group had 20% five-year survival rate despite of N2 metastases [26]. Riquet et al reported on 32% five-year survival rate in a large series consisting of 1466 patients of whom 342 had extended pneumonectomy [27]. In that study advanced age, advanced tumor stage, extended pneumonectomy, and adenocarcinoma adversely affected the survival, but right pneumonectomy did not affect the survival when compared to left side. In the current study the five-year survival rate was found 21%. The possible reason for this relatively low survival rate could be higher number stage III cases than stage II. Similarly, advanced age and advanced tumor stage adversely affected the survival. The reason for lower survival rate in the intrapericardial group could be higher tumor stage in the group.

Limitations of the study

The retrospective nature of the study, limited number of patients, insufficient number of cases representing the subgroups, and inhomogeneity of the groups with respect to tumor stage were the limitations of the current study. Moreover, the study comprises limited number of variables affecting the morbidity, mortality, and the survival. Other limitations of the study might be missing clinical characteristics of the cases like TNM subsets and insufficiencies in the follow up such as local and systemic recurrences.

As a conclusion, intrapericardial dissection could be necessary in the treatment of locally advanced non-small cell lung cancer to reach a complete resection with all negative tumor margins. Invasion of proximal pulmonary vessels, pericardium or left atrium may adversely affect the prognosis, but they do not affect the operability. Though intrapericardial approach increase the supraventricular arrhythmia rates it can be performed with acceptable morbidity and mortality rates.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

Ethics approval

The study was approved by the Ethics Committee of Health Sciences University (No: 2020-31).

Authors' contributions

AP; Conceived and designed the analysis, collected the data, contributed data/analysis tools, performed the analysis, co-wrote the paper, MN; contributed data/analysis tools, co-wrote the paper MM; co-wrote the paper.

References

1. Kara F, Ilter H, Keskinilic F. Turkish Cancer Statistics 2015, Ministry of Health. Ankara 2018; 1-64.
2. Hasdiraz L, Oguzkaya F, Bilgin M. An evaluation of pulmonary resections accompanied by intrapericardial ligation for pulmonary cancers. *Turkish J Thorac Cardiovasc Surg* 2007; 15: 123-6.
3. Olcmen A, Kutlu A, Dincer I, Bekar Y, Olcmen M. Intrapericardial approach in lung resections (27 cases). *Turkish J Thorac Cardiovasc Surg* 1996; 4: 109-13.
4. Sobin LH, Wittekind C. International Union Against Cancer (UICC) TNM classification of malignant tumours. 6. New York: Wiley; 2002.
5. Loscertales J, Jime'nez-Mercha'n R, Congregado- Loscertales M, Arenas-Linares C, Giro' n-Arjona JC, Arroyo Tristan A et al. Usefulness of videothoroscopic intrapericardial examination of pulmonary vessels to identify resectable clinical T4 lung cancer. *Ann Thorac Surg* 2002; 73: 1563-6.
6. Bemard A, Deschamps C, Allen MS, Miller DL, Trastek WF, Jenkins GD et al. Pneumonectomy for malignant disease: factors affecting early morbidity and mortality. *J Thorac Cardiovasc Surg* 2001; 121: 176-82.
7. Harpole DH Jr, DeCamp MM Jr, Daley J, Hur K, Oprian CA, Henderson WG, Khuri SF. Prognostic models of thirty-day mortality and morbidity after major pulmonary resection. *J Thorac Cardiovasc Surg* 1999; 117: 969-79.
8. Stephan F, Boucheseiche S, Hollande J, Flahault A, Cheffi A, Bazelly B, Bonnet F. Pulmonary complications following lung resection. A comprehensive analysis of incidence and possible risk factors. *Chest* 2000; 118: 1263-70.
9. Spaggiari L, D'Aiuto M, Veronesi G, Pelosi G, de Pas T, Catalano G et al. Extended pneumonectomy with partial resection of the left atrium without cardiopulmonary bypass for lung cancer. *Ann Thorac Surg* 2005; 79: 234-40.
10. Allison PR. Intrapericardial approach to lung root in the treatment of bronchial carcinoma by dissection pneumonectomy. *J Thorac Surg* 1946; 15: 99.
11. Johnson J, Kirby CK, Blakemore WS. Should we insist on radical pneumonectomy as a routine procedure in the treatment of carcinoma of the lung? *J Thorac Surg* 1958; 3: 309.
12. Rendina EA, Venuta F, Ibrahim M. Intrapericardial pneumonectomy. *Multimed Man Cardiothorac Surg* 2006; (109): mmcts.2004.000091.
13. T Fukuse, H Wada, S Hitomi. Extended operation for non-small cell lung cancer invading great vessels and left atrium. *Eur J Cardiothorac Surg* 1997; 11: 664-9.
14. Darteville PG, Mitilian D, Fadel E. Extended surgery for T4 lung cancer: a 30 years' experience. *Gen Thorac Cardiovasc Surg* 2017; 65: 321-8.

15. Wang KY, Lin CY, Kuo-Tai J, Yuan L, Chang HJ. Use of trans-esophageal echocardiography for evaluation of resectability of lung cancer. *Acta Anaesthesiol Sin* 1994; 32: 255-60.
16. Loscertales J, Jimé'nez-Mercha'n R, Congregado- Loscertales M, Arenas-Linares C, Carlos Giro'n-Arjona J, Arroyo Tristan A et al. Usefulness of video thoracoscopic intrapericardial examination of pulmonary vessels to identify resectable clinical T4 lung cancer. *Ann Thorac Surg* 2002; 73: 1563-6.
17. Pompeo E, Tacconi F, Mineo TC. Flexible videopericardioscopy in cT4 nonsmall-cell lung cancer with radiologic evidence of proximal vascular invasion. *Ann Thorac Surg* 2007; 83: 402-8.
18. Ginsberg RJ, Hill LD, Eagan RT, Thomas P, Mountain CF, Deslauriers J et al. Modern thirty-day operative mortality for surgical resections in lung cancer. *J Thorac Cardiovasc Surg* 1983; 86: 654-8.
19. Pricopi C, Mordant P, Rivera C, Arame A, Foucault C, Dujon A et al. Postoperative morbidity and mortality after pneumonectomy: a 30-year experience of 2064 consecutive patients. *Interact Cardiovasc Thorac Surg* 2015; 20: 316-21.
20. Krowka MJ, Pairolero PC, Trastek VF, Payne WS, Bernatz PE. Cardiac dysrhythmia following pneumonectomy. *Chest* 1987; 9: 490.
21. Foroulis CN, Kotoulas C, Lachanas H, Lazopoulos G, Konstantinou M, Lioulas AG. Factors associated with cardiac rhythm disturbances in the early post-pneumonectomy period: a study on 259 pneumonectomies. *Eur J Cardiothorac Surg* 2003; 23: 384.
22. Deschamps C, Bernard A, Nichols FC 3rd, Allen MS, Miller DL, Trastek VF et al. Empyema and bronchopleural fistula after pneumonectomy: factors affecting incidence. *Ann Thorac Surg* 2001; 72: 243.
23. Park B, Cho JH, Kim HK, Choi YS, Zo JI, Shim YM, Kim J. Long-term survival in locally advanced non-small cell lung cancer invading the great vessels and heart. *Thorac Cancer* 2018; 9: 598-605.
24. Ramnath N, Demmy TL, Antun A, Natarajan N, Nwogu CE, Loewen GM et al. Pneumonectomy for bronchogenic carcinoma: analysis of factors predicting survival. *Ann Thorac Surg* 2007; 83: 1831-6.
25. Deslauriers D, Ugalde P, Miro S, Deslauriers DR, Sylvie Ferland S, Bergeron S et al. Long-term physiological consequences of pneumonectomy. *Semin Thoracic Surg* 2011; 23:196-202.
26. .Shah AA, Worni M, Kelsey CR, Onaitis MW, D'Amico TA, Berry MF. Does pneumonectomy have a role in the treatment of stage IIIA non-small cell lung cancer? *Ann Thorac Surg* 2013; 95: 1700-7.
27. Riquet M1, Mordant P, Pricopi C, Legras A, Foucault C, Dujon A et al. A review of 250 ten-year survivors after pneumonectomy for non-small-cell lung cancer. *Eur J Cardiothorac Surg* 2014; 45: 876-81.

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To cite this article: Onay Mahmuti MS, Sezen CB, Erdogan V, Unver N, Metin M. Cyst of Mullerian Origin in anterior mediastinum: a case report Curr Thorac Surg 2021 Feb; 6(1): 33-35.

Case Report

Cyst of Mullerian Origin in anterior mediastinum: a case report

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ABSTRACT

In this report, a case of Hattori's cyst of Mullerian (HMC) origin, located in the anterior mediastinum is evaluated in light of the literature. A 33-year-old woman presented to our clinic with chest pain. A computed tomography scan of the patient's thorax revealed a 5x6 cm lesion located on the left paracardiac region. Following the excision of the cyst, a diagnosis of mediastinal HMC was made. Our case shows that cases of MHC, which are rare in the posterior mediastinum, can also be seen in the anterior mediastinum and should be included in the differential diagnosis.

Keywords: Hattori's cyst, Mullerian cyst, surgery, mediastinal cyst, mullerian differentiation

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Doi: 10.26663/cts.2021.0006

Received 21.10.2020 accepted 15.11.2020

Introduction

Primary congenital mediastinal cysts are rare and make-up 10-12% of mediastinal masses [1]. Several types of cysts can be seen in the mediastinum such as thymic, parathyroid, pericardial, neurogenic, bronchogenic, esophageal, and coelomic cysts. However, the most frequently seen type is bronchogenic cysts. When Hattori first identified a mediastinal cyst with Mullerian origin in 2005, he determined that this cyst was lined by ciliated non-stratified cuboidal or columnar epithelium with no cytological atypia [2]. To date, these cysts have been described as rare in the literature. In this report, we evaluate a case of Hattori's Cyst of Mullerian origin, which we found to be located in the anterior mediastinum, in the light of literature.

Case Report

A 33-year-old woman presented to our clinic with non-specific chest pain. She was a non-smoker and had no comorbidities. A CT scan of her thorax revealed a 5x6 cm lesion located on the left paracardiac region (Figure 1).

Surgical resection was planned. The patient underwent video-assisted thoracoscopic surgery (VATS). On exploration, a lesion of 5x5 cm, filled with serous fluid, on the left paracardiac region was seen. The cyst showed invasion to the mediastinal pleura; however, it had no invasion to the lungs. Total excision of the cyst was performed. Postoperative histopathological examination showed the cyst wall consisted of smooth muscle and connective tissues lined by ciliated epithelium with no cytological atypia. Immunohistochemical examination showed a positive reaction for Estrogen Receptor (ER) and Wilms' Tumor Gene 1 (WT-1), and negative for Calretinin (Figures 2a, b). Based on these findings, the patient was diagnosed with Hattori's Cyst of the mediastinum.



Figure 1. Thorax CT scan showing Hattori's Cyst (arrow).

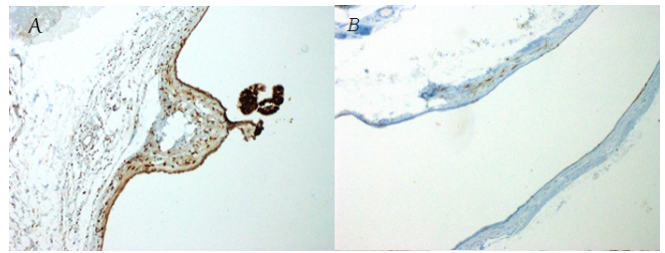


Figure 2. (A) Immunohistochemical staining showing a positive reaction of cell lining for estrogen receptor (x100), (B) immunohistochemical staining showing the negative reaction of the cell lining to calretinin (x100).

Written informed consent was obtained from the patient for publication of her data.

Discussion

Extra genitourinary tract or pelvic cysts with Mullerian differentiation are rare. They are generally seen in the skin and retroperitoneal cavity in women [3]. Primary congenital mediastinal cysts are rarer and constitute 12-30% of all masses seen in the mediastinum [1]. Hattori found that prior to describing this cyst, mediastinal cysts were misdiagnosed as bronchogenic cysts due to their ciliated epithelium. Thomas-de-Montpreville et al. [3] evaluated 163 consecutive mediastinal non-neoplastic cysts retrospectively and detected cysts conforming to Hattori's Cyst definition in only 9 cases (5.5%). They underlined that three of these 9 cases were diagnosed with a pleuropericardial cyst at first glance due to the benign cystic nature. Our case was acknowledged to be Hattori's Cyst, since ER and WT-1 were positive and Calretinin negative.

Regarding mediastinal cysts, a decision to operate is frequently made if the patient is symptomatic. As the size of the cyst increases, symptoms (chest pain, shortness of breath, palpitations, coughing, etc.) due to compression increase as well. Follow-up in the outpatient clinics is usually recommended to those patients with asymptomatic, small cysts [4]. Since our patient had symptoms of chest pain, and the cyst was 5 cm, we decided to perform surgery.

To date, 26 cases of Mediastinal Hattori's Cyst have been published in the literature, including our case. In these cases, the size, location, and symptoms caused by the cyst were investigated, and it was determined that cysts were more common in the left thoracic cavity compared to the right [5].

The cyst of Mullerian origin in the mediastinum is still unclear. The reason for the cysts being at the thoracic location is because of the developmental misplacement of the endosalpingeal or endo-salpingeal epithelium. One theory is that coelomic epithelium develops on the cranial end of the plica mesonephrica at the level of the third to fifth thoracic vertebral blastema [6]. All of the cases published in the literature define the cyst in the posterior mediastinum and paravertebral area. The case we present is the first case of a cyst of embryonic Mullerian origin in the anterior mediastinum.

The prognosis of all cases of Hattori's Cyst published to date has been shown to be good. Recurrence after surgical resection has not been reported. We performed total excision of the cyst in order to prevent a recurrence. It is difficult to make a preoperative diagnosis; therefore, it is essential that the differential diagnosis of these cysts should be made after resection. This way differentiation of these cystic tumors from bronchogenic or neurogenic cysts can be achieved. Detailed histopathological and immunohistochemical evaluation is imperative for definitive diagnosis.

Previously published 25 cases refer to Hattori's Cyst in the posterior mediastinum. Our case shows that Hattori's Cyst can also be seen in the anterior mediastinum and should be included in the differential diagnosis. Further clinical studies are needed to have more information on this subject.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support.

Authors' contributions

MSOM; Collected the data, performed the analysis, co-wrote the paper, CBS; performed the analysis, co-wrote the paper, VE, MM; co-wrote the paper, NU; contributed data/analysis tools.

References

1. Simmons M, Duckworth LV, Scherer K, Drew P, Rush D. Mullerian cysts of the posterior mediastinum: report of two cases and review of the literature. *J Thorac Dis* 2013; 5: E8-E10.
2. Hattori H. Ciliated cyst of probable mullerian origin arising in the posterior mediastinum. *Virchows Arch* 2005; 446: 82-4.
3. Thomas-de-Montpréville V and Dulmet E. Cysts of the posterior mediastinum showing müllerian differentiation (Hattori's cysts). *Ann Diagn Pathol* 2007; 11: 417-20.
4. Kocaturk CI, Sezen CB, Aker C, Kalafat CE, Bilen S, Kutluk AC et al. Surgical approach to posterior mediastinal lesions and long-term outcomes. *Asian Cardiovasc Thorac Ann* 2017; 25: 287-91.
5. Sekimura A, Iwai A, Funasaki A, Motono N, Usuda K, Uramoto H. Müllerian cyst in posterior mediastinum: A report of a case. *Int J Surg Case Rep* 2018; 49: 163-5.
6. Batt RE, Mhawech-Fauceglia P, Odunsi K, Yeh J. Pathogenesis of Mediastinal Paravertebral Müllerian Cysts of Hattori: Developmental Endosalpingiosis-Müllerianosis. *Int J Gynecol Pathol* 2010; 29: 546-51.

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To cite this article: Ceylan KC, Heskiloğlu C, Cansun F, Örs Kaya Ş, Yener AG. A case of destroyed lung caused by a chronic lymphocytic leukemia with mass effect. *Curr Thorac Surg* 2021 Feb; 6(1): 36-38.

Case Report

A case of destroyed lung caused by a chronic lymphocytic leukemia with mass effect

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ABSTRACT

Tuberculosis and bronchiectasis are the most common causes of the destroyed lung. Mediastinal masses, which cause bronchial compression, can also cause bronchiectasis. Chronic lymphocytic leukemia (CLL) is the most common subtype of leukemia, and it can rarely cause bronchiectasis and destroyed lungs by causing a mass effect in the mediastinum. A 50-year-old female patient with a history of tuberculosis in her childhood admitted to our clinic with dyspnea, cough, and chest pain. During the clinical examinations, a solid mass with approximately 46x33 mm in size was observed in the posterior mediastinum, compressing the left main bronchus and the entire left lung was destroyed. Since the patient had no definite diagnosis and was symptomatic, a surgical treatment was planned, and left pneumonectomy was performed together with mediastinal mass excision. As a result of the extracted specimen histopathology, bronchiectasis was present, and the mediastinal mass was consistent with chronic lymphocytic leukemia. The patient did not experience any postoperative complications and was referred to the oncology clinic for follow-up and treatment. Herein, we aimed to present a case with chronic lymphocytic leukemia mass in the posterior mediastinum compressing the left main bronchus, which caused bronchiectasis and destroyed lung with the literature's accompaniment.

Keywords: destroyed lung, bronchiectasis, mediastinal neoplasm, chronic lymphocytic leukemia, thoracotomy, pneumonectomy

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Doi: 10.26663/cts.2021.0007

Received 22.09.2020 accepted 14.01.2021

Introduction

The term “destroyed lung” is used for widespread lung injury caused by pulmonary infectious diseases [1]. The most common causes are bronchiectasis and tuberculosis [2]. Chronic lymphocytic leukemia (CLL) is a disease that occurs with the increase of mature lymphocytes without proliferation in the spleen, blood, bone marrow, lymph nodes. Thoracic symptoms of CLL can be classified as leukemia or treatment-related immunodeficiency, pleural effusions, and specific bronchopulmonary involvement because of lymphocytic infiltration. It is rare for CLL to cause bronchial compression due to the mass effect.

Accompanied by the literature, we aimed to present a destroyed lung case caused by CLL's mass effect in the posterior mediastinum, since it is infrequent.

Case Report

A 50-year-old female patient was applied to another hospital 5 years ago due to screening for a job admission and a mediastinal mass was detected in computed tomography. In this center, a transbronchial biopsy was performed. However, a definitive diagnosis could not be done. At that time the patient applied to our clinic, and in the computed tomography report a 2x1.7 cm soft tissue lesion in the left paraesophageal area was detected. Hospitalization was recommended for further examination and treatment, but the patient refused, as she had no symptoms and discontinued her follow-ups.

The second application of the patient to our clinic was 5 years later with complaints of shortness of breath, cough and chest pain. In her anamnesis, she had a history of tuberculosis during the childhood period. At the physical examination, respiratory sounds could not be detected on the left hemithorax and there was no palpable lymphadenopathy at any other part of the body. The sedimentation rate was 25mm/h. The other laboratory parameters were in normal ranges except mild leukocytosis. There was no growth in the tuberculosis culture of the bronchial sample taken from the patient. Abdominal ultrasonography was normal. Computed tomography of the thorax revealed a well-circumscribed, 46x33 mm mass lesion in the left para-esophageal area, springing the descending aorta to the left and compressing the left main bronchus. The left lung was destroyed, mediastinal shift was apparent together with the hyperaeration of the right lung (Figure 1).

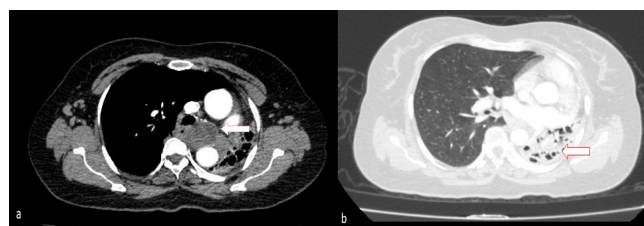


Figure 1. Thoracic CT images showing the mass lesion in the left para-esophageal area (a), the destroyed lung (b).

During the fiberoptic bronchoscopy, a long segment external compression was detected starting from the trachea's distal level descending to the left main bronchus. Diffuse edema and abundant mucopurulent secretion was present in the left main bronchus. *Pseudomonas aeruginosa* was reproduced in the culture. Antibiotic treatment of piperacilin-tazobactam in compliance with the culture taken was initiated. Respiratory function test results were as follows; FEV1: 1.07 (51%), FVCex: 1.57 (57%), FEV1/FVC: 76% (96%). According to lung ventilation-perfusion scintigraphy results, no functional lung tissue was reported in the left lung area and the patient was appropriate for left a pneumonectomy. With the present findings, an operation was planned for both the diagnosis and treatment. Mediastinal mass excision and pneumonectomy was performed via left thoracotomy. The patient, was discharged on the 5th postoperative day without any complications. The histopathological diagnosis was bronchiectasis, and the mediastinal mass was compatible with chronic lymphocytic leukemia (Figure 2). The patient was referred to the oncology clinic for further treatment.

Written informed consent was obtained from the patient for publication of her data.

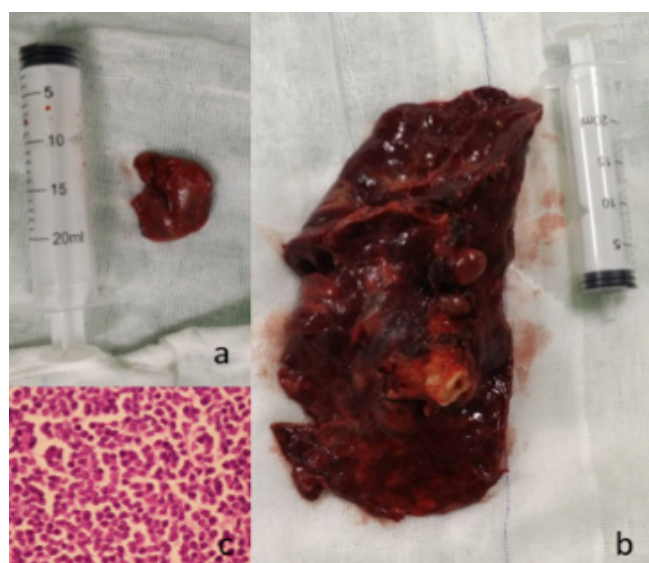


Figure 2. Excised material of the mass lesion (a), pneumonectomy specimen (b) and histopathological view of small 129 atypical lymphoid cells (H&E; x1000) (c).

Discussion

Tuberculosis comes first among the causes of the destroyed lung, followed by chronic pulmonary infections such as bronchiectasis, chronic interstitial pneumonia, organizing pneumonia, and aspergillosis [3]. Pneumonectomy is necessary due to complications such as massive hemoptysis caused by destroyed lung, secondary fungal infections, secondary amyloidosis, or pulmonary-systemic shunt [4]. There was a history of tuberculosis in childhood, and the patient had a destroyed lung due to bronchiectasis that developed with the compression of the main bronchus by the mediastinal mass. Although the CT images of 5 years ago were not available, a report for a bronchial compression or a destroyed lung were not mentioned at that time. Current thorax CT showed that, the mediastinal mass doubled in size and due to the bronchial compression the lung parenchyma was destroyed.

Differential diagnosis is important in patients with mediastinal mass. For this reason, establishment of the diagnosis by preoperative PET/CT and a tissue biopsy is recommended [5]. Such as, a diagnosis of lymphoma obtained by biopsy will direct the primary treatment of the patients mostly medically. In our case, the mediastinal mass was suitable for a transbronchial biopsy and PET-CT could have been done. However, the patient with the destroyed lung had a definitive indication for a surgical intervention so the former interventions had not been performed. Left pneumonectomy and mediastinal mass excision were performed for definite diagnosis and treatment.

CLL patients may be asymptomatic at the time of diagnosis or present with B symptoms (weight loss, fever, night sweats), pallor caused by anemia, hemorrhage due to thrombocytopenia, symptoms due to lymph node or organ involvement, and frequent infections because of hypogammaglobulinemia. The most common finding on physical examination is lymphadenopathy (LAP), and splenomegaly. Hepatomegaly can also be seen [6]. Thoracic complications are not uncommon in hospitalized patients with CLL, but the specific etiology and incidence of these complications are limited [7]. Our case had nonspecific symptoms such as cough and chest pain at the time of admission. When the literature is reviewed, CLL cases with bronchial compression due to mass effect after mediastinal involvement and causing destroyed lung are rare [8].

In conclusion, the coexistence of CLL, which causes bronchiectasis and destroyed lung by compressing the bronchi with mass effect, is rare. Hematological malignancies should be kept in mind in the presence of bronchiectasis and mediastinal mass for which surgery is considered.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support.

Authors' contributions

CH, KCC; conceived and designed the current case report. FC; collected the clinical data, AGY; examined the pathological preparates. KCC, CH, FC; co-wrote the paper. All authors discussed the case with under the literature data and contributed to the final manuscript.

References

1. Conlan AA, Lukanich JM, Shutz J, Hurwitz SS. Elective pneumonectomy for benign lung disease: modern-day mortality and morbidity. *J Thorac Cardiovasc Surg* 1995; 110: 1118-24.
2. Yalçınkaya İ, Özbay B. Harap akciğer (iki olgu sunumu). *Van Tıp Der* 2001; 8: 79-81.
3. Halezeroglu S, Keleş M, Uysal A, Celik M, Senol C, Hacıbramoğlu G et al. Factors affecting postoperative morbidity and mortality in destroyed lung. *Ann Thorac Surg* 1997; 64: 1635-8.
4. Mısırlıoğlu AK, Bayram S, Kırıl H, Ağca MÇ, Akylı FT, Alpay L et al. Factors affecting complication rates of pneumonectomy in destroyed lung. *Türk Gogus Kalp Damar Cerrahisi Derg* 2018; 26: 272-8.
5. Kim BT, Lee KS, Shim SS, Choi JY, Kwon OJ, Kim H et al. Stage T1 non-small cell lung cancer: preoperative mediastinal nodal staging with integrated FDG PET/CT - a prospective study. *Radiology* 2006; 241: 501-9.
6. Rai KR, Sawitsky A, Cronkite EP, Chanana AD, Levy RN, Pasternack BS. Clinical staging of chronic lymphocytic leukemia. *Blood* 1975; 46: 219-34.
7. Carmier D, Dartigeas C, Mankikian J, Rousselot-Denis C, Lissandre S, Diot P et al. Serious bronchopulmonary involvement due to chronic lymphocytic leukaemia. *Eur Respir Rev* 2013; 22: 416-9.
8. Ahmed S, Siddiqui AK, Rossoff L, Sison CP, Rai KR. Pulmonary complications in chronic lymphocytic leukemia. *Cancer* 2003; 98: 1912-7.

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Case Report

Extracorporeal membrane oxygenation after blunt trauma: when? how?

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ABSTRACT

In patients with acute respiratory distress syndrome (ARDS), mechanical ventilators (MV) are still key devices in the treatment. However, in cases where MV remains insufficient, extracorporeal membrane oxygenation (ECMO) is the most important treatment modality. Venovenous extracorporeal membrane oxygenation (VV-ECMO) was applied to a 42-year-old female patient due to ARDS developed after an in-car traffic accident, and it was successfully terminated. The case was presented to discuss the management of MV and ECMO in patients with ARDS developed after blunt trauma in the light of current literature.

Keywords: multiple trauma, acute respiratory distress syndrome, mechanical ventilation, extracorporeal circulation

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Doi: 10.26663/cts.2021.0008

Received 14.12.2020 accepted 14.01.2021

Introduction

Mechanical ventilators (MV) constitute the most important part of the treatment in patients with acute respiratory distress syndrome (ARDS) developed after blunt trauma. However, in cases where MV remains insufficient, the use of extracorporeal membrane oxygenation (ECMO) for appropriate patients reduces mortality [1-3].

Venovenous ECMO (Vv-ECMO) was applied to a 42-year-old female patient due to ARDS developed after an in-car traffic accident, and it was successfully terminated. The case was presented to discuss when and how MV and ECMO should be performed in patients with ARDS developed after blunt trauma in the light of current literature.

Case Report

A 42-year-old woman who was evaluated in the emergency clinic after an in-car traffic accident had a pulse of 85 beats/min, arterial blood pressure of 128/72 mm/Hg, and peripheral oxygen saturation (SpO₂) of 95% while breathing ambient air. In her physical examination, she was conscious, breathing sounds were natural. Palpation revealed tenderness in both posterior ribs, left arm, and pelvic area. The biochemical analysis was normal. Complete blood count values were as follows: Hb: 11.5 g/dl, Htc: 35.3%, Wbc: 21700/mm³, Plt: 220/mm³. Arterial blood gas (ABG) values were as follows: pH: 7.39, PaO₂: 93 mmHg, PaCO₂: 38 mmHg, and HCO₃: 24. No hemopneumothorax was observed at anteroposterior chest radiography (APCR) and thoracic computed tomography (CT), whereas there were displaced fractures in the left 3rd-12th ribs and the right 6th and 7th ribs, and a moderate contusion on the left lower lobe posterior (Figure 1).

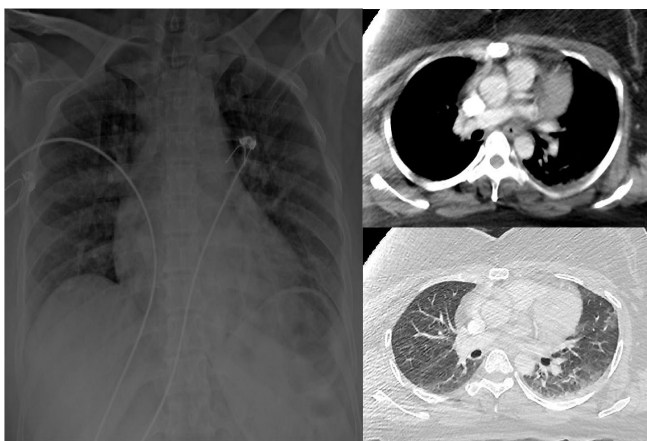


Figure 1. Anteroposterior chest X-ray and thorax computed tomography showing rib fractures and moderate contusion on the posterior lower lobe on the left.

Other X-ray graphs showed fractures in the pelvis and left humerus. On the second day, the thoracic CT showed progression of the pulmonary contusion (SpO₂ 85%). Despite non-invasive ventilation (NIV), the patient's clinical condition deteriorated, and the patient was intubated. After observing bilateral infiltrations in APCR (Figure 2), the absence of right heart overload findings on echocardiography (ECHO), the value of PaO₂/FiO₂ (P/F ratio) below 80, SpO₂ not exceeding 45% despite maximum support with MV, and PaO₂ not exceeding 40 mmHg in ABG, the patient was diagnosed with ARDS. As a result, Vv-ECMO application was decided.

During ECMO noradrenaline infusion was started for the normotensive target. After the first 24 hours, enteral nutrition and an empirical antibiotic therapy were started. Due to resistant hypoxemia on the first day of ECMO, PEEP was set to 14, FiO₂ to 100%, pressure support above PEEP to 18 mmHg, and respiratory rate to 16 in P-SIMV mode at MV. The ECMO was set to "full flow" while the heparin infusion was titrated according to the activated clotting time. Upon achieving the target in ABG in the first 24 hours, PEEP remained constant and the FiO₂ ratio was gradually lowered first in MV and then in ECMO. ECMO was terminated on the 5th day, when spontaneous respiration was observed and bilateral resolution of infiltrates were seen in APCR (Figure 3). During ECMO, no additional problem was encountered except for the transfusion requirement. However, fiberoptic bronchoscopy was performed on the 3rd day of ECMO due to increased airway pressure in MV and the absence of right lung ventilation.



Figure 2. Anteroposterior chest X-ray showing bilateral infiltrations.



Figure 3. Anteroposterior chest X-ray showing resolution of infiltrates bilaterally.

On the 10th day of intubation, the patient who succeeded the spontaneous breathing in trials was extubated. Nasal high-flow O₂ and NIV support were given. The patient was provided with respiratory physiotherapy. The patient, on the 3rd day of the extubation, was transferred to the orthopedics clinic on the 21st day of hospitalization for the treatment of her existing fractures.

Written informed consent was obtained from the patient for publication of her data.

Discussion

ARDS is an acute, common, inflammatory lung injury that may be associated with different etiologies. Identifying the patient with ARDS and starting treatment quickly is very important in reducing the high rate of mortality. ARDS should be suspected in patients with progressive dyspnea complaints, increased oxygen demand, and bilateral non-cardiac alveolar infiltration in the lungs within the first 6-72 hours in the imaging. The definition and severity of ARDS were classified in the Berlin Definition [1].

No specific treatment has been developed in ARDS. MV support may be necessary for its severe forms. However, ECMO is the most commonly used extracorporeal treatment strategy in severe ARDS cases where MV support is also insufficient [2,3]. ECMO was first successfully used in 1972 in a patient with post-traumatic respiratory failure. According to the records of "Extracorporeal Life Support Organization", the most important organi-

zation related to ECMO, for the last 10 years, the number of cases tends to increase over the years [4,5].

In their review study on the causes and treatments of ARDS in the last 50 years by Yavan et al [6], the researchers revealed that sepsis, aspiration pneumonia, pancreatitis, smoke inhalation, multiple trauma, fat embolism, as well as, blood transfusion, drug toxicity, although less frequently, were the reasons and examined whether they were preventable. In the present case, the presence of trauma causing multiple fractures and a history of blood transfusion may be ranked among the possible causes. In a study conducted by Yuksek et al [7], 72.7% of patients who were subjected to ECMO were observed to be applied to secondary pneumonia. The diagnosis of pulmonary embolism was excluded due to the absence of right overload in echocardiogram, low pulmonary artery pressure, lack of hypotension, and negative Doppler ultrasonography of lower extremity which was performed to exclude the diagnosis. Although thoracic CT angiography was considered for definitive diagnosis, it could not be performed due to hemodynamic instability and ECMO.

The treatment was continued with Vv-ECMO since the patient was young, P/F ratio was below 80 mm Hg, SpO₂ not exceeding 45% in MV, and PaO₂ not exceeding 40 in MV with maximum support. Although the prone position was recommended to ARDS patients [2,3,5], ECMO was decided to be applied because of insufficient clinical experience for the prone position in our center and the presence of severe and deep hypoxemia. In the guidelines [2,3,5], although intermittent recruitment maneuvers (RM) were recommended in ARDS, RM was kept for a short period due to the presence of hypotension, heparin use during ECMO, an excessive number of rib fractures, and the risk of hemodynamic pneumothorax due to overdistension.

During applying ECMO, it is recommended to provide deep sedation and muscle relaxation to rest the lungs, to prevent air embolism during cannulation, and to reduce oxygen consumption [5]. Neurological examination with sedation interruptions after the first 12-24 hours prevents masking of the complications that may occur. In our case, infusions of muscle relaxant and sedation were given during ECMO. Neurological evaluation was performed by sedation interruptions. Several studies in the literature revealed that neuromuscular blockade reduced the development of MV-associated

and MV-induced lung injury (VILI/VALI) by allowing the synchronization of MV and patient and controlling transpulmonary pressures [5]. In a meta-analysis, it was observed that muscle relaxant agents reduced the risk of pneumothorax [8]. In the present case, barotrauma-related pneumothorax was not developed.

The main approach to the use of inotropic and vasodilator agents in ECMO should be to rest the heart by minimizing the need. Low-dose inotrope in a manner that ensures adequate contractility and left ventricular contraction, is recommended [5,8]. In the present case, noradrenaline infusion was given during ECMO to achieve normotensive targets.

In critically ill patients, corticosteroids are used to create a strong anti-inflammatory effect and to prevent corticoadrenal insufficiency [5,8]. In the present case, hydrocortisone was added to the treatment due to post-traumatic ARDS-induced hypotension. Similar to all critically ill patients, a full-calorie and protein dietary support is essential for the patient in ECMO [5,8,9]. Our patient was given enteral nutrition support after the first 24 hours.

Although anticoagulant therapy is recommended to prevent clot formation in the ECMO circuit, heparin-induced bleeding during ECMO is also possible [5-9]. The transfusion is recommended up to the hematocrit level required for adequate oxygen delivery [5-9]. The humerus and pelvic fractures of our case increased the already existing bleeding risk. Although intermittent erythrocyte suspension and fresh frozen plasma replacements were performed, any complication due to heparin infusion was not developed.

In patients who require ECMO, a large part of the lung is collapsed and under consolidation, and only small areas called 'baby lungs' remain as functional lung tissue. Since excessive stress and difficulty may be encountered in the lungs due to conventional lung-protective strategies, it is open to the development of VILI [2,3,10]. The most important point in the treatment of ARDS is to monitor low volume and pressure ventilator management while continuing the treatment of the underlying disease [2,3,11]. Pressure controlled modes were also used in ventilator management during ECMO in the present case. Low pressure was maintained during MV by keeping the Ppeak below 30 cmH₂O and Pplateau below 20 cmH₂O. In this way, the driving pressure was kept at the specified levels.

In conclusion, the decision to apply ECMO to the appropriate patients with ARDS and to disconnect the patient from ECMO to eliminate the complications of ECMO should be given before being late. It should be kept in mind that successful ECMO management in a patient with ARDS is multidisciplinary teamwork.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support.

Authors' contributions

MÖ; Conceived and designed the analysis, co-wrote the paper, collected the data, performed the analysis, DFE; Contributed data/analysis tools, co-wrote the paper.

References

1. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E et al. Acute Respiratory Distress Syndrome. The Berlin Definition. JAMA 2012; 307: 2526-33.
2. Fan E, Del Sorbo L, Ewan CG, Hodgson CL, Munshi L, Walkey AJ et al. An official american thoracic society/european society of intensive care medicine/society of critical care medicine clinical practice guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2017; 195: 1253-63.
3. Griffiths MJD, McAuley DF, Perkins GD, Barrett N, Blackwood B, Boyle A et al. Guidelines on the management of acute respiratory distress syndrome. BMJ Open Resp Res 2019; 6: 1-27
4. Morris JA, Pollock R, Zwischenberger BA, Croft B, Zwischenberger JB. The story of ECLS: History and future. In: Schmidt GA editors. Extracorporeal life support for adults. New York: Springer; 2016. p.233-260.
5. elso.org [Internet]. Ann Arbor: Extracorporeal Life Support Extracorporeal Life Support Organization (ELSO) Guidelines for Adult Respiratory Failure, Version 1.4 August; c2017 [cited 2017 Aug] Available from: <https://www.elseo.org/>.
6. Yadav H, Thompson BT, Gajic O. Fifty Years of Research in ARDS. Is Acute Respiratory Distress Syndrome a Preventable Disease? Am J Respir Crit Care Med 2017; 195: 725-36.

7. Yüksel A, Tecimer EM, Özgöz MH, Yolgösteren A, Kan İris İ, Doğan İmran A et al. Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: our single-center experience. *Türk Gogus Kalp Dama* 2017; 25: 61-7.
8. Pappalardo F, Montisci A. Adjunctive therapies during venovenous extracorporeal membrane oxygenation. *J Thorac Dis* 2018; 10(Suppl 5): 683-91.
9. Bayar MK, Kosovalı DB. Ekstrakorporeal membran oksijenasyonu. In: Karadağ M editor. *Mekanik Ventilasyonda Son Gelişmeler*. Ankara: Akciğer Sağlığı ve Yoğun Bakım Derneği; 2018. p.93-103. Available from: <https://ghs.asyod.org/Konular/2018-6-11.pdf>.
10. Terragni PP, Rosboch G, Tealdi A, Corno E, Menaldo E, Davini O et al. Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2007; 175: 160-6.
11. Del Sorbo L, Goffi A, Goligher E, Fan E, Slutsky AS. Setting mechanical ventilation in ARDS patients during VV-ECMO: where are we? *Minerva Anestesiol* 2015; 81: 1369-76.

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