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Original Article

Pneumonectomy; a risky type of resection in non-small cell lung cancer: survival and mortality analysis

Serkan Yazgan[1*], Soner Gursoy[1], Ahmet Ucvet[1], Ozgur Samancilar[1], Ahmet Emin Erbaycu[2], Mehmet Unal[1], Tarik Yagci[1]

[1]Department of Thoracic Surgery, University of Health Sciences, Dr. Suat Seren Chest Diseases and Surgery Medical Practice and Research Center, İzmir, Turkey

[2]Department of Chest Diseases, University of Health Sciences, Dr. Suat Seren Chest Diseases and Surgery Medical Practice and Research Center, İzmir, Turkey

ABSTRACT

Background: This study aims to evaluate the mortality and survival rates of patients undergoing pneumonectomy due to primary non-small cell lung cancer (NSCLC) and to identify the factors which affect these variables.

Materials and Methods: This retrospective single center cohort study included a total of 250 patients who underwent pneumonectomy due to NSCLC between January 2007 and July 2015. 30- and 90-day mortality rates and survival rates of the patients were analyzed. The factors which affected survival and mortality were evaluated.

Results: The mean age was 59 (range: 35 to 77) years. The median survival was 48.1 months (95% C. I. 30.6 – 65.6 months) and five-year survival rate was 45.6%. The 30- and 90-day mortality rates were 6.4% and 7.6%, respectively. Age, nodal disease, and complete resection were factors to affect the survival ($p = 0.002$, $p = 0.0001$ and $p = 0.017$, respectively). Age was also effective on 30- and 90-day mortality ($p = 0.004$, RR: 3.3 and $p = 0.006$, RR: 2.5, respectively). The early rethoracotomy rate was 5.6% (n = 14) and the postoperative mortality rate in these patients was 28.6% (n = 4).

Conclusions: Although implementation of pneumonectomy due to lung cancer seems fearful, the present study found lower survival rates only depending on advanced age and N2 disease. The high levels of 30- and 90-day mortality and the increased mortality after early rethoracotomy was associated with advanced age and comorbidity. In terms of postoperative mortality, the selection of eligible patients is important in elderly patients who are candidates of pneumonectomy due to lung cancer.

Key Words: non-small cell lung cancer, pneumonectomy, survival rate, early mortality

Corresponding Author*: Serkan Yazgan, MD. SBÜ Dr Suat Seren Göğüs Hastalıkları ve Cerrahisi SUAM, Göğüs Cerrahisi Bölümü, K-Blok, 3. Kat, Yenişehir – Konak / İzmir, Turkey.
E-mail:serkanyazgan@gmail.com - Phone: +90 536 5835085
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Introduction

Prior to 1930, pneumonectomy was fatal due to bleeding, the lack of durable bronchial closure methods and antisepsis. Later, lobectomy were shown to have similar efficacy along with less morbidity, leading to gradually reduced indications for pneumonectomy [1]. However, pneumonectomy may be still inevitable due to anatomical and technical reasons. As it is associated with higher morbidity and mortality, compared to other lung resections, the effect of pneumonectomy on long-term survival is still controversial.

In the present study, it was aimed to evaluate the mortality and survival rates of patients who underwent pneumonectomy due to primary non-small cell lung cancer (NSCLC) and to identify the factors affecting these variables.

Materials and Methods

A written informed consent was obtained from each patient. The study was approved by the institutional study board and was conducted in accordance with the principles of the Declaration of Helsinki.

This retrospective study included a total of 250 patients who had pneumonectomy due to NSCLC between January 2007 and July 2015. Patients who had completion pneumonectomy, pneumonectomy due to an indication other than NSCLC were excluded. Data including age, histology, lymph node metastasis, T status, neoadjuvant therapy, adjuvant therapy, and the state of complete and incomplete resection at the surgical margin during post-resection histopathological examinations were obtained from hospital records operation reports, patient charts, and national survival database. All patients were analyzed in terms of 30- and 90-day mortality rates and survival. The survival time was calculated as the duration between the days of operation and death. The factors affecting survival and mortality were assessed statistically. Cardiac disease, hypertension, diabetes mellitus and previous tuberculosis were recorded as comorbidities.

Preoperative assessment included posteroanterior chest x-ray, thoracic, and upper abdominal computed tomography (CT), bronchoscopy, positron emission tomography, cranial magnetic resonance imaging or CT, pulmonary function tests (PFT) and blood gas analysis as a standard procedure. For eligible patients, transthoracic fine-needle aspiration biopsy, and mediastinal lymph node staging with endobronchial ultrasonography and/or mediastinoscopy were performed. The patients with the forced expiratory volume in 1 second (FEV1) level >2 l or 70% as measured by PFT underwent pneumonectomy prior to any advanced respiratory assessment. For the patients with PFT levels considered insufficient; quantitative perfusion scintigraphy, maximal oxygen consumption (VO2peak) and stair climbing tests were performed. Respiratory physiotherapy was applied as guided by physiotherapists in the postoperative period. Smoking patients were ensured to quit smoking at least one week before the operation.

Prior to thoracotomy, all patients were administered antibiotic and pulmonary embolism prophylaxis. During the operation, anesthesiologists conducted double-lumen intubation, arterial and central venous pressure monitorization and epidural analgesia as a standard procedure. The serratus anterior muscle was preserved and posterolateral thoracotomy was performed. To achieve a complete resection, additional procedures such as intrapericardial procedures or chest wall resection as well as extended pneumonectomy were performed when necessary. For bronchial closure, mostly stapler was used upon surgeon's choice. Each patient underwent systematic mediastinal and hilar lymph node dissection. The surgical margins were assessed by a pathologist using the frozen-section procedure. At the end of the operation, a thoracic drain was inserted. Extubation was ensured in the operating room as far as possible and the patients were kept under supervision for 24 to 48 hours in the intensive care unit. The amount of fluid drainage was followed and the thoracic drain was removed within the first 72 hours. The discharged patients were followed in the outpatient setting. All complications and mortalities were recorded.

Statistical Analysis

Data were collected from hospital database, operational reports, patient charts and national mortality database. Excel software (Microsoft Corp, Seattle, WA) was used to analyze the data. The means and standard deviations of the continuous variables, and number and percent of categorical variables were given by using descriptive statistics. Statistical analysis was performed using the SPSS 16.0 software program (SPSS Inc., Chicago, IL,

USA). All cumulative survival curves were estimated using the Kaplan–Meier method, and differences between the groups were evaluated by the log-rank test. The overall survival (OS) was considered as the time from the date of initial surgery to the date of death from any cause or the date of the last follow-up. Variables with a P-value less than 0.1 were selected for further multivariable analysis. Multivariable analysis for OS was performed to identify the prognostic factors using the Cox proportional hazard model.

Results

During the study period, there were a total of 1,267 patients who had lobectomy and pneumonectomy due to primary NSCLC in our clinic, and 1,017 (80.3%) of these cases were lobectomy and 250 (19.7%) were pneumonectomy. The lobectomy / pneumonectomy rate was 4.1. The mean age of the pneumonectomy patients was 59 (range: 35 to 77) years. There were 32 patients (12.8%) aged under 50 years, 88 patients (35.2%) aged between 50 and 60 years, 98 patients (39.2%) aged between 60 and 70 years, and 32 patients (12.8%) aged above 70 years. The majority of the patients were males (94.8%), and the most common histopathological type was squamous-cell carcinomas (72.8%). In terms of T status, most of the patients were T2 with 168 patients (67.2%). In addition, 55 patients (22%) had comorbidities. A total of 72 patients (28.8%) were operated following neoadjuvant chemotherapy, while postoperative 50 patients (20%) were found to have N2 disease. Also, 106 patients (42.4%) received adjuvant chemotherapy (Table 1). Adjuvant therapy was given to 27 patients (37.5%) who received neoadjuvant therapy. Most of the patients (70%) had left pneumonectomy and R0 resection was implemented at a rate of 97.2%.

Table 1. Demographics and the characteristics of the study population and the survival data.

		n	Rate (%)	5 year survival (%)	Median survival (months)	P
Total		250		45.6	48.1	
Gender	Female	13	5.2	19.5	20.1	0.06
	Male	237	94.8	46.1	56.8	
Age	< 50	32	12.8	58.6	NA	0.002
	50 ≤ age < 60	88	35.2	51.2	61	
	60 ≤ age < 70	98	39.2	43.7	42.4	
	≥ 70	32	12.8	24.1	20.7	
Comorbidity	Yes	55	22	41.9	56.8	0.49
	No	195	78	46.7	42.4	
Neoadjuvant	Yes	72	28.8	39.1	33.2	0.24
	No	178	71.2	48.4	59.3	
Adjuvant	Yes	106	42.4	49.5	59.7	0.07
	No	144	57.6	42.9	39.6	
Histology type	Squamous	182	72.8	48.2	58.7	0.09
	Nonsquamous	68	27.2	38.4	30.5	
Tumor size	≤ 3 cm	82	32.8	40.5	30.5	0.06
	3-7 cm	143	57.2	44	48.1	
	≥ 7 cm	25	10	68.8	NA	
T stage	T0/1	12	4.8	54	NA	0.67
	T2	168	67.2	45.2	49.7	
	T3/4	70	28	47.4	31.3	
N stage	N0/1	200	80	50.1	60.3	0.001
	N2	50	20	28	22.4	
Side	Left	175	70	44.3	40.3	0.81
	Right	75	30	48.8	58.7	
Resection	Complete	243	97.2	46.1	49.7	0.02
	Incomplete	7	2.8	28.6	4.1	

NA: Not available; Bold values: P < .05

The mean follow-up was 36.2 ± 28.6 (range: 0.1 to 104.9) months, and the median survival was 48.1 months (95% C. I. 30.6 – 65.6 months). The five-year overall survival rate was 56.6% (Figure 1).

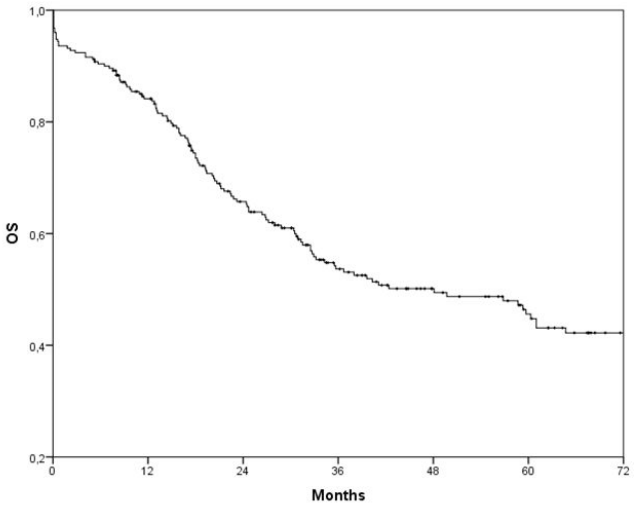

Figure 1. Overall survival of patients with pneumonectomy (Abbreviation: OS, overall survival).

The survival rates were lower in female patients (p = 0.06), non-squamous-cell carcinoma patients (p = 0.092), and those who did not receive adjuvant chemotherapy (p = 0.07); however, it did not show any statistical significance (Table 1). The difference in age groups (p = 0.002), detection of N2 disease (p = 0.001) and incomplete resection (p = 0.017) were found to significantly affect the survival rates. The five-year survival rate was 58.6% under 50 years of age, compared to 24.1% at the age of 70 and above (Figure 2).

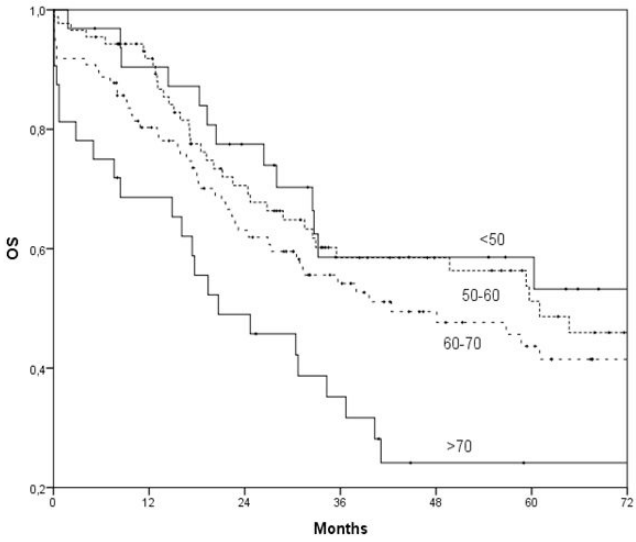

Figure 2. Overall survival of patients shows significant difference according to the age groups. (Log – rank test, P = 0.002) (Abbreviation: OS, overall survival).

The five-year survival rate was 28%, and median survival was 22.4 months for N2 disease (Figure 3) and 28.6% and 4.1 months, respectively for incomplete resection (Figure 4). The five-year survival was lower among patients receiving neoadjuvant therapy compared to those who did not (39.1% vs. 48.4%, p = 0.24).

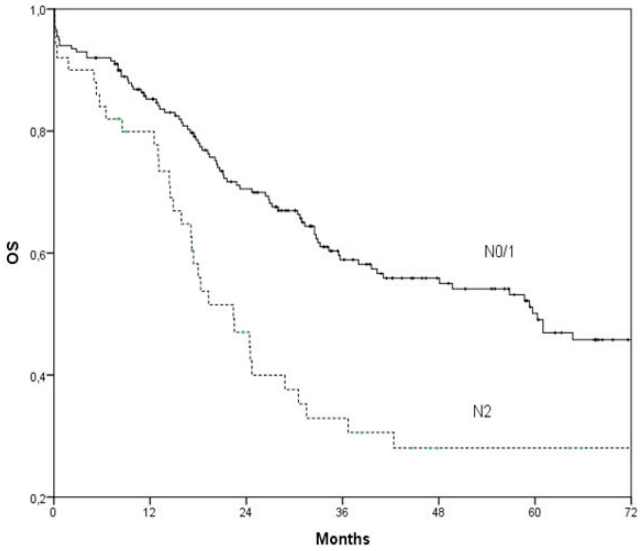

Figure 3. Overall survival of patients with N0/1 (n = 200) is significantly higher than patients with N2 (n = 50) disease (Log – rank test, P = 0.001) (Abbreviation: OS, overall survival).

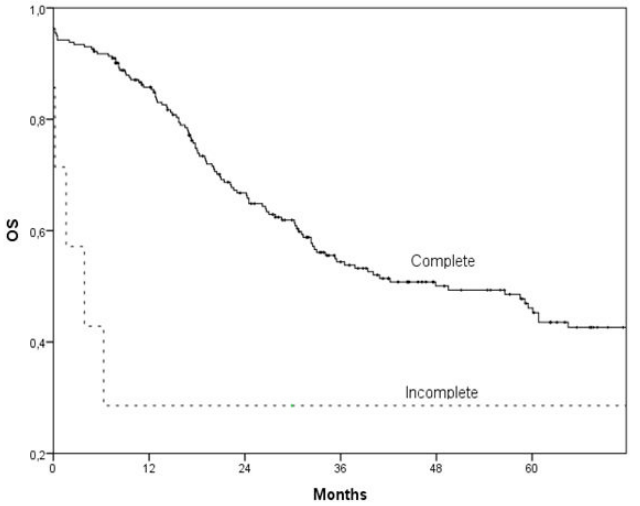

Figure 4. Overall survival of patients with complete resection (n = 243) is significantly higher than patients with incomplete resection (n = 7) (Log – rank test, P = 0.02) (Abbreviation: OS, overall survival).

During follow-up, disease progression was occurred in 80 patients (32%); 13 of them (16.2%) were local recurrence, 18 (22.5%) were both local recurrence and distant metastasis, and 49 (61.2%) were distant metastasis. Early rethoracotomy was performed in 14

patients (5.6%) within the postoperative 30 days; after left pneumonectomy in 10 and right pneumonectomy in four patients. The reasons for early rethoracotomy were bronchopleural fistula in seven patients, bleeding in six patients, and chylothorax in one patient. Six of the seven patients with fistula were cases with right pneumonectomy. Postoperative mortality occurred in four patients from early rethoracotomy group; two were due to bronchopleural fistula and two due to bleeding. The postoperative mortality rate after early rethoracotomy was 28.6% (4/14 patients).

The 30- and 90-day mortality rates were 6.4% and 7.6%, respectively. The review of national database revealed that 126 patients (50.4%) died and 70 of these patients (28%) died due to progression of NSCLC. Of the patients, 114 (45.6%) are alive and disease-free. The other 10 patients (4%) alive despite local recurrence or metastasis.

The Cox's regression analysis revealed statistically significant results for the analyses related to age groups, nodal disease, complete resection, histology, and adjuvant therapy (Table 2).

Table 2. Multivariable analysis of age, nodal status, adjuvant therapy, complete resection and histopathological type on survival.

	Subgroup	P	Ratio
Age	< 50, 50 ≤ age < 60, 60 ≤ age < 70, ≥ 70	0.0001	1.5
N status	N0 or N1 versus N2	0.0001	2.9
Adjuvant therapy	Yes versus No	0.001	2.2
Resection	R0 versus R1	0.019	3.1
Histology type	Squamous versus nonsquamous	0.018	1.6

The most influential factor in 30- and 90-day mortality was found to be age (p = 0.004 and p = 0.006, respectively) (Table 3), and the odds ratio from the logistic regression analysis was 3.3 (p = 0.001) and 2.5 (p = 0.003), respectively. The 30- and 90-day mortality in the presence of comorbidity was 12.7% and 14.5%, respectively (p = 0.05 and p = 0.04, respectively).

Table 3. Demographics and the characteristics of the study population and 30 and 90 days mortality.

		n	30 days mortality n (%)	P	90 days mortality n (%)	P
Total		250	16 (6.4)		19 (7.6)	
Gender	Female	13	1 (7.7)	0.58	1 (7.7)	1
	Male	237	15 (6.3)		18 (7.6)	
Age	< 50	32	0 (0)	0.004	1 (3.1)	0.006
	50 ≤ age < 60	88	2 (2.3)		3 (3.4)	
	60 ≤ age < 70	98	8 (8.2)		8 (8.2)	
	≥ 70	32	6 (18.8)		7 (21.9)	
Comorbidity	Yes	55	7 (12.7)	0.05	8 (14.5)	0.04
	No	195	9 (4.6)		11 (5.6)	
Neoadjuvant	Yes	72	2 (2.8)	0.16	4 (5.6)	0.6
	No	178	14 (7.9)		15 (8.4)	
Histology type	Squamous	182	11 (6)	0.77	12 (6.6)	0.42
	Nonsquamous	68	5 (7.4)		7 (10.3)	
Tumor size	< 5 cm	186	11 (5.9)	0.56	14 (7.5)	1
	> 5 cm	64	5 (7.8)		5 (7.8)	
Side	Left	175	9 (5.1)	0.26	11 (6.3)	0.3
	Right	75	7 (9.3)		8 (10.7)	

Bold values: P <.05

Discussion

Pneumonectomy has a higher operative risk compared to more limited resections and there are different opinions about its effect on long-term survival [1]. Nevertheless, this procedure is still performed due to anatomic or technical reasons. Pneumonectomy accounts for 10 to 35% of all lung resections [2,3]. The tumors for which pneumonectomy is needed are often larger and centrally

localized. Therefore, mediastinal lymph node metastasis are more common, and performing preoperative invasive staging is important for these patients.

The former studies report that the five-year overall survival rate is 21 to 41% [1,2,4,5]. In this study, we found median survival to be 48.1 months and five-year overall survival rate to be 45.6% in 250 pneumonectomy cases. These rates were 48.8% and 44.3% for right and left pneumonectomy, respectively. The long-term overall survival rate for pneumonectomy was slightly higher in our study, than previously reported. This can be attributed to the fact that advanced stage diseases are detected more and surgical treatment is not performed on such patients in recent years as we have used advanced imaging techniques and invasive staging methods. This is also supported by our patient group 80% of which consisted of N0 and N1 patients. Similar two series reported higher postoperative N2 disease rate as 26% and 41% [1,6]. Of our patients with detected N2 disease, 60% had a squamous-cell carcinoma and 32% had an adenocarcinoma. This finding is contrary to some reports indicating that squamous cell carcinomas have a lower biological potential for mediastinal lymph node metastasis [6].

According to the tumor size in patients with postoperative N2 disease, it was found that 34% of the patients had a tumor <3 cm, whereas 66% had a tumor >3 cm in diameters. This finding suggests that there is a link between increased tumor size and N2 detection. The subgroup analyses of our study revealed that advanced age, incomplete resection and N2 disease have a significantly negative effect on long-term survival, whereas sex, histology, tumor size, the side of the operation, presence of comorbidity and adjuvant or neoadjuvant therapy did not have any statistically significant effect. The age group analysis showed that survival rates were higher in the younger group. The five-year survival rate was 58.6% among patients under 50 years of age compared to 24.1% among patients the age of 70 and above. It is known that R0 resection is one of the most important variables affecting survival. The rate of patients with detected R1 is reported to vary between 1.2% and 10.6% in various series [5,7]. This rate was 2.8% in our study and only one patient received neoadjuvant therapy. In our study, the five-year survival rate was 28.6% in R1 group compared to 46.1% in R0 group ($p = 0.017$). This can be considered as a proof that microresidual disease is an indicator of poor prognosis.

Currently, the lobectomy/pneumonectomy rate is on the increase due to sleeve lobectomies that are performed as an alternative to pneumonectomy. The lobectomy/pneumonectomy rate was four in our series. There are series with such rate of 4.9 in consistent with our study [5]; however, we believe that this rate should be further higher. A study that investigated the chronological changes in lung cancer surgery during the past 41 years found that the lobectomy/pneumonectomy rate has increased to 15.6 from 5 [4]. Similarly, the sublobar resections has increased (3% vs. 38%), whereas the pneumonectomy rate has significantly reduced (16% vs. 4%).

It is important for surgeons to reduce the higher morbidity and mortality risk of pneumonectomy and identify the causes of early postoperative deaths. Our study demonstrated that 19.7% of the resections performed due to NSCLC were pneumonectomy, and the 30- and 90-day overall mortality rates were 6.4% and 7.6%, respectively. These values are in strong agreement with the results of studies conducted at some experienced centers, which were published within the past five years (Table 4). However, early mortality rates are expected to be even lower upon developing technology and novel surgical methods and more modernized intensive care units. In the literature, an analysis including 1949 and 2002 reports showed that post-pneumonectomy 30-day overall mortality varied between 3.1 and 17% [8], whereas this rate has been reported to vary between 3.2% and 8.3% for the past five years [9-12].

Table 4. Mortality rates of pneumonectomy for nonsmall cell lung cancer in different series.

	Year	n	30 days mortality-n (%)	90 days mortality-n (%)
Powell et al.[10]	2013	1121	78 (7%)	129 (11.5%)
Pezzi et al.[12]	2014	7949	663 (8.3%)	1110 (13.7%)
Frick et al.[9]	2015	186	6 (3.2%)	11 (5.9%)
Pricopi et al.[11]	2015	1805	110 (6.1%)	140 (7.8%)
Our study	2017	250	16 (6.4%)	19 (7.6%)

Furthermore, the present study also showed that advanced age had an adverse effect on mortality. The analysis of 30-day mortality revealed that there was no patient aged under 50, and 14 of 16 patients died

were above the age of 60. Post-pneumonectomy 30-day mortality was significantly higher among elderly patients, compared to other resections [1,3]. Therefore, it is obvious that a more serious care is required for elderly patients. A study examining post-pneumonectomy prognosis among elderly lung cancer patients reported a significantly higher level of pneumonia and bronchial fistula in the older patient group compared to the younger patient group [13]. In addition, the aforementioned study showed a significantly higher rate of operation-related mortality in the older patient group.

Nonetheless, the role of neoadjuvant therapy is still questionable. Some series report lower postoperative mortality following neoadjuvant therapy [2], while others report higher early postoperative mortality [14] or higher mortality only in right pneumonectomy [15]. Our study showed a statistically significant difference in early mortality following neoadjuvant therapy. However, contrary to many other studies, we found 30-day mortality lower among patients that received neoadjuvant therapy compared to those who had pneumonectomy without any preoperative therapy (2.8% vs. 7.9%, p = 0.16). This difference is likely to result from the fact that the patients to whom surgery was recommended following neoadjuvant therapy were selected among patients with best conditional status. A meta-analysis carried out between 1990 and 2010 analyzed 27 studies and found the mean 30-day mortality rate for pneumonectomy following neoadjuvant therapy to be 7% [16]. The study emphasized higher 30- and 90-day mortality in right pneumonectomies compared to left pneumonectomies. Although there was no significant difference in the morbidity rates, some authors reported that early mortality was significantly higher in right pneumonectomies [9]. Similarly, we also observed higher early mortality rates in right pneumonectomies (9.3% vs. 5.1%, p = 0.26). The common reason for high mortality in right pneumonectomy include more bronchopleural fistula rate at the right side, the postoperative cough not being adequately effective due to the lengthiness and position of the left main bronchus, and the functional predominance of the ablated lung [2,11]. Among our study population, 10 of 14 patients undergoing early rethoracotomy following pneumonectomy had right pneumonectomy. Additionally, six of seven patients undergoing rethoracotomy due to bronchopleural fistula also had right pneumonectomy. This indicates that right pneumonectomy is associated with higher morbidity and mortality.

In conclusion, based on the findings from our single-center study, we suggest that preoperative evaluation should be made more meticulously and invasive staging should be performed to exclude N2 disease in all patients especially in advanced-age indicated for pneumonectomy. As early mortality following neoadjuvant therapy seems low, pneumonectomy can be performed safely in these patients. In addition, it should be kept in mind that pneumonectomy is likely to be curative when not avoidable, when performed by experienced professionals following a thorough assessment.

Declaration of conflicting interests

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Original Article

Is surgical treatment effective option for survival of small cell lung cancer?

Celal Buğra Sezen*, Umut Kilimci, Oğuz Girgin, Yunus Aksoy, Ozkan Saydam, Seyyit İbrahim Dincer, Muzaffer Metin

Department of Thoracic Surgery, Health Sciences University, Chest Diseases and Thoracic Surgery Health Application and Research Center, Istanbul, Turkey

ABSTRACT

Background: Small cell lung cancer (SCLC) accounts for 10% of all lung cancers. Due to the fact that it is an aggressive tumor, there is still no consensus on treatment. Our aim in this study was to evaluate prognostic factors affecting survival in early-stage small cell lung cancer.

Materials and Methods: Between 2008 and 2017, 21 patients who underwent resection due to early-stage SCLC were evaluated retrospectively in the study. 16 (76.2%) stage I and 5 (23.8%) stage II patients were included in the study. All patients received adjuvant therapy after surgery.

Results: Sixteen (76.2%) male and 5 (23.8) female patients were included in the study. The mean age was 60.19 ± 7.13 years. Patients were followed for a mean of 33 months. There was 16 (76.2%) small cell, and 5 (23.6%) combined small cell carcinoma. The 5-year survival rate was 48.6% (59.6 ± 10.6 months). In 7 patients (33.3%) postoperative morbidity was observed. No statistically significant difference was found between N status and survival. Statistically significant differences were found between tumors smaller than 1 cm and tumors greater than 1 cm in terms of T stage ($p = 0.043$).

Conclusions: In conclusion, multimodal treatment is very important for survival in early-stage small cell lung cancer. Although our results in our study are aggressive tumors of the SCLC, survival outcomes in the early stages are quite satisfactory. Early stage survival outcomes, especially after stage I tumors, are as successful as non-small cell lung cancers.

Key Words: small cell lung cancer, lobectomy, prognostic factors

Corresponding Author*: Celal Bugra Sezen, MD. Yedikule Göğüs Hastalıkları Hastanesi, Belgrad Kapı Yolu Cad. No: 1, Istanbul, Turkey.
E-mail: info@bugrasezen.com
Phone: +90 553 160 55 31
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Introduction

Lung cancer is still the leading cause of cancer-related deaths. Especially as the population of elderly rise, the incidence of lung cancer increases. The small cell lung cancer (SCLC) accounts for 10% of all lung cancers [1]. For the potential of rapid growth and metastasis of the mediastinal lymph nodes and/or distant metastasis, SCLC's are regarded as a high-grade malignity. Even though they are chemoradiosensitive tumors; the prognosis is very poor. 5-year survival rates are 5% in the chemotherapy patients [2].

Some authors recommend the surgery as a treatment of early-stage SCLC, but the mutual treatment modality is still absent [3]. Our aim in this study is to observe the survival rates of surgically treated SCLC patients and the prognostic factors that affected.

Materials and Methods

The ethical committee approval of this study is acquired from Istanbul Education and Research Hospital.

Prospectively held data of the surgically treated SCLC patients in our hospital from 1.1.2008 to 1.7.2017 were evaluated retrospectively. Out of 1759 lung cancer patients, 34 were included in the study. 2 of them are lost at follow-up. Seven non-anatomic resection patients and four late-stage patients are excluded from the data. 21 early-stage SCLC patients that underwent a complete resection have evaluated retrospectively. Flowchart of the study has shown in figure 1.

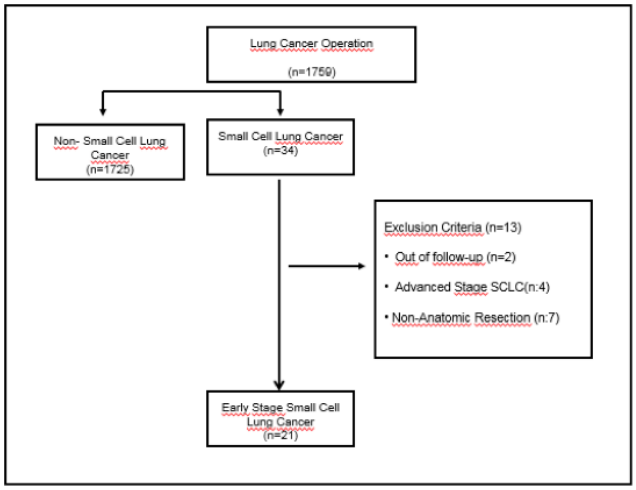

Figure 1. Flowchart of the study.

Preoperative Evaluation

Positron emission tomography (PET-CT), cranial magnetic resonance imaging and computerized thorax tomography (CT) have been used for exploring distant metastasis. Upper and lower abdominal evaluation were performed with CT and PET-CT scans. MRI was requested in the patients who had a lesion in CT. Respiratory function tests and electrocardiography have been used for evaluating preoperative pulmonary and cardiac capacity. Patients with lower than 40% FEV1 results were requested carbon monoxide diffusion test and pulmonary perfusion scintigraphy. All patients were assessed by diagnostic bronchoscopy before surgery. Mediastinal evaluations were performed by endobronchial ultrasonography and /or mediastinoscopy.

Postoperative Follow-up

Demographic data, comorbidities, length of hospitalization, histopathologic features, mortality and 1-2-5 years of survival rates were evaluated in the study.

Comorbidities are examined under three groups. Those groups are; respiratory problems (chronic obstructive pulmonary disease, asthma), cardiac problems (history of myocardial infarction, arrhythmia, history of the coronary stent), endocrinologic problems (diabetes mellitus, goiter) and nephrologic problems (chronic kidney deficiency).

The morbidities that occurred during the hospitalization period or within a month following the operation were included in the study. In this study, we observed empyema, pneumonia, wound infections, arrhythmia and prolonged air leak as morbidities.

Pathologic staging was done according to the 8th edition of the TNM classification system [4]. Patients were followed with chest CT and physical examination every three months for the first two years, every six months between two and five years, and once a year thereafter. All patients were given chemoradiotherapy in the postoperative period.

Surgical Procedure

Following double-lumen selective intubation, patients were placed in the lateral decubitus position for surgery. The patients were operated with posterolateral thoracotomy. After lung resection (lobectomy, pneumonectomy), systematic lymph node dissection was performed. 2, 4, 7, 8, 9, 10 and 11 on the right side and 5, 6, 7, 8, 9, 10, and 11 on the left side lymph node stations were

dissected. A single 28-F chest tube was placed in all patients. All patients were extubated in the operation room and transferred to the surgical intensive care unit. They were monitored in the intensive care unit until their general condition stabilized.

Statistical Analysis

SPSS Version 22.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. The chi-squared ($\chi 2$) test was used to calculate frequency values as descriptive statistics. A t-test was used to compare the means of independent groups and the Mann-Whitney U was used to compare medians. Survival analysis was conducted according to the Kaplan-Meier method and curves were compared using the log-rank test. The statistical significance level was accepted as $p < 0.05$ for all analyses.

Results

Out of the 21 patients, 16 patients (76.2%) were male, and five patients (23.8) were female, and the mean age was 60.19 ± 7.13 years (min: 40 max: 71). 15 of the patients (71.4%) were smokers in the preoperative period. Preoperative mean FEV1 value was 77.18 ± 22.2% (min: 42-max: 116). Preoperative comorbidity was present in 12 patients (57.1%). Demographic characteristics of the patients are listed in table 1.

Table 1. Demographic characteristics of patients with early stage SCLC.

Variables		n	%
Gender	Female	5	23.8
	Male	16	76.2
Age (Year)		60.19 ± 7.13	
Age	< 65	18	85.7
	> 65	3	14.3
Smoking (Package / Year)		31.5	±14.2
Comorbidity	Cardiac problems	5	23.8
	Respiratory problems	6	28.6
	Endocrinological problems	6	28.6
	Nephrological problems	3	14.3
Hospitalization		7.67 ± 4.46	
Diagnosis method	TTNA	9	42.9
	Bronchoscopic biopsy	4	19
	Frozen section	8	38.1
Clinical stage	Stage 1	19	90.5
	Stage 2	2	9.5

TTNA: transthoracic needle aspiration

Nine patients (40.9%) underwent lung resection on the right side and 12 patients on the left side (59.1%). Most common resection was left upper lobectomy (%31.8). Pneumonectomy was performed in 2 patients with the central tumor. Preoperative tumors of these patients were reported as non-small cell lung cancer. Postoperative pathology was reported as combined small cell carcinoma. Mean tumor diameter was 2.02 ± 1.80 cm. 16 (76.2%) of the patients, were small cell carcinoma and 5 (23.8%) patients were combined small-large cell carcinoma. Intraoperative mean 4.7 ± 1.64 lymph node stations were sampled. The number of lymph nodes removed was 12.19 (min: 4 - max: 34). The surgical and histopathological features of the patients mentioned in table 2.

Table 2. Surgical and histopathological characteristics of patients.

Variables		n	%
Operation side	Right	9	42.9
	Left	12	57.1
Resection type	Lobectomy	19	90.5
	Pneumonectomy	2	9.5
Tumor diameter		2.02 ± 1.80	
N Stage	N_0/N_1	17/4	81/19
Stage	1a1	4	19
	1a2	7	31.3
	1a3	5	23.8
	2b	5	23.8

There was no mortality in the following 30 days of surgery. Postoperative morbidity was observed in seven patients (33.3%). 13 morbidity was observed in seven patients. Seven patients with prolonged air leak (33.3%), one patient had (4.8%) pneumonia, three patients developed (14.3%) atrial fibrillation, one patient had (4.8%) wound infection and one (4.8%) patient with empyema. Air leakage was spontaneously regressed in 5 patients, and two patients needed blood pleurodesis. Medical cardioversion treatment was applied to patients with atrial fibrillation. Antibiotic therapy was performed according to the culture results to patients with empyema. There was no statistically significant relationship between morbidities with co-morbidity, age, sex, side, and operation pattern ($p > 0.05$).

Mean follow-up time for patients is 33 months. 5-year survival rate was calculated as 48.6% (59.6 ± 10.6 months). No statistically significant difference was found between N status and survival ($p = 0.416$). No difference was found in isolated SCLC when group analysis was performed ($p = 0.733$). When compared in the T stage,

there was no significant difference in survival rates (p = 0.240). The analysis revealed a statistically significant difference (p = 0.043) in the group analysis between 1 cm and below tumors and above than 1 cm ones. The 5-year survival rate for 1 cm and below tumors was found 100%, while the survival rates of the patients with tumors above than 1 cm was 27.1%. Table 3 shows prognostic factors affecting survival in early stage SCLC.

Table 3. Factors affecting survival in early stage SCLC.

Variables		1 Year survival %	2 Year survival %	5 Year survival %	Mean survival (Month)	%95 (CI)	p
Gender	Male	93.3	62.2	46.7	58.0	36.1-79.9	0.756
	Female	100	80	---	28	22.7-33.2	
Histopathology	SCLC	93.3	70.5	47	67.7	13.7	0.531
	Combined SCLC	100	40	40	43.6	19.3	
N Stage	0	93.8	74	27.8	64.7	11.3	0.416
	1	100	33.3	---	31.3	6.8	
Stage	1	93.3	72.2	54.2	63.5	40.9-86.1	0.591
	2	100	33.3	---	31.3	17.9-44.7	
CPRT	No	66.7	44.4	---	16.5	12.3-20.6	0.050
	Yes	100	65.3	54.4	41.5	30.6-52.4	

CPRT: Cranial Prophylactic Radiotherapy

Postoperative metastasis was detected in 10 patients (52.4%). 4 patients (19%) had lung, 4 patients (19%) had cranial, and 2 patients (9.5%) had vertebral metastasis. The disease-free survival was 28 months, the 2-year DFS 60% 5-year disease-free survival rate was 0%. 5-year disease-free survival was 41.9% in patients undergoing prophylactic cranial radiotherapy (PCI) and 0% in non-patients (p = 0.041). Kaplan Meier survival graph was shown in figure 2. There was no statistically significant difference in DFS in terms of resection type, stage, N status, sex, and histopathology.

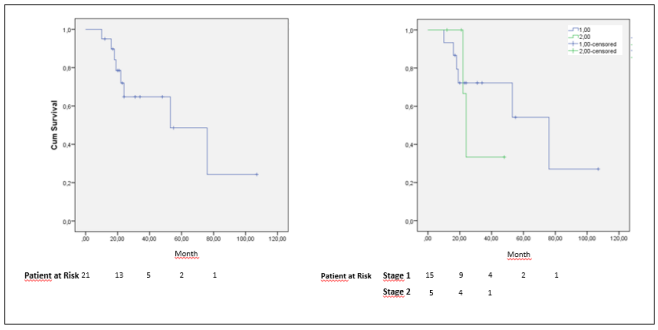

Figure 2. Kaplan Meier survival graph (left: general survival, right: survival by stage).

Discussion

The prognosis of SCLC is very poor because they are aggressive tumors. Survival rates of patients treated with chemoradiotherapy, even when they are detected at an early stage, is only 15% [5-7]. In today's standards, place of surgical treatment of SCLC is not clear, only to be used in a part of bi-trimodal treatments. The main reasons for this are; the difficulty of diagnosing SCLC at early stages while they still have resection potential [5], the insufficiency of standalone surgical treatment. (especially in the 1970's British Medical Research study, the outcomes of surgical treatment alone were quite bad) [8]. Therefore, surgical treatment is recognized as a component of multimodal treatment [9-11].

In a retrospective study of 39 patients with Bischof et al [12], the 5-year survival rate was 49%. In a 67 patient study of Badzio et al [13] showed that the five-year survival of patients who were performed surgery was 27%, while chemoradiotherapy-only patients' survival rate was 4%. Japan Clinical Oncology Group found that 5-year survival was 67% in stage 1A and 73% in stage 1B in SCLC. They have performed prophylactic cranial radiotherapy to reduce the risk of cranial metastasis. Local recurrence was observed in 10% of patients, and cranial metastasis was observed in 15% of patients in that study. In 2009, 13,290 SCLC cases were identified from the IASLC database. 349 of which had performed R0 resection. Five-year survival rates for them were 48%, 39% and 15% in stage I, II and III respectively [14]. It was also found that the survival outcomes were inversely proportional to T and N. In 2018, Paximadis et al [3] compared the surgery with SBRT and external beam radiation therapy (EBRT) in Stage 1 SCLC. Overall survival (OS) was more successful than EBRT and SBRT

in patients who underwent surgery ($p < 0.001$). Additional use of chemotherapy with any treatment modality resulted in improved OS ($p < .001$). Che et al [15] reported better survival rates in patients who underwent surgery in stage I and II ($p < 0.001$). Survival was observed in patients who did not undergo surgery for two months, and the survival of patients who were undergoing lobectomy was 34 months In our study, the 5-year survival rate in stage I tumors were 54.2% in patients with SCLC, and the 2-year survival rate was 33%. Comparison between the studies is shown in table 4.

Table 4. Assessment of survival in the presence of literature.

Author	Year	Number of patients	Methods	5 Year survival (%)
Fujimori [16]	1997	22	Prospective	73
Rea [17]	1998	104	Prospective	52
Rostad [18]	2004	38	Retrospective	45
Brock [19]	2005	23	Retrospective	86
Tsuchiya [20]	2005	61	Prospective	70
Granetzny [21]	2006	95	Retrospective	43
Bischof [12]	2007	39	Retrospective	49
Lim [22]	2008	59	Retrospective	60
Vallieres [14]	2009	349	Retrospective	48
Schreiber [23]	2010	863	Retrospective	52.6
Varlotto [24]	2011	584	Retrospective	47.4
Weksler [25]	2012	895	Retrospective	30.1
Takei [26]	2014	243	Retrospective	58.3
Stish [27]	2015	54	Retrospective	48
Current Study	2018	20	Retrospective	54.2

It is recommended to perform detailed mediastinal and distant lymph node metastasis assessment to all patients that planning surgery for primary SCLC [14,28]. In a study done by using Surveillance Epidemiology and End Results (SEER) database, Yu et al [29] Found that the survival outcomes in patients with mediastinal lymph node involvement were worse than those without mediastinum involvement. They also found that the stage I patients that underwent lobectomy had a 50% survival rate [29]. Schreiber et al [23] have found similar survival outcomes in a study of 861 SCLC patients, done with the SEER database (5-year survival 53%). However, N1 and N0 have been reported to be beneficial to patients. In this study, we found N0 patients' 5-year survival rate of 54.2% and N1 patients' 2-year survival rate of 33%. No statistically significant results were found due to the low number of patients in the study. Similar to the literature, T1a tumors have better survival outcomes than the other stages in terms of T stage.

In our study, DFS was 60% in 2 years and 0% in 5 years. Prognostic factor affecting especially DFS is prophylactic cranial radiotherapy. Bang et al reported that there was a statistically significant difference in overall survival in patients receiving PCI (HR 0.55; 95% CI: 0.39-0.77; P = .0005) and time to brain metastasis (HR 0.40; 95% CI: 0.23-0.66; P = .0004). Although our results were found to be similar to the literature, no subgroup analysis could be performed due to the small number of patients in the study.

The main limitations of this study are the low number of patients, being retrospective and lack of a control group of patients who only treated with chemoradiotherapy. However, retrospective comparisons will not be feasible as the performance status of patients receiving surgery is better than patients receiving chemoradiotherapy. Furthermore, there aren't any studies in the literature that compared surgical treatment with chemoradiotherapy treatment as of today.

In conclusion, multimodal therapy is very important for survival in early stage SCLC. Even though SCLC's are very aggressive tumors, the results of our study show that survival outcomes in the early stages are quite satisfactory. Especially, in stage 1 tumors short-term survival rates are shown as successful as non-small cell lung cancers. Therefore surgical treatment should be considered before definitive chemoradiotherapy in early stage SCLC. However, further prospective studies are needed for the evaluation of surgical treatment versus medical therapy.

Declaration of conflicting interests

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

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Original Article

Can neutrophil to lymphocyte ratio and platelet to lymphocyte ratio predict the severity of sternum fractures?

Muharrem Özkaya[1*], Cihan Bedel[2]

[1]Department of Thoracic Surgery, Health Sciences University, Antalya Training and Research Hospital, Antalya, Turkey

[2]Department of Emergency Medicine, Health Sciences University, Antalya Training and Research Hospital, Antalya, Turkey

ABSTRACT

Background: Although the NLR and PLR are cheap and widely available biomarkers, literature regarding their usage in trauma patients is scarce. It seemed to us interesting to evaluate the prognostic value of the NLR and PLR for trauma patients. In this manner, we selected a small group of trauma patients with sternal fractures and aimed to investigate their correlation with the serum NLR and PLR. To the best of our knowledge, this is the first study investigating the clinical value of these cheap and widely available biomarkers in trauma patients.

Materials and Methods: We designed a retrospective study examining the utility of NLR and PLR in estimating trauma severity in sternum fracture patients who admitted to our hospital between January 2013 and April 2018. Patients were divided into two groups: isolated sternum fracture group (36 patients with sternal fracture and without any complications in thorax or other system and/or only 1 or 2 rib fractures) and complicated sternum fracture group (19 patients with sternal fracture and with associated complications in thorax or other systems). Injuries were not graded but referred as severe according to the associated complications in thorax or other systems. The key clinical parameters, including NLR and PLR were compared among the groups.

Results: Based on the ROC curve, the best NLR cut-off value to predict complicated sternum fracture group patients was 2.1, with 88.9% sensitivity and 28% specificity, whereas the best PLR cut-off value was 123.8, with 72% sensitivity and 68% specificity.

Conclusions: The results may indicate a clinically useful marker that can be easily and reliably measured from a blood sample to predict outcome of trauma patients with sternal fractures.

Key Words: sternum fracture, neutrophil, lymphocyte, platelet, ratio

Corresponding Author*: Muharrem Özkaya, MD. Health Sciences University Antalya Practice and Research Center, Department of Thoracic Surgery, Muratpasa, 07100, Antalya, Turkey
E-mail: muharrem.ozkaya@sbu.edu.tr - Phone: +90 532 6543438 15
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Introduction

Thoracic trauma is responsible for 25% of post-traumatic deaths [1]. Sternal fracture (SF) accounts for about 3–8% of admissions for thoracic trauma. Isolated sternal fracture (ISF) may be defined as a SF without any other thoracic injury such as rib fracture, hemothorax, or pneumothorax. The incidence of ISF has been rising by the increasing use of seatbelts since legislation was implemented in 1983 [2,3].

Stimulation of a variety of inflammatory mediators takes place immediately after trauma. Although the level of CRP has been used in clinical practice for many years, it is relatively non-specific and many clinical studies have shown that there is no correlation between the serum CRP and the severity of injury or prediction of survival in poly traumatized patients. In this manner several studies have been published addressing the search for a clinically useful marker that can be easily and reliably measured from a blood sample [4].

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been defined as novel markers of inflammation and thrombotic events which can be easily measured from the complete blood cell count (CBC). NLR possesses diagnostic value in certain pathologies characterized by systemic or local inflammatory response such as acute coronary syndrome, non-ST myocardial infarcts, ischemic and hemorrhagic strokes, pulmonary embolisms, and several types of cancer [5-7]. PLR is currently considered to be a more sensitive marker and also assumed as a prognostic factor in breast cancer, and ovarian and colorectal cancers [8].

Although the NLR and PLR are cheap and widely available biomarkers, literature regarding their usage in trauma patients is scarce. It seemed to us interesting to evaluate the prognostic value of the NLR and PLR for trauma patients. In this manner, we selected a small group of trauma patients with sternal fractures and aimed to investigate their correlation with the serum NLR and PLR. To the best of our knowledge, this is the first study investigating the clinical value of these cheap and widely available biomarkers in trauma patients.

Materials and Methods

The study was approved by Institutional Review Board with the approval number 2018-142 and the tenets of the Declara¬tion of Helsinki were followed. After the approval we car¬ried out a retrospective hospital record review of the data of the thoracic trauma patients between January 2013 and April 2018 (64 months). Inclusion criteria of the study were: (1) admission with thoracic trauma, (2) presence of sternal fracture on x-ray (lateral chest x-ray or sternal view x-ray) or chest computed tomography (CT), (3) age over 18 years. Patients with missing data of clinical, laboratory or radiographic findings and the patients with a history of malignant disease were excluded from the study.

Injuries were not graded but referred as severe according to the associated complications in thorax or other systems. An ISF was considered as a sternal fracture without other thoracic or concomitant injuries except two or less rib fractures. A complicated sternal fracture (CSF) was regarded as a severe injury including a sternal fracture with associated other thoracic (more than two rib fractures) or concomitant injuries. Patients were divided into two groups: isolated sternum fracture (ISF) group (36 patients with sternal fracture and without any complications in thorax or other system and/or only 1 or 2 rib fractures) and complicated sternum fracture (CSF) group (19 patients with sternal fracture and with associated complications in thorax or other systems) (Figure 1).

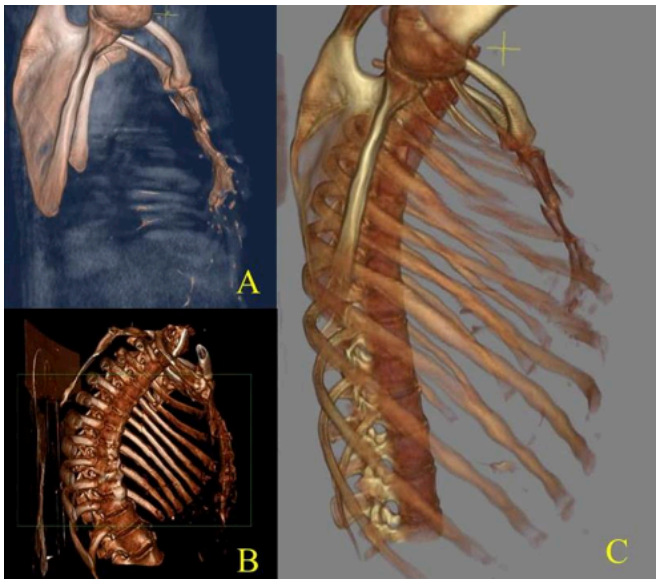

Figure 1. Three dimensional (3D) computed tomographic reconstruction views of sternal fractures. A. Ribs and thoracic vertebrae are extracted, B. Right hemi-thoracic structures are extracted, C. All bony structures are present.

Patient demographics (age and sex), cause of trauma, type of care (inpatient, outpatient), laboratory results (including NLR and PLR from complete blood count), length of stay data were gathered and analyzed. Imaging investigations included x-ray (lateral chest x-ray or sternal view x-ray) and chest CT in all cases. The SF was diagnosed by x-ray or chest CT. An electrocardiogram (ECG) was also performed. An Echocardiogram (ECHO) was performed only in patients with pathological ECG or suspected pericardial effusion on chest CT. Investigations including cardiac

enzymes such as creatine phosphokinase (CPK), myocardial branch of creatine phosphokinase (CKMB) and high sensitive troponin (Hs-Tn) were also recorded.

Pericardial effusion, myocardial contusion and vascular pa¬thologies were considered as abnormal ECHO findings. ST segment changes were accepted as abnormal ECG findings. Hs-Tn and CK-MB tests were evaluated; levels above 14 ng/L of Hs-Tn and/or above 5% of CK-MB (percentage of total CK) were con¬sidered as cardiac enzyme elevation.

Laboratory parameters

The laboratory results were evaluated according to the first venous blood samples taken on admission to the emergency department. Samples were analyzed within 1 h of collection using an automated blood cell counter (Coulter® LH 780 Hematologic Analyzer, Beckman Coulter Inc. Brea, USA). Reference values were 2.1–6.1×103/mm3 for neutrophils, 1.3–3.5×103/mm3 for lymphocytes, 156– 373×103/mm3 for platelets. The NLR was calculated as the ratio of the neutrophil count to the lymphocyte count, and the PLR was calculated as the ratio of platelet count to lymphocyte count.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 16.0 software (SPSS Inc., Chicago, IL). Median and inter quartile range (IQR) were used as descriptive statistics for continuous variables. To compare qualitative variables, Fisher's Exact Test was used.

Mann–Whitney U test was used for analysis of non-parametric continuous data. p value < 0.05 was considered as statistically significant.

Results

A total of 55 patients with a diagnosis of SF were included to the present study. There were 41 (74.5%) male and 14 (25.5%) female with a male to female ratio of 2.92:1. The median age was 50 years and their age ranged from 19 to 90 years with a mean of 52.2 ± 14.6. There were 36 patients (65.5%) in the isolated sternum fracture group and 19 patients (34.5%) in the complicated sternum fracture group. Baseline characteristics of the study population and the comparisons of demographic and laboratory values between the groups are shown in tables 1 and 2, respectively. There were statistically significant differences between ISF and CSF groups. The mean platelet count, PLR, NLR, CKMB, LDH and duration of hospital stay were significantly higher in CSF group than in ISF group and lymphocyte count and CPK levels were significantly higher in ISF group than in CSF group.

Table 1. Baseline characteristics of the study population.

	n (%)
Gender	
Male	41 (74.5%)
Female	14 (25.5%)
Type	
Isolated	36 (65.5%)
Complicated	19 (34.5%)
Age (year)	52.2 ±14.6
Cause of trauma	
Motor vehicle accident	33 (60%)
Fall	20 (36.4%)
Violence	2 (3.6%)
Hospital stay (day)	4.5 ±6.2

Table 2. Comparison between isolated and complicated sternum fracture group regarding the studied parameter

Parameter		Isolated sternum fracture group	Complicated sternum fracture group	P
Age (years)	Mean ± SD range	51.1 ± 15.2	54.2 ± 13.4	0.46
Gender	Female Male	(9;25%) (27;75%)	(5; 26.3%) (14; 73.3%)	0.91
Hemoglobin	Mean ± SD range	13.7 ± 1.4	13.3 ± 2.1	0.39a
Neutrophil count (×103/mm3)	Mean ± SD range	6.5 ± 3.1	7.8 ± 4.8	0.56
Lymphocyte count(×103/mm3)	Mean ± SD range	2.5 ± 2.1	1.6 ± 1.2	0.016
Platelet count (×103/mm3)	Mean ± SD range	227 ± 389.7	257 ± 813.3	0.13
PLR	Mean ± SD Range	124.6 ± 71.8	311.9 ± 504.7	0.010
NLR	Mean ± SD Range	3.4 ± 2.2	9.1 ± 11.5	0.024
CPK	Mean ± SD Range	427.9 ± 428.8	319.6 ± 264.1	0.41
CKMB	Mean ± SD Range	13.1 ± 8.3	21.2 ± 10.1	0.04
LDH	Mean ± SD Range	240.7 ± 41.9	431 ± 313.8	0.006
Hospitalisation day	Mean ± SD Range	2.2 ± 0.7	7.2 ± 8.5	0.001

Abbreviations: NLR (neutrophil-to-lymphocyte ratio), PLR (platelet-to-lymphocyte ratio), CPK (creatine phosphokinase), CKMB (myocardial branch of creatine phosphokinase), LDH (lactate dehydrogenase).

The most common associated pathology was rib fracture (36.3%) in 20 patients with SF. Other intrathoracic injuries associated were; pneumothorax in one (5.2%) patient, hemopneumothorax in one (5.2%) patient, pulmonary contusion in two patients (10.5%) and hemothorax in two patients (10.5%) in CSF group. The most common extrathoracic associated injuries were extremity fractures in seven patients (36.8%) in CSF group. Other extrathoracic associated injuries were vertebral injuries in three (15.7%) patients and head injury in one (5.2%) patient.

Control of pain with analgesics was the one and only therapeutic option in ISF group. Sternum fixation was performed in two (10.5%) patient and tube thoracostomy was performed in four (21.0%) patients in CSF group.

There was no mortality or morbidity in ISF group. The mortality and morbidity rates in CSF group were 3.6% (n =2), 16.2% (n = 9), respectively ($p < 0.001$). Causes of morbidity were atelectasis in 5 patients, respiratory insufficiency in 1 patient, and clotted hemothorax in 1 patient. Two patients with flail chest were intubated and died because of pulmonary infection.

Abnormal ECG findings were detected in 11 of 36 patients in ISF group and 6 of 19 patients in CSF group. There was no statistically significant difference in the pres¬ence of abnormal ECG findings among patients in both groups. Also, abnormal ECHO findings were detected in one (with a previous history of mitral regurgitation) of 18 patients in ISF group and two of 14 patients in CSF group. The difference was not sta¬tistically significant ($p = 0.22$). There was no statistically significant difference in the presence of cardiac enzyme eleva-tion between two groups ($p = 0.25$) (Table 3).

Table 3. Cardiac assesment of isolated sternal fracture vs. complicated sternal fracture (SF) subjects.

	Isolated SF	Complicated SF	p*
Abnormal ECG (n/N)	11/36	6/19	0.93
Abnormal Echo (n/N)	1/18	2/14	0.22
Cardiac enzyme elevation (n/N)	2/22	3/15	0.25

The cutoff NLR was obtained regarding the differences between the ISF and CSF groups by using ROC analysis. For the NLR, the AUC was estimated as 58.5% (95% CI, 51.34–65.41%), and the best cutoff NLR was 2.1 (sensitivity, 88.9%; specificity, 28%) (Table 4, Figure 2).

The cut off PLR was obtained regarding the differences between the ISF and CSF groups by using ROC analysis. For the PLR, the AUC was measured as 70% (95% CI, 63.1-76.3%), and the best cutoff PLR was 123.8 (sensitivity, 72%; specificity 68%) (Table 4, Figure 2).

Table 4. Prediction performance of the NLR and PLR for complication

	NLR (Cut-off: 2.1)	PLR (Cut-off: 123.8)
Sensitivity	88.9(81.17-94.38)	72(62.1-80.5)
Specificity	28(19.48-37.87)	68(57.9-76.9)
Positive likelihood ratio	1.24(1.08-1.43)	2.25(1.65-3.1)
Negative likelihood ratio	0.39(0.21-0.74)	0.41(0.29-0.58)
Positive Predictive Value	55.28(51.79-58.72)	69.2(62.2-75.4)
Negative Predictive Value	71.79(57.31-82.84)	70.8(63.3-77.4)
Accuracy	58.5(51.34-65.41)	70(63.1-76.3)

Abbreviations: NLR: neutrophil–lymphocyte ratio; PLR: platelet–lymphocyte ratio

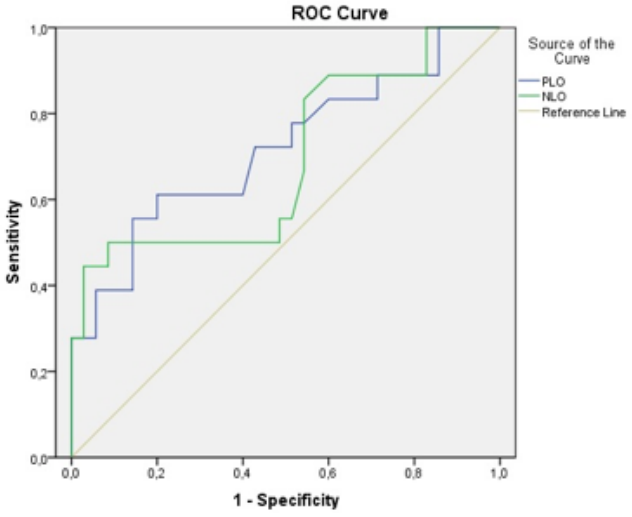

Figure 2. Receiver-operating curve for the relationship between NLR and PLR.

A multivariate logistic regression analysis using the laboratory parameters that have a significance level of $p < 0.05$ in the univariate analysis demonstrated that PLR (OR: 0.33; 95% CI: 0.1-1.06; $p = 0.52$), NLR (OR: 0.29; 95% CI: 0.1-1.06; $p = 0.078$), the difference between ISF and CSF groups was not statistically significant (Table 5).

Table 5. Effect of univariate variables on the presence of associated injuries in patients with sternal fractures.

Variables	p	Odds ratio	95% CI
Lymphocyte	0.32	2.90	0.31-26.84
Platelet	0.52	0.68	0.21-2.15
PLR	0.59	0.33	0.1-1.06
NLR	0.078	0.29	0.07-1.19
CKMB	0.21	0.48	0.15-1.53
LDH	0.001	0.13	0.03-0.48

Discussion

Thoracic traumas are the most important injury in severely injured patients, and about 50% of those with multiple trauma suffer from an associated thoracic trauma [9]. Sternal fractures is observed in 3-8% of blunt thoracic traumas and can either occur in isolation, or with other associated injuries [10]. Although the prognosis is excellent for isolated sternal fractures, the overall mortality is 0.7% [11,12]. However, two-thirds of sternal fractures have concomitant injuries with an associated mortality ranging from 25-45 % and the morbidity and mortality of sternal fractures increase in the presence of associated injuries [13,14]. Our results were similar with the literature. There was no mortality or morbidity in ISF group whereas the mortality and morbidity rates in CSF group were 3.6% (n = 2), 16.2% (n = 9), respectively ($p < 0.001$). It has also been reported that two or more rib fracture was the most common (46.9%) associated injury in patients with SFs [15] .Similar with the literature; the most common associated pathology was rib fracture (36.3%) in our patients with SF.

The mean platelet count, PLR, NLR, CKMB, LDH and duration of hospital stay were significantly higher in CSF group than in ISF group in our study results.

There is still debate whether the associated injuries affect the length of hospital stay or not. According to Wiener et al [16] the length of hospital stay varies with the presence of an accompanying pathology. Potaris et al [17] on the other hand reported that there is no significant difference in the length of hospital stay between SF patients with or without associated injuries. Perez et al [18] also reported that patients with associated injuries have longer hospital courses than ISF patients. In our study, average duration of hospitalization in sternal fractures was 4.5 ± 6.2. The average duration of hospitalization was significantly higher in CSF group than ISF group ($p = 0.001$).

In patients with SF, cardiac injury should be excluded. The incidence of cardiac injury following blunt chest trauma has been reported up to 90% [19]. And also, the frequency of myocardial contusion was reported as 18% in patients with SF [20]. In a recent study Perez reported that of 184 patients that underwent at least one of the three cardiac contusion work-up tests, 24.4% had abnormal ECG, 15.9% had abnormal Troponin, and 8.8% had abnormal ECHO findings [18]. All of our patients were monitored for ECG and cardiac enzyme levels. Patients with pathologic findings at ECG and elevated cardiac enzyme levels were evaluated with ECHO. We detected 17 (30.9%) ECG changes and 5 (13.5%) elevated cardiac enzymes in our patients. We also had three patients (9.3%) with minimal pericardial effusion and one them was in ISF group with a previous history of mitral regurgitation. Although, there was no statistically significant difference in the pres¬ence of abnormal ECG findings and cardiac enzyme eleva¬tion among patients in both groups in our study, higher levels of PLR in CSF group may indicate an undiagnosed cardiac injury.

The three most common causes of the fracture were motor vehicle accident 33 (60%), 20 fall (36.4%) and violence 2 (3.6%), respectively. Wojcik [20] reported that motor vehicle accidents (59%) were the most common cause of SF in their retrospective study. Rashid et al [21] reported that patient age ranged between 30 and 92 years and the mean age was 64. Velissaris et al [19] reviewed 73 patients with SF so that most of the cases were male (69.8%), with a median age of 51. In our study, the median age of the cases was 50 (19-90) years and the most frequent cause of the fracture was motor vehicle accident (60%).

NLR is a simple, cheap and effective biomarker that has been studied properly in the literature in order to predict severity of multiple diseases, including inflammatory conditions, neoplastic diseases like gastric cancer, thyroid cancer, breast cancer, and solid tumors [22,23]. But literature regarding their usage in trauma patients is scarce. According to our results, NLR were a useful indicator for severity of sternum fractures. In the present study, we found that the sensitivity, specificity, negative predictive value and positive predictive value of NLR count were 88.9, 28, 71.79, and 55.28%, respectively, with 58.5% diagnostic accuracy for a cut-off value of 2.1.

PLR has been identified and used for these purposes and as a sign of severe inflammation. In prior studies PLR were also investigated in patients with myocardial infarction, peripheral arterial occlusive disease, end-stage renal diseases, malignancies [15,24-27]. Lack of publication in the English literature regarding the relation between serum biomarkers and severity of SF didn't allow the possibility of proper comparing our results, so that in our discussion we mainly presented our results about this topic. According to the results of our study, PLR were a useful indicator for severity of SF and the sensitivity, specificity, negative predictive value and positive predictive value of PLR count were 72, 68, 70.8, and 69.2%, respectively, with 70% diagnostic accuracy for a cut-off value of 123.8.

Our study had limited number of patients, which can be attributed to the rarity of sternal fractures and ISF being even rarer. Lack of publication in the English literature regarding the topic of the study didn't allow the possibility of proper comparison of our results. The small patient population and the retrospective nature of the study do not allow us to draw any further conclusion.

To our knowledge, there is no literature data exists regarding relation between serum biomarkers and severity of SF. In our opinion, the present study is the first report about the association of NLR and PLR with the severity of SF. Even with the above-mentioned limitations, we can conclude that these results may indicate a clinically useful marker that can be easily and reliably measured from a blood sample to predict outcome of patients with SF. Further studies are necessary to externally cross-validate our findings in a larger cohort of SF patients.

Declaration of conflicting interests

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Original Article

Comparison of the outcomes of the implanted subcutaneous ports in cancer patients: six-years single center experience

Ali Cevat Kutluk*, Hasan Akın

Department of Thoracic Surgery, Yedikule Chest Disease and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

ABSTRACT

Background: The preferred site of venous access ranges from deep veins (internal jugular or subclavian veins) to superficial veins (external jugular, anterior jugular, and upper limb veins). The aim of the study is to evaluate experience of single surgeon and compare the outcomes of the subclavian (SCV), internal jugular (IJV), and external jugular (EJV) veins in terms of procedure time and complications retrospectively.

Materials and Methods: The study included 327 patients who had port placement between 2012 and 2018. The mean age of all cases was 55.67 years, and the patients were divided into 3 groups according to venous sites; subclavian (SCV), internal jugular (IJV), and external jugular veins (EJV). Only local anesthesia was given and no antibiotic prophylaxis was provided before the intervention. The 3 groups were compared regarding age, sex, primary tumor site, procedure time, and complications.

Results: The procedure was significantly longer in the SCV group than the other 2 (43.35 min vs 34.58 and 33.71 min). Removal of the catheter was less common in the IJV group than the other 2 groups. Overall complications in the IJV group were lower than the other 2 groups, especially catheter malposition and pneumothorax rates were lower in the IJV group.

Conclusions: In light of the findings of the study implantable port placement via internal jugular vein is safe and had lower complication rates than either the subclavian or external jugular veins.

Key Words: cancer, chemotherapy, implantable venous port.

Corresponding Author*: Ali Cevat Kutluk, MD. Yedikule Gogus Hastanesi. Belgradkapi C. No:1. 34020. Zeytinburnu, Istanbul, Turkey.
E-mail: dralikutluk@gmail.com
Phone: +90 505 630 91 87
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Introduction

According to Turkish statistics 167.463 new patients had cancer in 2015 [1]. Most of these patients are diagnosed in the late stages of their diseases. Therefore, chemotherapy comes about as the only treatment method for these patients. Because chemotherapy is a long-term treatment method the access site to administer the chemotherapeutics is important for patient comfort. The implantable venous sites are not only used to deliver chemotherapy regimens but also used to administer fluids, blood products and parenteral nutrition solutions.

At the beginning subclavian vein was used fort port placement. But later on jugular vein gained popularity due to its advantages over subclavian vein. The aim of the study is to compare the duration and the complications of the implantable ports of subclavian and jugular veins.

Materials and Methods

After approval by the Ethics Committee (Institutional Review Board of Istanbul Education and Research Hospital of Health Sciences University26/10/2018-1481), we designed a retrospective cohort study and included 327 patients who had subcutaneous implantable ports (Power Loc® port access needle, C.R. BARD, Salt Lake City, Utah, USA) between April 2012 and April 2018. The ports were placed one of the three sites, subclavian, internal, or external jugular veins. The choice of the site was based on the initial surgery site, radiotherapy status, and the experience of the surgeon. All ports were placed by the same thoracic surgeon. Informed consent was taken from all patients. The files of the patients were evaluated retrospectively and age, gender, source of the primary tumor, access site, mean of catheter days, and complications were recorded.

Most of the patients were referred by the oncologists. The thorough physical examinations of all patients were performed, and detailed medical and surgical histories were recorded. Complete blood count, routine blood chemistry, prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR), electrocardiography, chest X-ray were taken. All patients were consulted with an anesthesiologist.

All procedures were in the operation room under sterile conditions. The patients were put in Trendelenburg position. The operation sites were cleansed with povidone-iodine twice and covered with sterile dresses. Local anesthesia was conducted with lidocaine hydrochloride 3mg/kg. Sedation was provided with midazolam 2-3 mg in un-cooperated patients. In all patients, venous entry was performed with an 18 G Seldinger needle and the tip of the guide-wire was advanced into the vena cava. After dilatation the catheter was placed into the vena cava. As for pocket preparation a 2-3 cm incision was made 5 cm below the clavicle. A tunnel was made between the venous site and the pocket by blunt and sharp dissection. The fatty tissue in the pocket was removed to place the port chamber. The catheter was connected to the port chamber with a trocar. The catheter was flushed with diluted heparin solution using a Huber needle. The Huber needle remained in the port chamber to prevent flip-over until the end of the procedure. The port chamber was fixed to the pectoral fascia by polyglactin sutures. The wound was closed with absorbable subcuticular sutures. Port efficacy was checked with an aspiration of blood, and the reservoir was flushed with heparin saline solution (9 cc 0.9% NaCl plus 1 cc heparin) to show any leakage. A chest x-ray was taken to check the position and the kinking of the catheter, and possibility of pneumothorax (Figure 1).

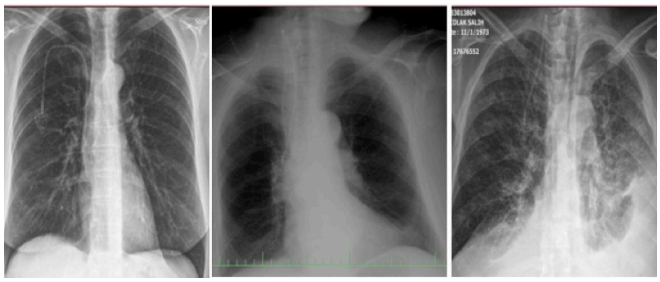

Figure 1. Placement of SCV, IJV, and EJV ports.

The malpositioned or kinked catheters were corrected under fluoroscopic guidance (Figure 2). The patient was discharged on the same day with paracetamol 500 mg, three times a day. Some catheters were placed during the operation performed to resect the pulmonary metastases.

Figure 2. Malposition of a SVC catheter.

Statistical Analysis

Descriptive statistics were used, including mean ± standard deviation, median and range, frequencies and proportions. Chi-square test or Fisher's exact test were used to compare the proportions and student t-test was used to compare the means. ANOVA was used to compare the groups. $P < 0.05$ is considered statistically significant.

Results

During the study period 327 patients had 342 implantation of ports either via subclavian vein (SC, 196 patients), internal jugular vein (IJC, 95 cases), and external jugular vein (EJV, 36 patients). The mean age of all patients was 55.86 ± 11.45 years. Male patients comprised 59% of the patients (193 cases). The 3 groups were homogenous in respect to age, sex, and intervention side (Table 1).

Table 1. Clinical characteristics of the patients.

	SCV	IJV	EJV	P
Age	55.67	56.43	56.71	0.86
Sex (M/F)	117/79	52/43	21/15	0.26
Side (R/L)	314/13	91/4	33/3	0.35
Tumor Origin				
Head and Neck cancer	42 (21%)	26 (27%)	(4%)	0,16
Lung cancer	38 (19%)	16 (17%)	(23%)	0.71
Gastrointestinal System	32 (16%)	22 (23%)	(29%)	0.52
Colorectal cancer	67 (34%)	23 (24%)	(31%)	0.79
Ovary cancer	17 (10%)	(9%)	(13%)	0.83
Procedure time (minutes)	43.35	34.58	33.71	0.001
Length of the catheter (cm)	19.80	26.16	23.71	0.001
Access Vein, N	196	95	36	
Removal for complication	14 (7%)	4 (4%)	4 (11%)	0.24

Colorectal cancers were the leading indications in all three groups, and gastrointestinal system followed them. Placing the port was faster in the ICV and EJV groups than the SC group, and the difference was significant. On the contrary, the port length was significantly longer in the ICV and ECV groups than SC group. Although occasion of port removal was least common in ICV group than the other 2 groups the difference did not reach significance.

Table 2. Complications in 3 groups.

Complications	SC	IJV	EJV	P
Catheter malposition	13 (7)	2 (2%)	3 (8%)	0.08
Thrombosis	4 (2%)	2 (2%)	1 (3%)	0.63
Pneumothorax	6 (3%)	1 (1%)	0	0.27
Arterial injury	5 (3%)	2 (2%)	1 (3%)	0.58
Hemothorax	2 (1%)	0	0	0.45
Pinch-off	1 (0.5%)	0	0	0.67
Change of access site	14 (7%)	5 (5%)	0	0.35
Wound infection	6 (3%)	2 (2%)	2 (6%)	0.21
Skin necrosis	5 (3%)	2 (2%)	1 (3%)	0.32

Change of access site and the catheter malposition were leading complications in all patients (Table 2). Although catheter malposition was more common in the SC and EJV approach the difference was not found significant. Similarly the rate of pneumothorax was highest in the SC group. The chance of arterial injury was higher in the SC and EJV than the IJV group. An interesting complication called pinch-off (spontaneous fracture of an implanted central venous catheter) occurred in only one case of SC group and treated successfully with thoracotomy (Figure 3).

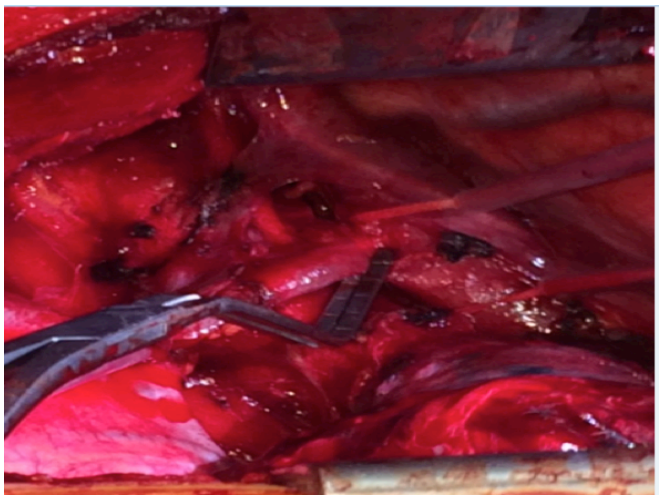

Figure 3. Removal of fractured catheter (pinch-off).

Discussion

The management of the patient with cancer is challenging for physicians in terms of venous access that is not only for chemotherapy but also for administering blood products, antibiotics, fluids, and access to the bloodstream for clinical monitoring. The use of implanted ports provides comfort to the patients by preventing repeated venipunctures. During the last 2 or 3 decades the type and the structure of catheters have changed, the calibers and lumen numbers of the catheters have increased. The placement and care of the implantable ports requires a multidisciplinary approach including surgeons, nurses, oncologists, and anesthesiologists.

According to the experience of the surgeon and the condition of the patient deep or superficial veins are used for entry sites. In the current study we started with the subclavian vein first and added the internal jugular vein, and used external vein in 36 patients in recent years. Our experience showed us that the best results were obtained by the IJV approach with the least complication rates. Li et al, in a 344-patient series, used SCV, IJV, and upper arm vein for access. They claimed that upper arm vein had superior to both IJV and SCV approach in terms of higher success rates and lower complication rates [2]. This study was a retrospective study like many other series in the literature.

A rare randomized study was reported from Biffi et al [3]. The study included 401 patients with 3 venous accesses; SCV, IJV, and cephalic vein. Unlike the findings of Li's the Biffi reported that all 3 groups were similar with respect to success rates and complication rates. A similar study by Aribas et al. compared the IJV and SCV for patency times and complication rates and they pointed out that there was no difference between the 2 methods [4]. Another study comparing 145 patients with IJV to 165 EJV patients, and reported that the venous insertion site did not influence the early or late complication rates [5].

There are also series reporting the outcomes of single venous sites. One of the largest series in the literature was reported by Ahn and et al [6]. They placed 1254 venous ports under the guidance of ultrasound and fluoroscopy. They pointed out that the IJV approach is a safe and effective method with an extremely high technical success rate, low peri- and post-procedural complication rates, and satisfactory clinical outcome. Only 4% of the cases experienced early or late complications. In a similar study, Cil et al reported one of the highest success rate (99.8%) and lowest complication rate (0.63%) in the literature. The study was performed by radiologists and under ultrasound guidance [7]. IJV access could be either high or lower, and when appropriate high jugular approach was reported to be good alternative to low jugular approach [8]. Similar success rates were reported from another radiology department [9].

Keum et al reported a series with 242 patients who had 245 ports inserted via subclavian vein [10]. All ports were placed by a thoracic surgeon and no radiologic guidance was used. They reported 4.5% complication rate and recommended that the use of radiologic guidance could decrease the complications.

There some series and case reports in the literature reporting the use of superficial veins (external jugular and anterior jugular veins). Pancholi et al reported the use of external jugular vein in 23 patients and recommended its use with excellent safety and short procedure time [11]. Rott and Boecker reported a case and reviewed the literature about the use of anterior jugular vein [12].

An interesting complication of spontaneous fracture of an implanted central venous catheter (pinch off syndrome) occurred in one our patients with SCV group. The fractured part was in the Azygos vein and the attempt to remove by angiography was unsuccessful. We performed thoracotomy and removed the fractured catheter. This complication was reported in the literature [2,13]. Biffi also reported the cost-effectiveness of different access sites, and pointed out that subclavian vein approach was the most cost-effective method of

central venous port placement and use [14].

American Society of Clinical Oncology (ASCO) published a clinical practice guideline for the central venous catheter care of the patient with cancer [15]. They pointed out there was insufficient evidence to recommend a specific type of CVC or insertion site, but femoral vein insertion should be avoided, except in certain emergency situations. They also recommended that port placement should be performed by well-trained health care providers, and not to give prophylactic use of systemic antibiotics before port placement.

This is a retrospective and non-randomized study. It comprised the cases during the learning curve. In the light of our findings port placement via the internal jugular vein is safe and the complication rate is lower than subclavian vein and external jugular vein. Though it was not found significant both malposition and pneumothorax rates are higher in the SCV and EJV groups.

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Original Article

Pediatric foreign body aspirations: experience of 263 cases

Ozgur Katrancioglu[1*], Sule Karadayi[2], Ekber Sahin[2]

[1]Department of Thoracic Surgery, School of Medicine, Omer Halisdemir University, Niğde, Turkey
[2]Department of Thoracic Surgery, School of Medicine, Cumhuriyet University, Sivas, Turkey

ABSTRACT

Background: Foreign body (FB) aspiration is a serious clinical situation due to its life-threatening status and especially common in the childhood period. We aimed to present the diagnosis and treatment of foreign bodies in pediatric age group.

Material and Methods: Files of 510 patients aged 16 years and below that underwent rigid bronchoscopy due to suspicion of FB aspiration between June 1994 and November 2017 were retrospectively reviewed. 263 cases were included to the study that underwent foreign body removal. The cases were assessed in terms of gender, age, type and localization of the foreign body, clinical complaint, radiological findings, treatment method, complication and mortality.

Results: Among the patients 45.6% were male and 54.4% were female. The aspirated foreign bodies varied from dried nuts to plastic, from hijab needles to beads. The most aspirated foreign body were dried nuts. 51% of them were removed from the right main bronchus, 31.9% from the left main bronchus, and 17.1% from the trachea. 97.8% of the foreign bodies were removed via bronchoscope. Thoracotomy was performed in 6 cases since the foreign bodies were not extractable with a bronchoscope or due to developing complications. No mortality occurred.

Conclusions: FB aspiration can lead to life-threatening complications in children aged 3 years or below. Bronchoscopy should be performed in all cases of foreign body aspiration, including suspicious cases. Notably, the bronchoscopy procedure should be carried out by a well-trained, experienced anesthesiologist-endoscopy team and with appropriate tools.

Key Words: childhood period foreign body aspirations, trachea, bronchus.

Corresponding Author*: Ozgur Katrancıoğlu, MD. Department of Thoracic Surgery Omer Halidemir University School of Medicine, 51240, Niğde, Turkey.
E-mail: ozgursongur@gmail.com
Tel: +90 388 2252583
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Introduction

Foreign body (FB) aspirations are situations that should be treated immediately due to its life-threatening status [1], and are most commonly seen in the pediatric age group [2]. The majority of the cases are children aged 3 years or below, and 7% of these children die due to aspiration [3,4]. The reasons of the high incidence rate in this age group are the fact that the molar teeth does not grind food items properly, speaking or playing while there is food in the mouth [5,6]. The aspirated foreign bodies may vary according to the sociocultural characteristics and nutritional habits of families and societies [7]. Liquids are more frequently seen in infants, organic food and parts of plastic toys are commonly encountered in children [2,8,9]. Golden standard in treatment is rigid bronchoscopy. However, flexible bronchoscopy is also useful in some cases [10]. In cases where rigid bronchoscopy is unsuccessful, foreign bodies are extracted with surgeries, including tracheostomy, bronchotomy and thoracotomy [11-13]. The immediate and reliable extraction of the aspirated foreign bodies is very significant in terms of preventing serious complications, including death [14].

In this study, we aimed to present the clinical findings and outcomes of our pediatric patients that underwent FB extraction in our clinic.

Material and Methods

Files of 510 patients aged 16 years and below that underwent rigid bronchoscopy due to suspicion of FB aspiration between June 1994 and November 2017 in our clinic were retrospectively reviewed. Approval of the ethical committee was obtained for the study.

For the diagnosis; history of aspiration, clinical findings, physical examination and radiologic methods were used. 263 cases that underwent foreign body extraction were included to the study. In all cases, rigid bronchoscopy was performed under general anesthesia using muscle relaxants. The cases were assessed in terms of gender, age, type and localization of the foreign body, clinical complaints, radiological findings, treatment method, complications and mortality. Patients were also divided into three groups according to their time of diagnosis: in the first 24 hours group, in the first week and after the first week group.

Statistical Analysis

SPSS 22.0 software was used. Mann-Whitney U test was used to compare the differences between two groups. Chi-square test were used to compare the frequency of two or more groups. A p value of < 0.05 was considered significant.

Results

Among the 263 cases that underwent foreign body extraction, 120 (45.6%) were male and 143 (54.4%) were female children. The age of the patients ranged between 5 months and 16 years (mean age: 5 years 4 months). In age-wise patient distribution, it was seen that the 0-3 years age group was listed first with 59.3%, followed by 10 years and above group with 25.9% (Table 1). The most common complaints of the patients were coughing, shortness of breath, wheezing and fever.

Table 1. Age distribution of cases that underwent bronchoscopy due to foreign body aspiration.

Age	n	%
0-3	156	59.3
3-7	22	8.4
7-10	17	6.5
> 10	68	25.9
Total	263	100

The most frequent radiological findings were radiopaque foreign body in 28.9% (76 cases) (Figure 1), followed by normal radiography in 24.7% (65 cases), unilateral hyperaeration in 19.8% (52 cases) and atelectasis in 15.2% (40 cases) (Figure 2).

Figure 1. Image of the aspirated construction nail on posteroanterior chest x-ray of a 2-year-old patient.

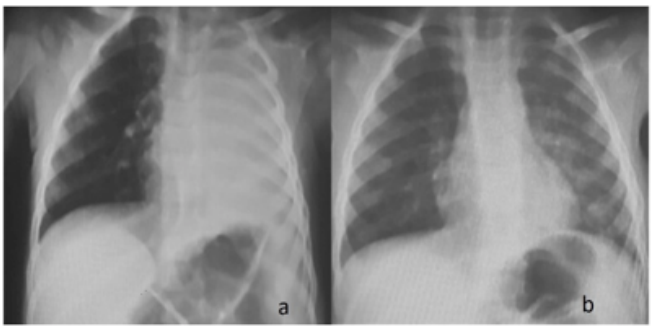

Figure 2a. PA chest x-ray image of the atelectasis after nut aspiration, **b.** image after bronchoscopy.

The foreign bodies were extracted from right main bronchus in 51% of the cases, from the left main bronchus in 31.9% and from the trachea in 17.1% (Table 2).

Table 2. Localizations of the foreign body.

	%
Right bronchial system	51
Left bronchial system	31.9
Trachea	17.1
Total	100

The aspirated foreign bodies were varying objects ranging from dried nuts to plastic nylon, from hijab needles to beads. The most frequently aspirated foreign body were dried nuts. One case aspirated a plastic whistle (Figure 3). When analyzing the cases according to their time of diagnosis, most (61.9%) of the cases were diagnosed in the first week (Table 3).

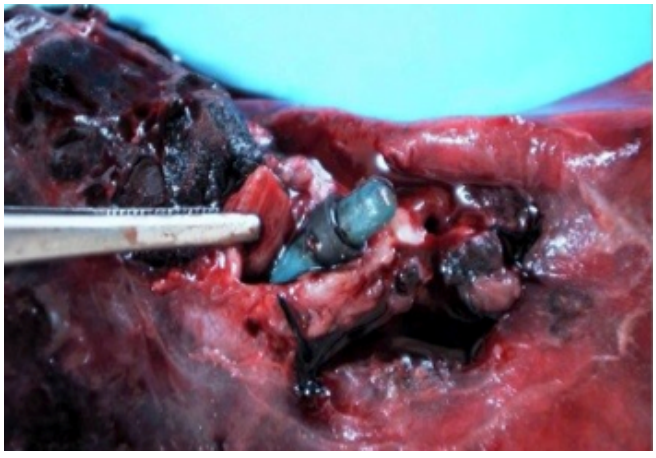

Figure 3. Intraoperative image of the plastic whistle.

Table 3. Distribution of cases according to time of intervention.

Time of intervention	n	%
In the first 24 hours	78	29.7
In the first week	163	61.9
After the first week	22	8.4

The minimum and maximum time of application period to the emergency department was identified as 15 minutes and 6 years, respectively. Rigid bronchoscopy was performed on all patients with general anesthesia. Thoracotomy was conducted in six (2.2%) cases, because rigid bronchoscopy was inadequate or due to developing complications. No mortality was seen in our study group.

Discussion

FB aspiration is a serious situation that potentially results in death. The majority of the aspirations are seen in childhood period. Specifically, it may lead to more serious outcomes in children [15]. In literature, FB aspirations are more frequently seen in male children due to unexplainable reasons. This rate is about 2/1 [15-17]. However, in contrast to the literature, according to our results, FB aspirations were more frequent in female children. This was explained with the fact that hijab needle aspiration was more frequent in our country and all of these cases were seen in girls.

Although FB aspirations are seen at every age, according to literature, it is most commonly seen between 1 and 3 years of age. This may be due to the tendency of children at this age to learn the world using their mouth [15]. Our patient group supports this fact.

Early diagnosis and treatment is important in preventing serious complications. In the pediatric patient group, the aspiration event is generally based on the observation of an adult. The presence of a witness is diagnostic. However, this observation may sometimes be unreliable [18]. The most important complaint of the patients at application to the hospital was coughing and rate of aspiration history among patients may be low. In our patient group, the history of aspiration rate was also low. However, this resulted from hiding the truth due to the social fear of the mother, rather than a witness not being present. Therefore, although there is no history of aspiration in the pediatric age group, FB aspiration should be considered in unexplainable and unresolved coughing despite treatment.

In many studies, organic foreign bodies were the most commonly aspirated foreign bodies, specifically in the pediatric age group. The rate of these foreign bodies ranges between 31.5% and 95% in literature [15].

Among organic bodies, the most common ones were dried nuts. This was supported in our study. However, the type and rate of foreign bodies varies according to country, diet and traditions. In developing countries, the majority of aspirated foreign bodies consist of organic bodies, while plastic bodies are more commonly seen in developed countries. In middle-eastern countries, like our country, aspiration of prayer beads, beads and hijab needle in girls is frequent due to cultural reasons [15]. In our study, hijab needle aspiration, particularly in female children, was common, although not being the most frequent.

Most of the aspirated foreign bodies (90%) are radiolucent, since most of them are food objects. Hence, indirect findings are seen in x-rays [19]. Of these, the most radiologically common ones are air trapping/hyperinflation (33%) and atelectasis (16%). Air trapping/hyperinflation are nearly perfect indicators of foreign bodies [20]. In our study group, since the most frequently aspirated object were food products, there were radiologically indirect findings supporting the literature.

Due to the anatomy of the bronchial tree, FBs are more common in the right main bronchus and its branches [15-17]. In the obtained data of our study, this hypothesis was supported with a foreign body aspiration rate of 51% in the right bronchial system.

In the literature, when analyzing the cases according to their time of diagnosis, the intervention rate at the first 24 hours ranges between 20.5% and 38.4%, and this rate varied between 57.6% and 71% at the first week [15]. Consistent with the literature, these rates were 29.7% for the first 24 hours and 61.9% for the first week in our study.

In our clinic all of the 510 cases that applied due to suspicion of foreign body aspiration underwent rigid bronchoscopy. Of these, foreign bodies were seen in 263 cases. The majority of the foreign bodies (97.8%) were extracted via rigid bronchoscopy. In our study, thoracotomy was performed in six (2.2%) patients due to inadequacy of rigid bronchoscopy or developing complications. Since the foreign body was too peripheral and was reachable via a forceps in 2 cases, since 2 cases that aspirated grass inflorescence developed massive hemoptysis, since one case that aspirated a plastic whistle developed bronchiectasis and the foreign body advanced to the pericardium in a case that aspirated a sewing needle, thoracotomy was performed. Moreover, laryngospasm was seen in 3 cases and cardiac arrest that resolved with intervention was seen in one case. The reason of the rarity of laryngospasm among patients was the use of corticosteroid before and after bronchoscopy, according to the recommendations in the literature [15]. In our study group, mortality was in none of the patients.

Conclusively, early diagnosis and treatment in pediatric foreign body aspirations are lifesaving. It should be noted that "suspicion" is the most important way to diagnosis. Notably, the bronchoscopy procedure should be performed by a well-trained, experienced anesthesiologist-endoscopy team and with appropriate tools. We consider that every possible problem may be resolved with education.

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Original Article

Evaluation of characteristics of the patients who undergo surgical treatment for lung hydatid cyst

Ersin Sapmaz[1*], Kuthan Kavaklı[1], Merve Sengul Inan[1], Hakan Isık[1], Okan Karatas[2], Deniz Dogan[3], Hasan Caylak[1], Sedat Gurkok[1]

[1]Department of Thoracic Surgery, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey
[2]Thoracic Surgery Clinic, Sinop Ataturk State Hospital, Sinop, Turkey
[3]Department of Pulmonology, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey

ABSTRACT

Background: Hydatid cyst is a public health problem, particularly where it is endemic. It is a benign disease and usually asymptomatic unless the symptoms and complications develop. Effective treatment is important because this benign disease can cause considerable mortality and morbidity. The aim of this study was to describe the epidemiological and clinical characteristics of HC, localization (bilateral lungs or multiple organ involvement) and perforation characteristics of HC.

Materials and Methods: 160 patients were operated on for pulmonary hydatid disease for about approximately 12 years of time period. Patients were evaluated according to their age, gender, distribution of cysts in the lung, extra-pulmonary organ involvements, presence or absence of perforations, and animal contact stories.

Results: Number of the cysts, the cyst diameter, gender, location of the cysts and the liver involvement were found unrelated with the perforation status of the cyst. But, there is a significant difference between the localization of the cysts in the lung and the involvement of the liver. The rates of presence of liver cysts in the case of unilateral right, unilateral left and bilateral cysts in the lung were found as 13%, 25% and 50% respectively.

Conclusions: Hydatid cyst is a public health problem and elimination is possible with rigorous work. In case of bilateral pulmonary cysts and the multiple number of cysts, the likelihood of a cyst in the liver is increased. It was concluded that there was no relationship between the presence of cysts in the liver and the absence of perforation in the lung cysts. However, it should be kept in mind in terms of the possible complications that may occur at high perforations in patients who received preoperative albendazole therapy.

Key Words: albendazole monohydrochloride, cystic echinococcosis, hydatid cyst, perforation of cyst

Corresponding Author*: Ersin Sapmaz, MD. Gulhane Training and Research Hospital, Thoracic Surgery Clinic, General Tevfik Saglam Street, No:1, Kecioren, Ankara, Turkey
E-mail: esapmaz@hotmail.com - Phone: +90 312 3045175
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Introduction

Turkey is one of the countries where hydatid cyst (HC) is considered endemic [1]. According to WHO, worldwide, 1 million people are living with these diseases at any one time. Annual costs are estimated to be 3 billion US $. The prevention programs are directed to the definitive hosts like dogs and lambs for cleaning them from the parasites. The WHO Informal Working Group on Echinococcosis (WHO-IWGE) continues to guide and set priority areas [2].

The disease is caused by the larvae in the metacestod stage of the Echinococcus granulosus. Four type of echinococcus have been defined. Echinococcus granulosus is the most common infestation type in human [3]. Echinococcus multilocularis is less common and causes alveolar echinococcosis. E. vogeli and E. oligarthus causes polycystic echinococcosis and they are endemic in South America.

Humans acquire the infection by oral ingestion of parasite eggs that contaminated water and food. Parasites in the mesenteric circulation reach the liver through the portal system. They cannot pass through the sinusoids and that's why this disease most commonly occur in the liver (55-70%). The second most frequent site is lungs (18-35%) [1]. Parasites can reach the lung by hepatic vein, vena cava inferior, right lung, pulmonary arteries road and also reach by transdiaphragmatic transition, lymphatically or by portocaval anastomosis. Both liver and lung can be affected in about 5-13% of all cases [4]. It's reported in different studies that it could be placed in almost all organs.

HC is a benign disease and usually asymptomatic unless the symptoms and complications develop. Clinical course varies according to the organ in which it is placed, effects on adjacent tissue, its superinfections and hypersensitivity reaction that can cause anaphylaxis. If lung HC is ruptured towards the bronchus, the patient can describe membrane and clear water expectoration and hemoptysis. Effective treatment is important because this benign disease can cause considerable mortality and morbidity [5].

The diagnosis of HC depends on clinical findings, imaging methods and serology. There is no common consensus on the HC therapy strategy, medical treatment (albendazole), surgery and percutaneous drainage. The definitive treatment of lung hydatid disease is surgery. In cases where there is a possibility of cyst spread, it is recommended to use albendazole and mebendazole as postoperative preservatives [6] .

The aim of this study was to describe the epidemiological and clinical characteristics of HC, localization (bilateral lungs or multiple organ involvement) and perforation characteristics of HC.

Materials and Methods

A total of 254 patients with pulmonary hydatid cyst diagnosed between January 2006 to March 2018, in Thoracic Surgery Clinic in our institution. Patients who were thought to be hydatid cysts in preoperative radiological examinations but could not be confirmed with postoperative pathology results were excluded from the study. In addition, patients who did not have evaluation for extrapulmonary organ involvement were also excluded from the study. Finally, 160 patients were studied retrospectively. An illuminated affirmation form of the permission or prohibition of the use of their medical information for medical research purposes is signed by all patients admitted to our clinic. Patients were evaluated according to their age, gender, distribution of cysts in the lung, extra-pulmonary organ involvements, presence or absence of perforations, and animal contact stories. This study has been approved by Institutional Review Board of our institution.

Statistical Analysis

SPSS for Mac Version 20.00 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis of the data obtained at the end of the study. Continuous variables were expressed as mean ± standard deviation (SS), while categorical variables were as number and percentage (%). The continuous variables were assessed by the Kolmogorov-Smirnov test for normal distribution. Chi-square test for intermittent variables and Student-t test for continuous variables were used for comparison of groups. Statistical significance was accepted as $p < 0.05$.

Results

160 patients were operated on for pulmonary hydatid disease for about approximately 12 years of time period. Age and gender characteristics of the patients, lung localization of the cysts, extra-pulmonary organ involvements, perforation status of the cysts and animal contact story of the patients were evaluated.

146 patients were male (91.25%), whereas the remaining 14 (8.75%) were female. Their mean age was 24.99 ± 9.6 (20-66). Mean age in females was higher than males (41.14 ± 15.8 versus 23.44 ± 7.2) ($p < 0.001$).

When compared to the number of cases according to years, it is seen that in 2009 and 2011 there were more cases, the number of cases has gradually decreased in recent years (Table1).

Table 1. Number of cases by years.

Year	Number of cases (n)
2006	12
2007	16
2008	17
2009	20
2010	19
2011	19
2012	14
2013	12
2014	12
2015	9
2016	6
2017	1
2018	3
Total	160

The mean number of cysts in all patients was 1.51 (min: 1, max: 9) and the mean cyst diameter was 6.42 cm (min: 1cm, max: 25cm). Both the number of the cysts and the cyst diameter were not statistically significant in relation with perforation status of the cyst (respectively, $p = 0.150$, $p = 0.843$). Also, there was no statistically significant relationship between gender and the perforation status of the cyst ($p = 0.392$).

62 (38.8%) of the patients had a history of animal contact, while 98 (61.2%) of them did not had. The history of animal contact was significantly higher in males than females (41.1% versus 14.3%) ($p = 0.049$).

There was a similar result between existence of extrapulmonary organ cyst and the history of animal contact which is not statically significant ($p = 0.984$). In 14 of 62 patients (22.6%) with the positive animal contact history had extrapulmonary organ cyst, while in 22 of 98 patients (22.4%) with no animal contact history had extrapulmonary organ cyst. On the other hand, cyst perforation ratio was higher in patients with no history of animal contact (44.9% versus 30%), but this is not statistically significant ($p = 0.063$).

When the distribution of the cysts according to lobes were evaluated, it was found that cysts were most frequently located unilateral 88.2% and in the right lung 51.2%. In 11.2% of all patients, cysts were located bilaterally.

There was no statistically significant difference between the localizations of the cysts and the perforation status (Table 2).

Table 2. Distrubution of cysts in the lung.

	Lober Localization (n)	Perfored / Intact	p
Right n,% (82, 51.2)	Upper lobe (n=22)	11/11	0.839
	Middle lobe (n=19)	8/11	0.547
	Lower lobe (n=45)	23/22	0.551
Left n,% (60, 37.5)	Upper lobe (n=25)	7/18	0.906
	Lingula (n=1)	0/1	0.534
	Lower lobe (n=34)	12/22	0.171
Bilateral n,% (18, 11.2)	Upper lobe (n=8)	2/6	0.502
	Middle lobe-Lingula (n=5)	1/4	0.457
	Lower lobe (n=17)	6/11	0.467

37 patients had extrapulmonary involvement. Except one case with spleen and heart involvement 35 (22.2%) patients had liver involvement.

The presence or absence of liver involvement did not affect the perforation status of the cysts ($p = 0.374$).

There was no significant difference between liver involvement and cyst diameter ($p = 0.938$), however, as the number of cysts in the lung increased, the rate of liver involvement increased ($p = 0.009$)

The rates of presence of liver cysts in the case of unilateral right, unilateral left and bilateral cysts in the lung were found as 13%, 25% and 50% respectively.

Discussion

Cystic hydatidosis continues to be a public health issue for endemic countries. According to health statistics Republic of Turkey, in 2001 annual incidence has been reported as 4.9 in 100000 [7].

This parasitosis is more common in areas where the livestock are existence and the work of men in this business is more usual in Turkey. In parallel with this, 91.25% of our patients were males.

Hydatid cyst is usually acquired in childhood, but most are diagnosed at age 30-40 [8]. Tor et al. reported that 31% of the patients were younger than 20 years of

age in their pulmonary hydatid cysts series which containing 288 patients [9]. Only adult patients were operated on in our clinic so in our study the mean age was found 24.99 (20-66 years).

In this study the number of annual cases decreased in an approximately 10-year period. While the hydatid cyst prevalence is closely related to poor sanitation conditions, this can be explained by the improvement of these conditions over the years and by the successful treatment of animals.

Perforation is the most common complication of pulmonary hydatid cysts [10]. In previous studies, perforation was thought to be related to the with the demographic characteristics of the patient, number of cysts, intra-cystic pressure and localization of the cysts [11,12].

The relationship of intrathoracic pressure with cyst perforation has also been investigated, previously. It is thought that the factors that increase intrathoracic pressures such as coughing and trauma may be responsible for perforation [12,13].

Intra-cystic pressure increases as the diameter of the cyst increases. So, even small increases in cyst size can lead to perforation by increasing intra-cystic pressure. It should be kept in mind that diagnostic invasive procedures may also be responsible for perforation [14].

There is no consensus to support the association of number and diameter of cysts with perforation of any of them. Kocer et al reported no significant relationship between increasing the diameter of the cyst reduces the risk of perforation [15]. Burgos et al claimed that increasing the diameter of the cyst reduces the risk of perforation [16]. We could not determine the relationship between number and diameter of cysts with perforation in our study. However, especially during childhood, as cysts grows, the pressure inside the cyst increases due to the low volume of the thorax. Therefore the rates of cyst perforation in children are reported higher [17] .

The number of literatures comparing cyst perforation with cyst localization is low. The rate of perforation in our study was 40%. This ratio is compatible with the rate ranging from %24.7 to 61% in the literature. In our study, the most frequently placed lobe of the cysts was the left lower lobe while the perforation was most frequently observed in the right lower lobe. This data is in contrast to Onal et al, which reports that perforation is most commonly seen in the right middle lobe cysts in their series of 134 cases [12].

People become infected by digesting parasite eggs in contaminated food, water or soil or by direct contact with the host. It is reasonable that the disease is more frequent in rural areas where there is more animal contact with humans. In our study, 38.8% of patients had an animal contact story. Compared to females there was higher ratio of animal contact in males (41.1% vs 14.3%). This can be explained by the fact that men are more engaged in animal livestock in rural areas.

There is no agreed evidence that more cysts are formed or more organs are involved in case of animal contact history. There was no statistically significant difference between extrapulmonary cysts existence and animal contact story in our study. Also, we found that cyst perforation is not related to animal contact history.

Albendazole treatment is accepted to be effective and safe in hydatid cysts of the liver. It is reported that preoperative use of albendazole reduces the viability of the cyst while the postoperative use of it decreases the recurrence [18].

In adults, lung is the second most common localization after liver. Most chest surgeons face with lung cyst hydatid on the chest x-ray that took for control while receiving albendazole treatment for liver cyst hydatid. Albendazole is able to penetrate into hydatid cysts, and active against protoscolices of Echinococcus granulosis in vitro cultures. Drug effect by interfering with glucose absorption in the parasite wall and ultimately cell autolysis comes to the forehead. This may result in cyst perforation for the lung. In our study, in 18 patients (48.6%) cysts were perforated from 37 patients who underwent preoperative medical treatment. This high perforation ratio is compatible with the literature [5,14].

In conclusion, hydatid cyst is a public health problem and elimination is possible with rigorous work. Compatible with the literature data, it was seen that animal contact was more frequent in male patients. The location of the cyst in the lung does not affect the risk of perforation. In case of bilateral pulmonary cysts and the multiple number of cysts, the likelihood of a cyst in the liver is increased. It was concluded that there was no re-

lationship between the presence of cysts in the liver and the absence of perforation in the lung cysts. However, it should be kept in mind in terms of the possible complications that may occur at high perforations in patients who received preoperative albendazole therapy.

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Case Report

An extraordinary bullet embolism after gunshot injury: a case report

Cenk Balta*

Thoracic Surgery Clinic, Şanlıurfa Training and Research Hospital, Şanlıurfa, Turkey

ABSTRACT

Gunshot injuries are the second most common cause of death following motor vehicle accidents. Embolization due to gunshot bullet is rarely reported in the literature. A 20-year-old male patient admitted to hospital due to chest pain where radiologic examinations demonstrated a bullet in his thorax. We learned that he was shot from his leg in Syrian civil war one year ago. This very interesting case of bullet embolism with its migration to left ventricle was reported.

Key Words: gunshot, bullet embolism, trauma

Corresponding Author*: Cenk Balta, MD. Department of Thoracic Surgery, Şanlıurfa Training and Research Hospital, Yenice yolu No:1, Eyyübiye, Şanlıurfa, Turkey.
E-mail: drcenkbalta@gmail.com - Phone: +90 555 6343937
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Introduction

War is a shame of humanity. 190 million people have died in 21th century due to wars and most of them were civilians. Injuries depended on gunshot are the second most common cause of death following motor vehicle accidents. Bullet embolism which is a rare but serious complication of penetrating trauma [1]. Most of the bullet embolisms are arterial and the victim has symptoms of ischemia. Venous bullet embolization is rare and generally the patient has no symptoms. However, if the bullet in the venous system migrates to the pulmonary artery it might cause serious problems [2].

Herein, we present a 20-year old male patient presented with chest pain where the radiologic examinations demonstrated a bullet in his thoracic cavity. We learned that, he was shot from his leg one year ago. He has no other injuries, i.e. gunshot, in his entire body. We discussed this very interesting case within the light of relevant literature.

Case Report

A 20-year-old male with a history of gunshot injury of leg one year ago in Syrian civil war, admitted to the clinic with the complaint of mild chest pain. He didn't receive any medical treatment after this injury. The physical examination was normal except the scar of the wound in his right upper leg with a deep indentation which resembles a direct entrance (Figure 1). There was no scars to be accepted as an exit.

Figure 1. The scar of the gunshot in the leg with a deep indentation.

The posterior-anterior (Figure 2a) and lateral (Figure 2b) chest X-ray examinations demonstrated a bullet core in the left anterior hemithorax. The thorax computed tomography (CT) (Figure 2c), showed a metal reflection close to the left ventricle and abdominal CT showed a 25×45 mm sized abscess formation in his right iliopsoas muscle (Figure 2d).

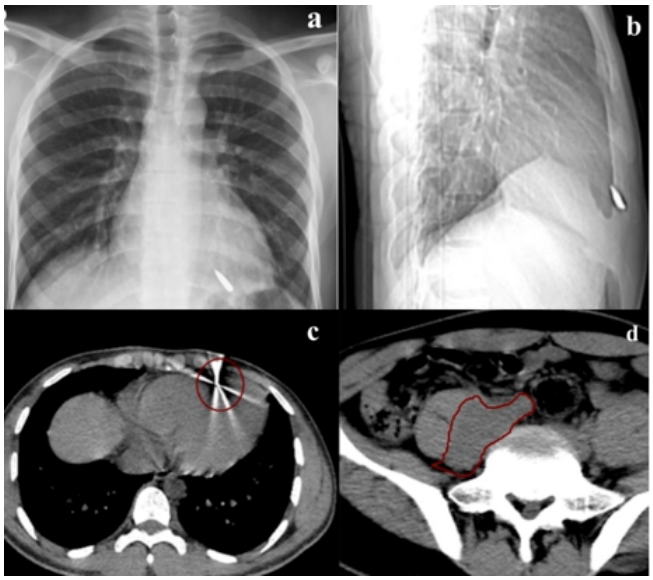

Figure 2a. Posterior-anterior and b. lateral chest X-ray showing the bullet core in the left anterior hemithorax, c. thorax CT showing metal reflection close to the left ventricle and d. abdominal CT showing a 25×45 mm sized abscess right iliopsoas muscle.

The echocardiography was normal and the bullet was seen not in his hearth chambers. Antibiotic treatment for the iliopsoas abscess was initiated.

An anterior approach via mediastinotomy was performed. During the peroperative exploration the bullet was seen within the myocardium of the left ventricular floor and consulted to cardiovascular surgery department. Eventually we left the bullet due to the close proximity to the left anterior descending artery. The first year follow up was uneventful.

Discussion

Thomas Davis reported a wood fragment embolism to the right ventricle in 1834 for the first time [1]. Many foreign bodies such as needles, intravenous catheters, bone fragments and bullets that migrate to the right ventricle were reported [3].

A review has reported 0.3% incidence of foreign body migration during Vietnam war [1,4]. Bullet

migration usually occurs immediately after trauma, but late migrations up to 14 years have been reported [1]. Bullet embolus can enter to the venous system nearly from any point of the injury by direct protrusion or by erosion of the vascular wall [5]. Various embolus pathways had been described in literature. These pathways are; from a peripheral vein to the heart [3,6], from a peripheral veins to the pulmonary artery [2], from a peripheral vein to another peripheral vein [7], paradoxical embolization from the right side to the left side [1] and from the heart to a peripheral veins [8].

Bullet core embolization must be suspected in gunshots entrance wounds without an exit or the final location of bullet does not confirm the expected pathway. Symptoms are associated with the location of the embolus. Arterial embolizations commonly presented with ischemic symptoms and venous embolism presented with valvular destruction, endocarditis, sepsis, venous thrombosis, dysrhythmia [3].

Management of foreign bodies in cardiovascular system depends on location and size of the foreign body. Common decision is to remove the foreign body. Knottnerus and colleagues suggest that follow up of the clinical course during an appropriate period is a good alternative. But some authors suggest that follow up of the clinical course is an alternative if the patient is symptomless [9]. There are such series of follow up to 20 years after Second World War where pericarditis was reported with an incidence of 25% [10]. Similar follow up series were also reported where no complications encountered [11]. Endovascular treatment is another option for the embolization of pulmonary artery and cardiac chambers [4,12]. The mortality of bullet embolism is 6% and mortality rate decreases 1-2% if the bullet is removed (13).

In conclusion bullet cores should be removed if they are symptomatic by considering profit and loss statement. If there is a risk of infection, embolization, or erosion even asymptomatic bullet cores should be removed. However, asymptomatic, risk free or late diagnosed cases might be treated conservatively.

Declaration of conflicting interests

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Appendix. Conference Discussion

Dr. Özpolat (Editor-in-chief, Kırıkkale, Turkey): Dr. Balta, this is an interesting case report presenting the migration of a bullet to the heart. Could you give the details of intra operative findings?

Dr. Balta: I performed a mediastinotomy from the fourth intercostal space. After opening the pericardium at the left ventricle apex, I palpated the bullet. The cardiovascular surgeons were invited to the operating theatre. Unfortunately due to the localization of the bullet they suggested that it could cause a catastrophe if it was removed on beating heart.

Dr. Özpolat: Dr. Şimşek, could you make a suggestion about the migration of the bullet to the left heart via the venous circulation?

Dr. Şimşek (Kırıkkale, Turkey): This is a case of paradoxical embolus and the most possible pathway for the bullet to pass to arterial circulation is via a patent foramen ovale.

Dr. Özpolat: Dr. Şimşek, why does an echocardiography miss a foreign object?

Dr. Şimşek: Transthoracic echocardiography, being not only a subjective diagnostic tool but also having a weak power in imaging apical views, can lead to missing a foreign object especially in the left ventricular apex.

Dr. Özpolat: Dr. Doğan, during the preoperative work up what other studies could be performed?

Dr. Doğan (Ankara, Turkey): First, a venography of the lower extremity shows the structure of the vein, helps to detect any possible venous anomaly and venous thrombosis. Second, a preoperative transesophageal echocardiography (even perioperative) shows a possible septal defect for migration of the bullet core to left side of the heart.

Dr. Özpolat: Dr. Şahan, could we use cardiac MR, to evaluate the exact localization of the foreign object within the heart and to decide a plan for the surgical intervention?

Dr. Şahan (Kırıkkale, Turkey): The majority of bullets tested were found to be contaminated by ferromagnetic metals and some contain steel. If such a metallic object is located near or within a vital anatomic structure, it has the potentially to move. Caution is advised as well as an assessment of risk versus benefit for the patient is mandatory. Every case should be interpreted on its basis and if we have no idea about the content of the bullet, I will definitely refuse to perform an MR.

Dr. Özpolat: Dr. Doğan, is it possible to remove a bullet from this localization on beating heart?

Dr. Doğan: It is exactly impossible to remove such an object when heart is beating. In such a situation, I just increase the length of the incision, place a pulmonary artery plus a femoral artery catheter for venous and arterial cannulations, give the cardioplegia solution and clamp the ascending aorta then via a small incision remove the foreign object from the apex of the left ventricle.

Dr. Özpolat: Dr. Şimşek, depending on the author's conclusion which states "asymptomatic, risk free or late diagnosed cases might be treated conservatively", should we give any other treatment to the patient?

Dr. Şimşek: I think, if the bullet was totally embedded in the myocardium no additional treatment is necessary. However, if a fragment is in the ventricle which should be confirmed via transesophageal echocardiography, warfarin should be prescribed just like the common follow up of mechanical prosthetic heart valves, in order to prevent thrombus formation.

Affiliations;

Rıza Doğan, MD, Professor of Cardiothoracic Surgery, Hacettepe University Faculty of Medicine, Ankara, Turkey

Berkant Özpolat, MD, Professor of Thoracic Surgery, Kırıkkale University Faculty of Medicine, Kırıkkale, Turkey

Mehmet Şahan, MD, Assistant Professor of Radiology, Kırıkkale University Faculty of Medicine, Kırıkkale, Turkey

Vedat Şimşek, MD, Associate Professor of Cardiology, Kırıkkale University Faculty of Medicine, Kırıkkale, Turkey

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Case Report

Intradiaphragmatic bronchogenic cyst: a very rare diaphragmatic mass

Goktan Temiz[1], Ozgur Omer Yildiz[2], Omer Cenap Gulyuz[3], Nurettin Karaoglanoglu[4]

[1]Department of Thoracic Surgery, Adana City Education and Research Hospital, Adana, Turkey
[2]Department of Thoracic Surgery, Yildirim Beyazit University, Yenimahalle Education and Research Hospital, Ankara, Turkey
[3]Department of Thoracic Surgery, Adiyaman University Education and Research Hospital, Adiyaman, Turkey
[4]Department of Thoracic Surgery, Yildirim Beyazit University, Faculty of Medicine, Ankara, Turkey

ABSTRACT

Bronchogenic cysts are generally asymptomatic and are detected incidentally by radiographic imaging as a smooth homogeneous mediastinal/pulmonary lesion. Isolated intradiaphragmatic bronchogenic cysts are extremely rare. Here, we report a case of intradiaphragmatic bronchogenic cyst mimicking a left lower lobe mass in a 56-year-old man suffering from chest pain. Imaging studies of the chest, including plain chest radiography and computerized tomography revealed a left sided mass in the lower zone. The patient underwent surgical resection of the mass. Intradiaphragmatic bronchogenic cyst was diagnosed by pathology.

Key Words: bronchogenic cyst, diaphragma, mass

Corresponding Author*: Ozgur Omer Yıldız, MD. Yildirim Beyazit University, Yenimahalle Education and Research Hospital, Department of Thoracic Surgery, Ankara, Turkey.
E-mail: dr.ooyildiz@gmail.com - Phone: +90 533 8147314
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Introduction

Bronchogenic cysts are uncommon congenital anomalies of foregut origin. They are most frequently found in tracheobronchial tree, mediastinum or within the lung parenchyma. Rarely, the cysts have occurred in other locations. They are generally asymptomatic in the adulthood age. They can cause symptoms only when infected, ruptured or pressing on neighbouring structures. Most of them presented as a smooth homogeneous water density shadows mediastinal or pulmonary opacity on chest radiographs or computed tomography (CT). If the cysts are asymptomatic or diagnosed in any way, to avoid possible complications should be treated by surgery [1,2].

Case Report

Our patient, a 56-year-old man, was referred to our institution for chest pain of one year duration. General physical examination and routine laboratory tests were unremarkable. The thorax CT revealed a lobulated, calcified, well-defined, and homogeneous mass, of 6x8x6 cm at the lower zone (Figure 1).

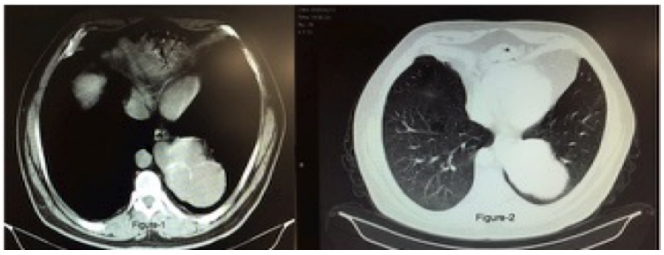

Figure 1. Thorax CT shows a lobulated, calcified, well-defined, homogenous soft-tissue density lesion with calcifications along the wall in the left posterior mediastinal region.

A left thoracotomy was performed for the resection of the lesion. Intraoperatively, a 6x8 cm sized cyst was found within the left hemidiaphragma. The mass has no connection with the left lung parenchyma. It was enucleated from the left hemidiaphragma (Figures 2,3). The diaphragma was repaired with a 6x8 cm sized polypropylene mesh. There were no intraoperative complications.

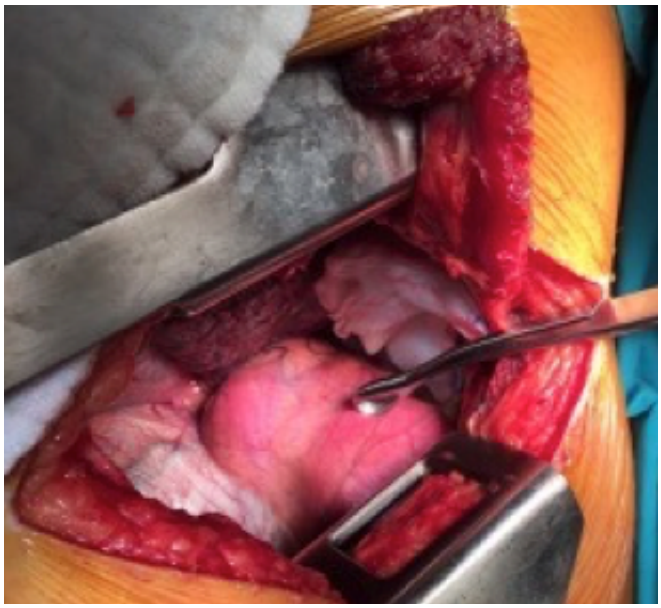

Figure 2. Intraoperative image shows the cyst within the left diaphragma.

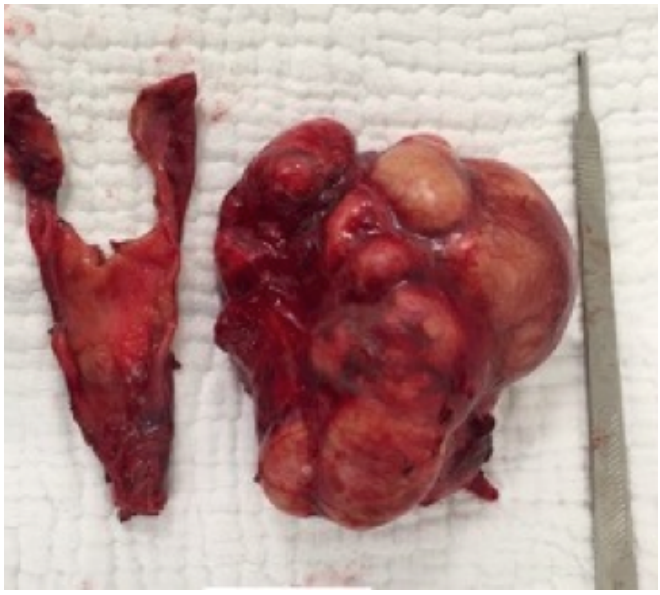

Figure 3. Excised cystic lesion.

On gross examination, the cystic mass was multilocular, thin-walled and filled with red, yellow fluid. On microscopic sections, the cyst had smooth muscle tissue, cartilage and mucus glands on its wall. It was lined with ciliated cylindrical respiratory mucus epithelium, thus established a histopathologic diagnosis of intradiaphragmatic bronchogenic cyst.

Discussion

Bronchogenic cysts are uncommon congenital anomalies of foregut origin [1]. They are most frequently found in tracheobronchial tree, mediastinum. Extra mediastinal bronchogenic cysts may be located in the lung

parenchyma, diaphragma or pleura [2]. Intrapulmonary cysts are usually found in the perihilar areas or rarely peripherally in the lower lobe. In our case, the cyst was found in diaphragma but on CT plains it appears as located in lower lobe.

Bronchogenic cyst is the most common mass lesion in diaphragma in general population and the most common benign cystic process in infants. They are observed within congenital cysts [3,4]. Two-thirds of the patients are asymptomatic and the cyst is detected incidentally. Symptomatic patients generally present with chest pain, cough, dyspnea, fever and dysphagia. Chest pain is the most frequent symptom. In our case, chest pain complaint was observed as symptom and lesion was detected during radiographic examination.

It is often enough to apply plain chest radiography, thorax CT and bronchoscopy from among the laboratory methods for diagnosis. On plain film examinations, bronchogenic cysts present as spherical or oval masses with smooth outlines and soft tissue. CT is an excellent method for demonstrating the size, shape, position and margin characteristics of the cyst. It is also useful to show mass effect on adjacent structures, cyst attenuation, homogeneity and calcification. Barium swallow can be useful in dysphagic cases. In our case, radiology, especially CT, helped to a great extent about lesion's nature, placement and size.

Life-threating complications such as airway obstruction, atelectasis, and compression are reported in pediatric age group. It is reported in current series that bronchogenic cysts in adults are more symptomatic. In our case, though it is adult, complications such as respiratory distress related with compression, atelectasis, and infection were not reported.

The cyst may show a solid appearance because of infection and its density increasing in parallel with its protein/calcium content. Cyst hydatid, lung abscess, infected air cyst, cavitary disease and malignancy should be kept in mind in differential diagnosis [2,5]. Bronchogenic cysts containing mucoid material are surrounded by a wall of bronchial cartilage, smooth muscle, elastic tissue and mucous gland [6,7]. In our case similar histopathological findings were reported.

Surgery may be considered as a treatment of choice even if the cyst is asymptomatic, to avoid complications such as infection, haemorrhage, or neoplasia within the cyst. Observation may be indicated for small, classic, asymptomatic cysts or high-risk patients.

Percutaneous catheter, drainage, sterile alcohol ablation or transbronchial cyst aspiration have been performed in selected cases [8,9]. Total excision of mediastinal bronchogenic cysts is adequate for treatment, minimal (wedge), segmental or lobar resection may be needed in parenchymal bronchogenic cysts [10].

Consequently, bronchogenic cysts must be kept in mind in all cystic lesions, in suppurated cyst appearance or in cases when tumor is not marginalized.

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Current Thoracic Surgery

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Case Report

Thoracic splenosis: a very rare cause of chest pain

Celal Bugra Sezen[1], Salih Bilen[1], Cem Emrah Kalafat[2], Cemal Aker[3], Celalettin Ibrahim Kocaturk[4]

[1]Department of Thoracic Surgery, Yedikule Chest Disease and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey
[2]Department of Thoracic Surgery, Mardin State Hospital, Mardin, Turkey
[3]Department of Thoracic Surgery Burdur State Hospital, Burdur, Turkey
[4]Department of Thoracic Surgery, İstinye University, Liv Hospital, Istanbul, Turkey

ABSTRACT

Intrathoracic splenosis presents a rare thoracic lesion occurring after splenectomy or abdominal trauma as a consequence of heterotopic autotransplantation and implantation of splenic tissue. We present a 38- year-old man with intrathoracic splenosis. He was admitted to hospital with chest pain. In computed tomography homogenous, smooth-edged multiple lesions were found. The patient was not able to be diagnosed with transthoracic fine needle aspiration biopsy. On the exploration, there were multiple lesions at the thoracic cavity and the masses were excised. Definitive pathology was reported as splenosis.

Key Words: thoracic splenosis, medical history, abdominal trauma, chest pain, splenectomy

Corresponding Author*: Celal Bugra Sezen, M.D. Yedikule Chest Disease and Thoracic Surgery Traning and Research Hospital, Kazlıçeşme Mh, Belgrat Kapı yolu Cad. No: 1, 34020 Zeytinburnu, Istanbul, Tukey
E-mail: info@bugrasezen.com - Phone: +90 553 1605531
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Introduction

Thoracic splenosis (TS) is a rare condition following diaphragmatic injury or an abdominal surgery, with autotransplantation of splenic tissue into the left hemithorax. TS typically presents in the chest radiography as solitary or multiple lung masses and the diagnosis is challenging if history of a previous abdominal injury is not obtained. Herein, we present a rare case of thoracic splenosis diagnosed 4 years after an abdominal trauma.

Case Report

A 38-year-old male patient admitted to the hospital with chest pain. On the posterior-anterior chest X-ray, there were homogeneous opacities in the middle zone and diaphragmatic pleura of the left hemithorax. On the computerized thorax tomography (CT), homogeneous, smooth-edged multiple lesions were found in the lower lobe of the left lung, including parenchymal, costal, and diaphragmatic pleura (largest diameter of 3.5 cm) (Figure 1). In positron emission tomography, FDG uptake level of the lesion was 2.5.

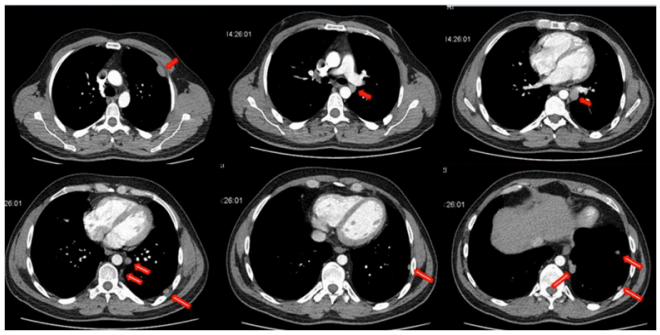

Figure 1. Thorax CT shows multiple round shape and homogenous lesions in the left hemithorax (red arrows).

Transthoracic fine needle aspiration biopsy was not diagnostic. We decided to perform an exploratory video-assisted thoracoscopic surgery (VATS) for the diagnosis and treatment. However, it was converted to a thoracotomy due to excessive adhesions. Upon exploration, multiple lesions on the chest wall, aortic adventitia, and lung parenchyma were observed. Excisional biopsy of one of the lesions performed and the frozen section reported a collection of lymphoid cells in the vasculature pattern and benign/malign discrimination could not be done on histopathological examination. All masses was resected from the defined regions report.

The final pathology examination of the specimens revealed that, there was perivascular mature lymphocyte population that formed nodules in the roof with rich interstitial vascularity which was compatible with typical spleen morphology (Figure 2). When the patient's anamnesis was detailed, a history of blunt trauma to the abdominal region, which was medically treated 4 years ago, was found.

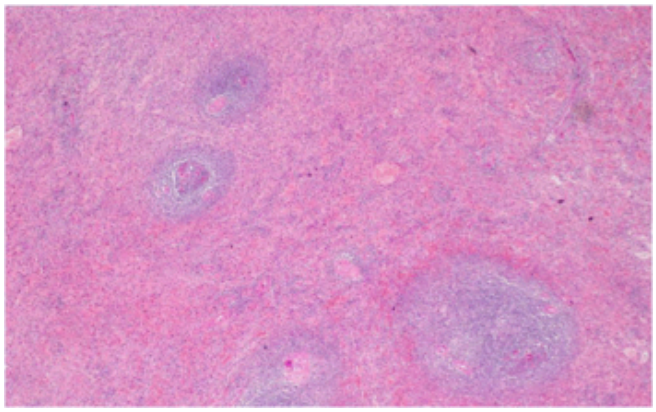

Figure 2. Mature lymphoid population with rich vascularity findings in frozen section.

Discussion

Accessory spleens and splenosis are two distinct forms of ectopic splenic tissue which might be found in the body. During the embryological period of development accessory spleens arise from the left side of the dorsal mesogastrium and moves to abnormal localizations. On the other hand splenosis is autotransplantation of splenic tissue through different anatomical localizations of the human body and it generally occurs after trauma, surgery or iatrogenic rupture of the spleen[1].

Shaw et al [2] reported for the first time in 1937 that splenic tissue autotransplantation after splenectomy to the thoracic cavity resulted in an incidence of TS. In 2016, Tulinský et al [3] stated that there were 75 patients in the English literature. A total of 81 cases were published until now. Most of the patients had abdominal trauma in their history. The splenic nodules may be few or up to hundreds in the peritoneal cavity and can be localized in the splenic bed, omentum, mesentery, liver, or diaphragm [4]. Splenic tissue could be found in intraperitoneal or extraperitoneal locations. Splenosis has also been reported rarely in the pericardium, subcutaneous tissue and even in the occipital pole of the brain [1].

The time interval between abdominal injury requiring splenectomy and thoracic splenosis detection varies

from several years to decades [3]. Most patients with splenosis are asymptomatic, but 10-15% of them may have pleuritic pain, pleurisy, recurrent hemothorax, or fever [3]. Patients with a diaphragm, phrenic nerve, and parietal pleural involvement may have pain. Our patient was symptomatic because of the location of lesions.

The differential diagnosis of intrathoracic splenosis includes lung carcinomas, pleural metastases, lymphoma, malignant mesothelioma, invasive thymoma, gossypiboma and fibrous tumors of the pleura. Scintigraphy with Tc-99m-labeled and heat-altered erythrocyte is the gold standard method [5,6]. Thorax CT shows a well-defined, homogeneous, pleural-based nodule in the left hemithorax [7,8]. Thorax CT of our patient had multinodular, well-defined masses in the lung. It is not necessary to surgically treat patients who are suspected of TS in the preoperative period.

A 99 m technetium□labeled heat□damaged red cell scan is highly specific for detection of splenosis and considered as the gold standard, due to reduced uptake in the normal liver. With the emergence of improved resolution of planar/single photon emission computed tomography/computed tomography (SPECT/CT) scans, Tc□99 m sulphur colloid scintigraphy can be a reliable for differentiating splenic tissue from non□splenic tissue [7,9].

Especially in splenectomy patients, surgical resection is unnecessary. Surgical resection should be considered only in symptomatic patients. In our 6 months follow-up after discharge, the patient's pain was ceased. If there are difficulties in diagnosing on left lower zone lesions, the history of trauma and splenectomy should be questioned in carefully.

Declaration of conflicting interests

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Case Report

Bilateral pulmonary nodular amyloidosis with positive FDG uptake

Koray Dural[1*], Berkant Özpolat[1], Nesimi Günal[1], Ekin Zorlu[1], Salih Kür[1], Pınar Atasoy[2]

[1]Department of Thoracic Surgery, Kırıkkale University Faculty of Medicine, Kırıkkale, Turkey
[2]Department of Pathology, Kırıkkale University Faculty of Medicine, Kırıkkale, Turkey

ABSTRACT

Amyloidosis is a disease characterized by extracellular accumulation of protein in fibrillary structure (amyloid protein) in various organs and soft tissues. Although the involvement of respiratory system is encountered in systemic amyloidosis, localized pulmonary amyloidosis has rarely been reported. The radiologic findings are nonspecific and show variations according to involvement pattern of amyloidosis. Here we present a 62-year-old female diagnosed as pulmonary nodular amyloidosis with the help of relevant literature.

Key Words: multiple pulmonary nodule, metastatic disease, pulmonary lesion, amyloidosis

Corresponding Author*: Koray Dural, MD. Department of Thoracic Surgery, Kırıkkale University Faculty of Medicine, Yenişehir, Yahşihan, Kırıkkale, Turkey.
E-mail: koraydural@yahoo.com
Phone: +90 505 4454548
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Introduction

Amyloidosis is a systemic disease characterized by extracellular deposition of abnormal protein fibrils -termed as amyloid protein- in various organs and tissues. Amyloid aggregates are insoluble and resistant to proteolysis. Although systemic amyloidosis is common and respiratory system is one of the affected tissues, certain forms are exclusively localized. Localized pulmonary nodular amyloidosis can be multiple or solitary. Peripheral or subpleural involvement is more frequent in lower lobes, which grow slowly. However, systemic type shows a diffuse alveolar septal involvement and radiologic changes may be absent [1-4].

Here we present a case of pulmonary nodular amyloidosis and discussion of the radiologic, invasive diagnostic and pathologic features of this rare disease with the help of relevant literature.

Case Report

A 62 year-old female with non-productive cough with a 6-month history was referred to our clinic with thoracic CT findings of nodular opacities. The physical examination was normal other than bilaterally heard rhonchi. The biochemical values were normal. The thoracic computed tomography showed bilateral pulmonary nodules of different sizes with irregular contours and some having microcalcifications. The largest nodule was 24x22 mm (Figure 1). Abdominal CT was normal. PET/CT reported that the lesion at right mediobasal segment showed increased FDG avidity with SUV max of 4.0 (Figure 2).

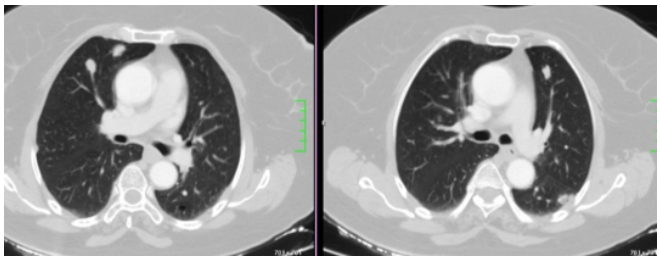

Figure 1. Preoperative thorax CT showing bilateral nodular lesions.

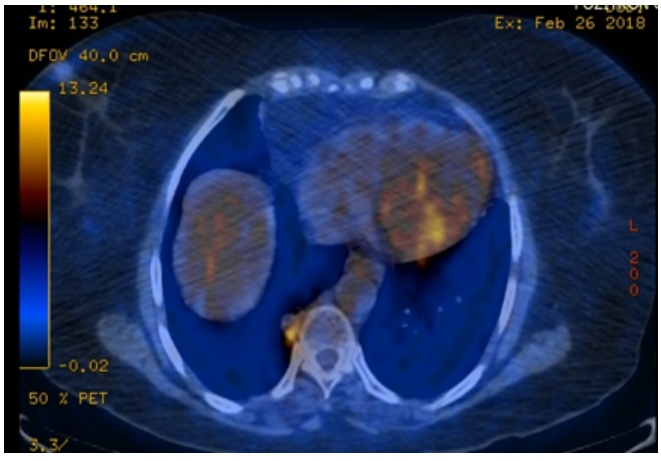

Figure 2. PET/CT image showing FDG uptake.

Fiberoptic bronchoscopy revealed non-diagnostic bronchoalveolar lavage for malignancy and minimal chronic inflammation was reported.

VATS wedge resection of two lesions one being the larges nodule with FDG uptake was performed which both were consisted with amyloidosis. Histologically the lesions were irregular nodules with diffuse acellular material accumulation at stroma and at wall of the vessels and, the lesions had limitations by mesothelial cells. On crystal violet stain, this deposit was confirmed to be amyloid. The final histopathologic diagnosis was pulmonary amyloidosis (Figures 3a,b). After the operation, the patient was referred to internal medicine department and the workup did not identify systemic amyloidosis. The 9th month follow up was uneventful with stabile nodules on control thoracic CT (Figure 4).

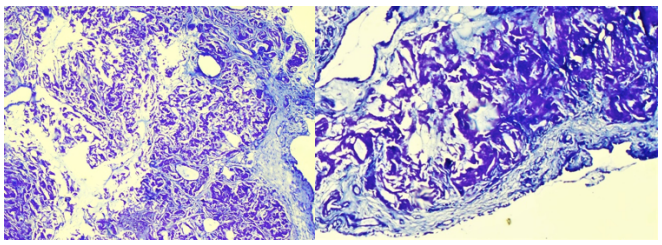

Figure 3. Histopathological examination demonstrating amyloidosis. Crystal violet stain (left x100, right x40).

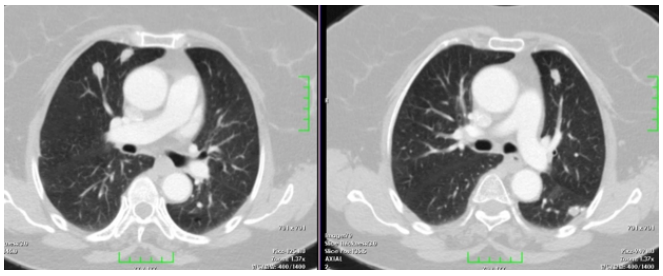

Figure 4. Postoperative thoracic CT showing stable lesions at 9th month follow up.

Discussion

Amyloidosis is a disease characterized by extracellular deposition of amyloid protein in tissue and organs such as kidney, liver, spleen, lung, gastrointestinal tract, endocrine organs, skin, heart or the autonomous nervous system [1,2]. Many types of amyloid have been described and all share the characteristics of fibrillary B-pleated sheet configuration. Although the involvement of respiratory system is encountered in systemic amyloidosis, localized forms such as pulmonary amy-

loidosis has rarely been reported. Four histopathologic forms of respiratory amyloidosis defined as; a. focal deposits in tracheobronchial tree, b. diffuse parenchymal deposits, c. single or multiple parenchymal nodules and d. senile form [2]. Amyloid generally found in alveolar interstitium at the periphery of the nodule. As compact amyloid mass consists of many giant cells, lymphocytes and plasma cells normal parenchymal structure generally does not exist at the central parts [3]. Congo red and crystal violet stains are used to demonstrate amyloid [5]. As the present case is a multinodular form, we will concentrate on this form in this report.

In nodular form the clinical signs and symptoms are nonspecific compared to other forms and although the patients are generally asymptomatic, cough, dyspnea and hemoptysis are the main complaints [2,6]. In this case, cough is the main symptom for a duration of 6 months.

The diagnosis of localized respiratory form is particularly difficult unlike the systemic form where in the systemic form workup involving blood, urine and imaging studies are generally diagnostic [3].

In the differential diagnosis of the multiple nodules showing calcifications, granulomatous diseases, tuberculosis, histoplasmosis, coccidiodomycosis, blastomycosis must be kept in mind. Multifocal calcifications are extraordinary in metastatic disease other than osteogenic sarcoma and chondrosarcoma. Lymphoproliferative diseases frequently accompanies multinodular form of the disease. In such cases, amyloidosis may be seen with parenchymal bullae or thin walled air cysts however the mechanism is not clear but hypothesized as, first, the occurrence of check valve mechanism due to the narrowed airway as a result of accumulation of inflammatory cells, second, increased alveolar wall destruction due to deposition of amyloid at alveolar wall and third, ischemic alveolar destruction due to deposition of amyloid at muscular wall of small blood vessels [3]. In the workup of this case, we did not identify such a co-existence.

Among radiologic imaging techniques HRCT makes the distinction of 5 types of nodular form; a. peripheral and subpleural localization which is generally bilateral and at the lower lobes, b. well defined, lobulated form, c. nodular form showing central (generally) or irregular calcifications, d. multiple nodules between 0.5 to 15 cm and e. slow growing nodular form without regression. Although mediastinal LAP is seen in 20% of amyloidosis, in localized form this is unusual and the presence should direct the surgeon to investigate the etiology [3,4].

Although calcifications in the nodules and other imaging and blood test did not support a primary malignancy, PET/CT was included to the diagnostic work up and the lesion at right mediobasal segment showed increased FDG avidity with SUV max of 4.0. Positive FDG uptake of pulmonary amyloidosis mimicking lung metastasis was rarely reported in the literature [4].

In amyloidosis fine needle aspiration biopsy has low field in diagnosis. Although CT-guided biopsies are reported to have a better chance of providing diagnostic material, most cases of pulmonary amyloidosis have been diagnosed only following surgical resection or at autopsy [1,2,4,7,8]. Similarly, in our case the final diagnosis was achieved following surgical resection. The nodule with positive uptake with high suspicion of malignancy and another one in the same lobe both were resected via VATS.

In systemic amyloidosis with respiratory involvement mean life expectancy was 16 months, however, in local form it is better. Mortality is due to obstruction of the airways and respiratory insufficiency [3,9]. To date there is still no effective treatment for systemic cases. Colchicine, melphalane and systemic steroid therapy and, conservative surgical excisions to protect the functional structure may be an option [5,9,10]. In this case, at the 9th month, follow up the nodules had remained stable at CT and annual radiologic controls was planned.

In conclusion, localized nodular pulmonary amyloidosis may mimic many benign and malign pulmonary disease radiologically without having clinical symptoms. In the differential diagnosis of multiple pulmonary nodules, localized amyloidosis should be kept in mind. Surgery plays an important role in the diagnosis.

Declaration of conflicting interests

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Images in Thoracic Surgery

Intraoperative findings of spontaneous hemopneumothorax

Kuthan Kavakli*, Hakan Isik, Gokhan Ayberik, Alper Gozubuyuk

Department of Thoracic Surgery, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey

Spontaneous hemopneumothorax is a life-threatening complication association with spontaneous pneumothorax and accumulation of more than 400 mL of blood in the pleural cavity [1]. Physiopathology includes ruptured vascularized bullae or lung parenchyma, an aberrant vessel or a hemorrhage from a torn parietal pleura [2].

A 25-year-old male was referred to our hospital with unexpanded lung and massive air leaks after chest tube insertion (Figure 1a). The patient was followed for two days at our clinic. Thoracoscopic bullae wedge resection was recommended for him because the air leak was not cease. He underwent thoracoscopic bullae wedge resection for curative intent. We determined a few vascularized bundles that were pending the bullae to apex of the chest intraoperatively (Figures 1b,c). It was seen that the lung did not separate from the thoracic wall and was attached through vascularized fibrous bundles when pneumothorax developed.

In our case, we detected the potential for spontaneous hemopneumothorax that can occur with the separation of these vascularized fibrous bands in the event of a sudden pulmonary collapse. We think that intraoperative findings of our case are important for explaining the physiopathology of spontaneous hemopneumothorax.

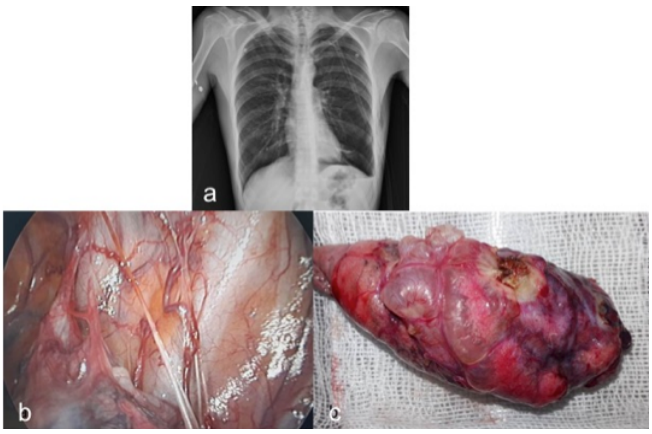

Figure 1a. Chest X ray of the patient revealed an unexpanded lung, **b.** intraoperative view of the vascularized bundle that was the cause of hemothorax after sudden collapse of the lung and **c.** wedge resection of the vascularized bullae.

Key Words: hemopneumothorax, spontaneous, thoracoscopic surgery

Declaration of conflicting interests

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Corresponding Author*: Kuthan Kavakli, MD. Department of Thoracic Surgery, SBÜ, Gülhane Eğitim ve Araştırma Hastanesi, Ankara, Turkey.
E-mail: kavaklikuthan@gmail.com
Phone: +90 312 3045171
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Review Article

Surgical approach for malignant pleural effusion

Hasan Akin[1]*, Ali Kilicgun[2]

[1]Department of Thoracic Surgery, Yedikule Chest Disease and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey
[2]Department of Thoracic Surgery, Bolu Abant Izzet Baysal University, Bolu, Turkey

ABSTRACT

In this review, the causes of pleural effusion were discussed. Pleural reactions and tumors were explained in the tables. Subsequently, radiographic findings and their role of guidance in the interventional procedures were briefly mentioned. Surgical diagnosis and treatment methods were explained. Malignant mesothelioma was discussed under a separate title. In the end, pleurodesis, a commonly used method in patients with malignant pleural effusion, was discussed.

Key Words: malignant pleural effusion, surgery, pleural fluid

Corresponding Author*: Hasan Akın, MD. Yedikule Gogus Hastanesi. Belgradkapi C. No: 1, 34020. Zeytinburnu, Istanbul, Turkey.
E-mail: akinhasan@gmail.com - Phone: +90 535 428 22 32
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Introduction and Etiology

The characteristic of malignant pleural effusion (MPE) is the presence of cancerous cells in pleural fluid or pleural tissue obtained at percutaneous needle biopsy or thoracoscopy, thoracotomy, or autopsy. Malignant pleural effusion is a highly morbid disease [1,2]. 80% of MPEs are caused by lung, breast, over, gastrointestinal cancers, and lymphomas. Primary malignancy may not be detected in about up to 10% of MPEs. 95% is unilateral. Lung cancer is the leading causes of MPE [1,2].

Almost all tumor types may cause a malignant pleural effusion. The prognosis is based on tolerability of the patients to systemic treatment; however, the presence of malignant effusion is not associated with pathologic diagnosis or indication for poor prognosis. There is no specific guideline for the treatment of malignant pleural effusion and evidence to dope out the survival of these patients [3]. The development of pleural effusion in a cancer patient does not indicate that this fluid is malignant. This may be due to atelectasis and pneumonia, due to bronchial constriction, or as a side effect of severe malnutrition, cardiac failure, chemotherapy drugs, or radiotherapy.

Table 1. List of the conditions that lead to pleural effusion via causing a pleural reaction [4].

Pleural infection
Radiation
Surgery
Trauma
Intracavitary therapies
Collagen vascular diseases
Systemic rheumatic diseases
Subpleural parenchymal diseases
Pneumothorax
Drug reactions
Pancreatitis
Uremia
Pneumoconiosis

Table 2. World Health Organization classification of pleural cancers [5].

A-Mesothelial Tumors	B-Lymphoproliferative Diseases	C-Mesenchymal Tumors
1-Diffuse malignant mesothelioma	1.Primary effusion lymphoma	1-Epitheloid hemangioendothelioma
Epithelioid mesothelioma	2. Lymphoma with pyothorax	angiosarcoma
Sarcomatoid mesothelioma		2-Synovial sarcoma
Desmoplastic mesothelioma		Biphasic
Biphasic mesothelioma		Monophasic
2-Localized malignant mesothelioma		3-Solitary fibrous tumor
3-Other tumors of mesothelial origin		4-Calcifying tumor of pleura
Well-differentiated papillary mesothelioma		5-Desmoplastic small round cell tumor
Adenomatoid tumor		

Rare pleural malignant tumors may also cause malign pleural effusion besides malignant mesothelioma and other common pleural tumors (Table 3).

Table 3. Malign tumors of pleura other than mesothelioma [6].

Localized malignant mesothelioma
Epithelioid hemangioendothelioma
Pleural angiosarcoma
Synovial sarcoma
Hemangiopericytomas
Primary smooth muscle tumor of pleura
Pseudomesotheliomatous angiosarcoma
Primary pleural liposarcoma
Non-skeletal primary myxoid chondrosarcoma of the pleura
Primary pleural thymoma
Primary pleural squamous cell carcinoma
Pleural primary melanoma
Malignant peripheral nerve sheath tumor
Pluronic chondroblastic osteosarcoma
Pleural mucoepidermoid tumor
Carcinosarcoma of Pleura
Pleural adenosquamous carcinoma

Radiological Findings

Posterior-Anterior Lung Graph;

The mediastinum is shifted to the rightward. 200-300 cc fluid is sufficient for blunting the costodiaphragmatic recess. Lateral chest graph, lateral decubitus graph or USG are crucial at the differential diagnosis of fluid, atelectasis, pneumonia, and pleural thickening. On PA roentgenogram the affected hemithorax shows completely homogeneous density.

When the collection was too much, the entire hemithorax is covered with homogeneous density and mediastinum was pushed to the opposite side. Chest x-ray appearance in intrapulmonary pleurisy mimics a diaphragm elevation [7].

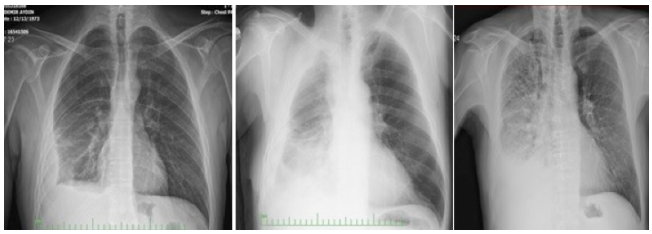

Figure 1. Chest x-rays showing pleural effusion.

Thorax ultrasonography

Using the B-Mode technique, the echo waves reflected from intra-thoracic structures are evaluated with the guidance of intercostal windows. The application process is easy, and sonographer can get results after the evaluation (Figure 2). Initial indications: Ultrasonography is essential in the diagnosis of localized fluids. It is critical to distinguish effusion locations to see pleural fluid without pleural thickening, before pleural biopsy or thoracic tube placement. It is used to determine the amount and localization of pleural effusion, to separate the pleural thickening from minimal pleural effusion and to obtain a parietal pleura biopsy. The preferences to use USG rather than computerized tomography in the pleural fluid could be summarised as follows: USG is easy and quick to handle, the patient does not take the radiation, it is cheap, and USG can be used as a guidance to locate the thoracentesis. USG detects pleural fluid septations with higher sensitivity than CT [7].

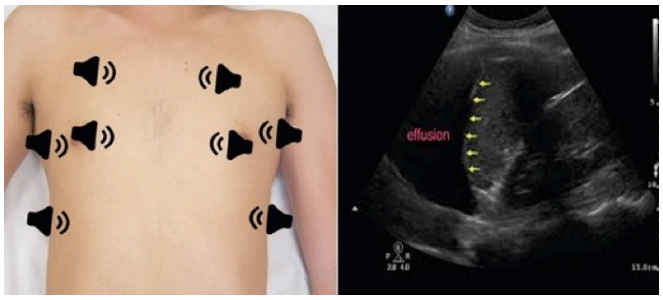

Figure 2. Thorax ultrasonography showing pleural effusion.

Computerized Thorax Tomography

CT is important for the diagnosis of local fluids. Since computerized tomography (CT) has become widespread and accessible, it is generally the first choice after the chest x-ray. Computerized tomography is crucial in every undiagnosed exudate fluid (Figure 3). In addition to exudate fluid, it is more useful at recognition and identification of the parenchymal pathology, pleural mass, and nodules [7].

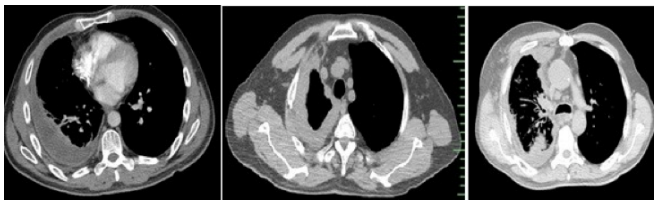

Figure 3. Computerized thorax tomography showing pleural effusion and thickening.

Surgical Diagnosis and Treatment Methods

After the physical examination of the patient with pleural effusion, the above-mentioned radiological examinations should be performed. If the patient has exposure to asbestos and there is a radiological suspicion of mesothelioma, these patients should also be assessed as described in the section of the malignant pleural mesothelioma. Transudate/exudate fluid differentiation should be made from the fluid collected via thoracentesis. Also, cytological, other biochemical, and microbiological examinations should be done. In doubt of malignancy, the patient should undergo bronchoscopy and interventional diagnostic procedures, according to results of tomography [8]. The methods are as shown in table 4.

Table 4. Surgical diagnosis and treatment methods.

1. Thoracentesis
2. Closed Pleural Biopsy
3. Biopsy with Imaging (CT, USG, MR)
4. Thoracoscopy with local anesthesia
5. VATS
6. Open Pleural Biopsy
7. Major Resection
8. Permanent Pleural Catheter / Pleuroperitoneal Shunt

1. Thoracentesis

The first procedure to perform in a patient with malignant pleural effusion is thoracentesis. Thoracentesis can be useful for both diagnosis and elimination of the most common complaint, the dyspnea. Also, lung expansion capacity can be evaluated during the procedure. If the patient's life expectancy is short (especially less than a month), then the treatment can be continued with evacuation thoracentesis. The ideal treatment choice should be tube thoracostomy and pleurodesis. In many patients, fluid is drained via repeated thoracentesis to provide symptomatic relief. But there are some disadvantages of this implementation. First, the fluid is recollected shortly after thoracentesis. In addition, the risk of infection is high, and inoculations may develop in the pleural fluid (Figure 4).

Figure 4. Thoracentesis procedure.

For thoracentesis, preferred application location is intercostal space under the fluid level. In order not to damage the intercostal vein and nerve pack, the punch is applied from the upper part of the costa. Major complications are cough, pneumothorax, chest pain, infection at the pleural cavity, hemothorax, vasovagal reflex stimulation (bradycardia, hypotension), and rarely diaphragm, liver or splenic injury [9].

2. Closed pleural biopsy

This technique can be applied with Abrams, Cope, Vim-Silverman needles (Figure 5). This procedure, like thoracentesis, is performed via inserting the notched end of the pleural biopsy needle into the pleura and by performing a biopsy with the drill inside. Diagnostic value of closed tubal pleura biopsy is 50-80%. If pleural fluid cytology is negative for malignant pleural fluid, a closed pleural needle biopsy may be performed, but in this case, the diagnosis rate is decreasing. A thoracoscopic biopsy is more commonly used in exudative pleural fluids that cannot be diagnosed instead of pleural needle biopsy. Thoracentesis and closed pleural biopsy can be done in outpatient clinics, but there are complication risks such as hemoptysis and hemothorax. Closed pleural biopsies are less preferred because of their low diagnostic yield and relatively high complications. This method can be preferable for the patients with tuberculous pleurisy [10].

Figure 5. Abrahams needle set.

3. Biopsy with imaging modalities

In the context of imaging modalities, especially with the guidance of thoracic tomography and thorax ultrasonography, a tru-cut biopsy is the preferred method with high diagnostic and low complication rate. MR and PET/CT guidance has begun to become the current method for biopsies [10].

4. Thoracoscopy with local anesthesia

Pleuroscopy method, thoracoscopy with local anesthesia, can be useful to take biopsies from pathological areas. Cryobiopsy, as a novel sampling method, which freezes the samples during flexible or rigid thoracoscopy, can be a new option in the undiagnosed effusions [10,11].

5. VATS

Video-Assisted Thoracoscopy (VATS) is frequently used due to its development in today's state-of-art technology, which is the procedure performed under the preference sedoanalgesia or general anesthesia according to the patient's choice (Figure 6).

With VATS, the hemithorax can be visualized in the best way, and the biopsies can be obtained with the highest diagnostic value. In selected eligible patients, partial pleurectomy can also be performed to provide lung expansions. The entire pleural field exploration is the procedure which allows complete pleurodesis, including complete confirmation of the lung expansion and application of talc with visual-assistance for the removal of the entire fluid. Thoracoscopy is a safe procedure and mortality is reported to be 0.1% in 1350 cases [3,12].

Figure 6. VATS procedure.

6. Open Pleural Biopsy

An open pleural biopsy may be performed in patients with pleural adhesions that are not appropriate for VATS. This procedure can also be performed under sedation, and local anesthesia where the general condition of the patient is not good and general anesthesia cannot be obtained [3].

7. Major Resections

Surgical options are VATS pleurodesis, VATS partial pleurectomy, pleurectomy / decortication, extended pleurectomy/decortication, and extrapleural pneumonectomy. In some studies, mortality and survival advantage has been shown to be comparable to the others in Extended Pleurectomy / Decortication surgery. However, there are prospective, randomized controlled trials studies which show the comparison between these surgical options (3). In the past, these procedures were performed with open thoracotomy and also with VATS since the early 1990s. Pleurectomy is performed in two conditions. First one is the thoracotomy for pleural effusion that is not diagnosed. If malignancy is detected, immediate parietal pleurectomy is performed to prevent fluid accumulation. The second condition is persisting pleural effusion, and sclerosing agent cannot be applied due to the restricted lung. Parietal pleurectomy is performed with decortication. Technically, dissection is advanced according to the location of the parietal pleural tumor. After reaching to the mediastinal surface, the primary aim should be not to damage the phrenic nerve, the recurrent laryngeal nerve, the sympathetic nerves or the stellate ganglia or vascular structures (Figure 7). Diagnosticians should care not to remove the diaphragmatic connection parts of the chest wall in the costophrenic sinus, because the application is unnecessary and often impossible, and decortication should be added only if the visceral lung pleura is not expansive depending on the fibrin texture. Another major resection is extrapleural pneumonectomy. Additional intra-operative or post-operative treatments should be performed when major resection is planned. These are hyperthermic intraoperative chemotherapy and photodynamic therapy. In addition, radiotherapy could be added [13,14].

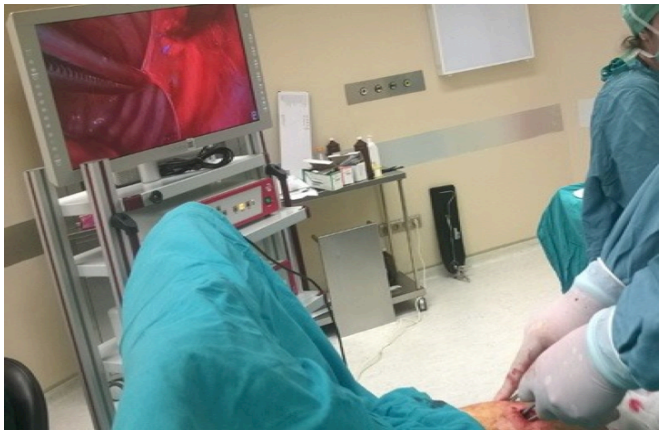

Figure 7. Application of parietal pleurectomy with VATS.

8. Permanent Pleural Catheter / Pleuroperitoneal Shunt

Persistent pleural catheters can be applied in cases where the pleural effusion cannot be drained, and the lung cannot be expanded. And patients may be monitored in the outpatient clinic [15]. Permanent pleural catheters used more frequently in recent years and recommended for patients with frequent, recurrent, and inoperable pleurodesis [16]. The pleuroperitoneal shunt is another option when patients are symptomatic, pleurodesis cannot be performed, and lung is not expansive. It is preferred in cases where the respiratory parameters are limited, the general condition is not very good, and the pleural function is not considered. It allows the lung to ventilate, prevents mucous retention, atelectasis, and pneumonia. Tumor cells have a risk of spreading to the peritoneal cavity and shunt failure due to catheter blockage may happen [17].

Malignant Mesothelioma

A separate section is needed to approach the patient with pleural effusion and doubt of malignant mesothelioma. Pleural effusion is usually the first clinical manifestation of malignant mesothelioma. The guidelines prepared by ERS and ESTS for diagnosis and treatment of malignant pleural mesothelioma include the following suggestions. Cytological examination in pleural effusions is the first choice in diagnosis. However, the cytological examination is not preferable for patients with doubt of the MPM, since the misdiagnosis rate is too high (Grade IB). When cytologically suspicious, this condition should be confirmed with tissue biopsy (Grade IB). Closed pleural biopsies (Abrams or Castelain's needles) have a higher error rate, as in cytologic diagnosis. Thoracoscopy is recommended as a diagnostic method (Grade IA). With thoracoscopy, the entire pleura could be observed, and deep biopsies could be obtained from both normal and pathological areas (Figure 8). Fat and muscle invasions can also be detected during the procedure [18].

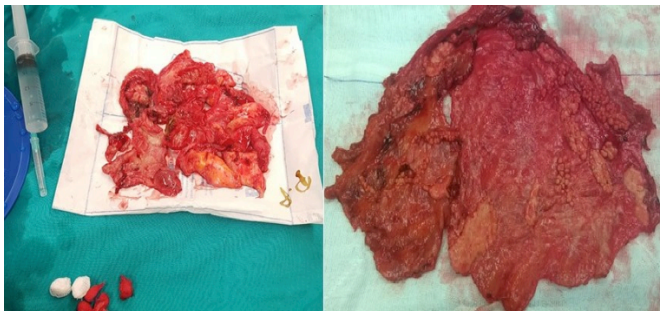

Figure 8. Surgically decorticated epithelioid type malign mesothelioma.

Pleurodesis

Side effects, cost-effectiveness, and ease of administration should be considered in selecting the preferred agent for pleurodesis. The success rate of talc pleurodesis is high. Large particulate talc pleurodesis should be preferred to avoid possible ARDS-like complications.

Before the pleurodesis procedure, a diluted local anesthetic is delivered via tube thoracostomy. After that, a sclerosing agent dissolved or suspended in 50-100 ml of saline should be administered to the pleural cavity. With this method, the irritation pain of the patient during the procedure can be alleviated. After the procedure, the tube is clamped and left in this position for 3-4 hours. The tube can be aspirated so that it does not exceed 20 cm H2O pressure.

If the patient develops severe pain or shortness of breath after the procedure, the tube should be opened immediately, and the talc should be drained. If the drainage falls below 50-100 ml, the tube thoracostomy should be terminated [19].

Pleurodesis can also be done with VATS technique. During VATS for diagnostic purposes, in patients suspicious for a pleural tumor or metastasis, frozen examination can be done. For those who will not undergo additional surgery, the fluid may be drained entirely, and talc may be applied after the adhesions have been removed [20].

Declaration of conflicting interests

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Charts must be prepared in 2 dimensions unless required by the data used. Charts unnecessarily prepared in 3 dimensions are not accepted.

Figures that are charts, diagrams, or drawings must be submitted in a modifiable format, i.e. our graphics personnel should be able to modify them. Therefore, if the program with which the figure is drawn has a "save as" option, it must be saved as *.ai or *.pdf. If the "save as" option does not include these extensions, the figure must be copied and pasted into a blank Microsoft Word document as an editable object. It must not be pasted as an image file (tiff, jpeg, or eps) unless it is a photograph.

Tables and figures, including caption, title, column heads, and footnotes, must not exceed 16×20 cm and should be no smaller than 8 cm in width. For all tables, please use Word's "Create Table" feature, with no tabbed text or tables created with spaces and drawn lines. Please do not duplicate information that is already presented in the figures.

Tables must be clearly typed, each on a separate sheet, and double-spaced. Tables may be continued on another sheet if necessary, but the dimensions stated above still apply.

Berkant Özpolat MD.
Editor-in-Chief, Current Thoracic Surgery
e-mail: cts@tgcd.org.tr
http : www.cts.tgcd.org.tr