

## The relationship of pneumothorax with acute respiratory distress syndrome and mortality in Covid-19

### ABSTRACT

**Background:** Pneumothorax is defined by the accumulation of air between the visceral and parietal pleura. The degree of collapse after rupture of the visceral pleura determines the clinic of the pneumothorax. Acute respiratory distress syndrome is an important lung disease responsible for morbidity and mortality in critically patients, including Covid-19 patients.

**Aims:** It was aimed to related pneumothorax with ARDS and mortality in Covid-19 patients hospitalized in the Intensive-care unit.

**Study Design:** This study was done retrospectively between 1 Sep 2020 and 31 Dec 2020 in Ersin Arslan Training and Research Hospital Covid Intensive-care unit.

**Methodology:** Patients older than 18 years of age, positive polymerase chain reaction test, with lung involvement in computed tomography and admitted in the Intensive-care unit were included in the study. Age, gender, comorbidities, severity of ARDS, presence and treatment of pneumothorax, hospital stays and mortality of the patients were retrospectively examined. Statistical analysis of the study was done with the Chi-square test.

**Results:** 79 of the patients were males (66.4%) and 40 females (33.6%). The mean age was  $68.2 \pm 1.93$  (33-92) years. 71.4% of them had a history of chronic illness. The order of comorbidities from most to least were hypertension, diabetes mellitus, and chronic obstructive pulmonary disease. Lung involvements in CT were 60.5% multifocal and 29.5% unifocal. ARDS severity were 36.9% mild, 39.5% moderate, and 23.6% severe. Pneumothorax was found in 10% of the patients. Surgical treatment (tube thoracostomy) was required in 58.3% of patients with pneumothorax. 68% of the patients were mechanical ventilated. The mean length of stays in the intensive-care unit were  $9.9 \pm 1.28$  (1-38) days. The mortality rate was 41.1%.

**Conclusion:** Covid-19 are more often in males and over 60 years of ages in patients admitted to intensive-care unit. Hypertension and chronic obstructive pulmonary disease are related with pneumothorax. Multifocal involvements of the lung are related with pneumothorax. Mild ARDS is not related with pneumothorax, but moderate and severe ARDS are related. Pneumothorax with severe ARDS is require surgical treatment. Pneumothorax is related with mortality in Covid-19.

*Keywords: ARDS, Covid-19, pneumothorax, surgical, treatment*

### 1.INTRODUCTION

Pneumothorax is defined by the accumulation of air between the visceral and parietal pleura. Occurs due to trauma or non-traumatic causes. The degree of collapse after rupture of the visceral pleura determines the clinic of the pneumothorax [1]. If it occurs due to an underlying disease, it is defined as secondary spontaneous pneumothorax (SSP). The incidence of SPP is 2 - 6.3 / 100.000, more often in males [2]. Interstitial involvement and endothelial damage occur after diffuse alveolar damage in acute respiratory distress syndrome (ARDS), and causes worsening of lung compliance and scarring [3]. ARDS is an important lung disease responsible for morbidity and mortality in critically patients, including Covid-19 patients [4]. An increase in pneumothorax rates was observed during the pandemic period. In this study, it was aimed to related ARDS with pneumothorax and mortality in Covid-19 patients hospitalized in the Intensive-care unit.

### 2.MATERIALS AND METHODS

This study was done between 1 Sep 2020 and 31 Dec 2020 in Ersin Arslan Training and Research Hospital Covid Intensive-care unit. Patients older than 18 years of age, positive Polymerase Chain Reaction (PCR) test, with lung involvement in Computed Tomography (CT) and admitted in the intensive-care unit were included in the study. A total of 119 patients compatible with these criteria were identified. Age, gender, comorbidities, presence of ARDS, lung involvements in CT, presence and treatment of pneumothorax, hospital stays and mortality of the patients were retrospectively examined. Berlin criteria were used for the diagnosis of ARDS. Statistical analysis of the study was done with the Chi-square test.

### 3.RESULTS

79 of the patients were males (66.4%) and 40 females (33.6%). The mean age was  $68.2 \pm 1.93$  (33-92) years (table 1). 71.4% of them had a history of chronic illness. The order of comorbidities from most to least were hypertension (HT, 44.7%), diabetes mellitus (DM, 31.7%), and chronic obstructive pulmonary disease (COPD, 15.2%). Lung involvements in CT were 60.5% multifocal and 29.5% unifocal. According to the number of lobes damaged in the lung, 1 lobe (36.9%) was most frequently affected, and at least 2 lobes (6.7%) affected. ARDS severity were 36.9% mild, 39.5% moderate, and 23.6% severe. Pneumothorax was found in 10% of the patients. Surgical treatment (tube thoracostomy) was required in 58.3% of patients with pneumothorax. 68% of the patients were mechanical ventilated. The mean length of stays in the intensive-care unit were  $9.9 \pm 1.28$  (1-38) days. The mortality rate was 41.1%.

**Table 1. Demographic characteristics of the study**

	Mean	Std Dev	95%(+/-)
Age	68.2 (33-92)	10.64	1.93
Male	66.4%	0.47	0.08
Female	33.6%		
Stay of hospitalized (days)	9.92	6.98	1.28

As a result, although not statistically significant, pneumothorax ( $p < 0.7$ ) and mortality ( $p < 0.3$ ) were more often in males. Despite pneumothorax was more often in those older than 60 years ( $p < 0.4$ ), it was statistically significant in the 18-40 ages group ( $p < 0.002$ ). The mortality was related with those older than 60 ages ( $p < 0.02$ ). Presence of chronic disease history was related with both pneumothorax ( $p < 0.0001$ ) and mortality ( $p < 0.01$ ), and mortality was more often in those with comorbidity (circa 3 times more) than in those without ( $p < 0.04$ ). HT ( $p < 0.01$ ) and COPD ( $p < 0.0001$ ) were associated with pneumothorax, and it was 14 times more with COPD. As is known, ARDS is a cause of mortality. Severe ARDS was related with a high value of evidence ( $p < 0.0001$ ) for mortality. Mortality with moderate ARDS ( $p < 0.004$ ) was increased approximately 7 times. Multifocal involvement in CT was related with both pneumothorax ( $p < 0.01$ ) and mortality ( $p < 0.06$ ). Regardless of the percentage of lung lobe involvement, of up to 3 lobes were not related with pneumothorax and mortality. However, affected of 4 lobes ( $p < 0.001$ ) were associated with pneumothorax, and affected of 5 lobes were associated with both pneumothorax ( $p < 0.02$ ) and mortality ( $p < 0.04$ ). Presence of mechanical ventilation ( $p < 0.0001$ ) was associated with pneumothorax, and pneumothorax ( $p < 0.0001$ ) was related with mortality. (table 2).

**Table 2. Statistical analysis of parameters with pneumothorax and mortality**

	n	Pneumothorax			Mortality		
		p<	CV	ODDS	p<	CV	ODDS
Gender							
Male	79	0.7	0.002	1.014	0.3	0.078	1.545
Female	40	0.7			0.3		
Ages							
18-40	1	0.002	0.275	1.091	0.3		
41-60	30	0.1			0.2		
>60	88	0.4			0.02	0.107	1.847

<b>Comorbidity</b>								
Yes	85	0.0001	0.026	1.224	0.01	0.181	2.700	
HT	38	0.01	0.229	0.645	0.0001	0.102	1.932	
DM	27	0.5			0.0001	0.093	0.576	
COPD	13	0.0001	0.419	14.286	0.0001	0.153	1.149	
No	34	0.7			0.04	0.181	0.370	
<b>ARDS</b>								
Mild	44	0.3			0.002	0.284	0.207	
Moderate	47	0.08	0.181	0.276	0.004	0.258	6.955	
Severe	28	0.002	0.275	5.733	0.0001	0.025	1.184	
<b>Lung Involvement</b>								
Unifocal	47							
Multifocal	72	0.01	0.213	8.295	0.06	0.164	2.829	
<b>Number of lobes</b>								
1	44	0.7		0.607	0.1		2.298	
2	8	0.8		1.299	0.7		1.355	
3	16	0.5		0.558	0.7		0.511	
4	27	0.001	0.285	6.090	0.2		1.684	
5	24	0.02	0.040	1.365	0.04	0.181	0.351	
<b>Mechanical Ventilated</b>								
Yes	81	0.0001	0.110	2.535	0.0002	0.341	6.500	
No	38			0.394			0.154	

Severe ARDS was related with medical ( $p<0.04$ ) and surgical ( $p<0.03$ ) treatment of pneumothorax. Based on the evidence, severe ARDS was required surgical treatment. Left pneumothorax ( $p<0.0001$ ) was related with medical treatment and right pneumothorax ( $p<0.0001$ ) with surgical treatment. Unifocal or multifocal involvements ( $p<0.3$ ) in CT were not related with medical treatment of pneumothorax, and both required surgical treatment ( $p<0.02$ ). Surgically treated pneumothorax patients were associated with longer (16-20 days,  $p<0.003$ ) hospital stays (table 3).

**Table 3. Statistical analysis of pneumothorax treatment**

		Treatment of Pneumothorax					
		Medical			Surgical		
		p<	CV	ODDS	p<	CV	ODDS
<b>ARDS</b>							
	Mild	0.4			0.6		
	Moderate	0.3			0.1		
	Severe	0.04	0.180	5.340	0.03	0.189	4.889
<b>Lung Involvement</b>							
	Unifocal	0.3			0.02		0.903
	Multifocal	0.3			0.02	0.202	1.108
<b>Stay of hospitalized (days)</b>							
	1-10	0.5			0.3		
	16-20	0.4			0.003	0.272	8.583
	>20	0.5			0.4		
<b>Pneumothorax</b>							
	Right	0.0001	0.446	32.700	0.0001	0.646	90.833
	Left	0.0001	0.426	37.333	0.0001	0.350	22.000

#### 4.DISCUSSION

Secondary spontaneous pneumothorax (SSP) is more often in patients aged 60-60 years, and 3 times more in males. The incidence of pneumothorax secondary to COPD is 26 / 100.000 [2]. In this study, SSP was more often in patients older than 60 years, and 2 times more in males than females. The pneumothorax rate was found to be 10% in Covid-19 patients hospitalized in the Intensive-care unit. It was understood that Covid-19 significantly increased the pneumothorax rates. It has been reported that a history of chronic disease in Covid-19 is associated with poor prognosis [5]. Patients with comorbidities (71.4%) in intensive-care were approximately 2 times more than those without. Comorbidity was associated with both pneumothorax and mortality. The comorbidities in the study, in order of frequency, were hypertension, diabetes mellitus, and COPD. Hypertension and COPD were related with pneumothorax.

ARDS is a deadly disease and frequently observed in Covid-19. Mortality rates in ARDS range from 34.9% to 40%, depending on its severity [6]. It has been reported that mortality rates due to ARDS in patients with and without Covid-19 are similar [7]. Therefore, as in ARDS, hypoxemia and lung dynamics are very important. ARDS severity of the patients were determined according to the Berlin criteria in the study. Regardless of ARDS severity, it was associated with mortality. Odds ratios according to their severity were mild 0.2, moderate 6.9 and severe 1.1. When the severity of ARDS increased, the mortality rates were increased. If ARDS was mild, it was not related with pneumothorax, and moderate or severe ARDS were associated with pneumothorax. Spontaneous pneumothorax, subcutaneous and mediastinal emphysema are a complication of Covid-19 pneumonia [8]. As it is known, pneumothorax is a treatable disease, and if tension progresses to pneumothorax, it can result with death. Early detection of pneumothorax in chest x-ray is possible. Therefore, pneumothorax should be investigated especially in Covid-19 patients. It has been reported that pneumothorax increases mortality in patients with ARDS, and it is seen at a rate of 1.7% to 77% [9,10]. In this study, pneumothorax was found to be associated with mortality in Covid-19. Since ARDS is related with pneumothorax, appropriate management of hypoxemia can prevent fatal pneumothorax complication. Because, mild ARDS was not found to be significantly associated with pneumothorax in the study.

More of lung involvement is logically indicates more common disease. Analysis of the findings in the study supported it. Multifocal affected of the lung were related with both pneumothorax and mortality. Therefore, unifocal involvement of the lung was not significant for pneumothorax. Multifocal involvements of lung were found to be a risk factor for pneumothorax in Covid-19. Any a rate involvement of up to 3 lobes of the lung were not related with pneumothorax and mortality. However, affected of 4 lobes of the lung were associated with pneumothorax, and affected of 5 lobes were associated with both pneumothorax and mortality. Hence, affected of 4 lobes were found as a risk factor for pneumothorax. Barotrauma is known as the cause of pneumothorax. This study was supported the relationship between mechanical ventilated and pneumothorax.

Treatment of pneumothorax is observation, tube thoracostomy, pleuridesis, thoracoscopy and thoracotomy. Pneumothorax patients with ARDS are critically ill and not suitable for thoracoscopy and thoracotomy [10]. Major surgery was not performed on any patient in the study. Classically, observation and oxygen support were preferred in patients with minimal pneumothorax (<5%). In patients with mechanical ventilated, low pressure support (PS) and low positive end expiratory pressure (PEEP) were recommended first. However, if there were no response to non-surgical methods, tube thoracostomy was performed. The thorax tube could not be removed until death, especially in severe ARDS patients, due to continued air leakage. Pneumothorax in patients with ARDS is associated with many factors such as smoking, COPD, severity of ARDS, and mechanical ventilation settings [11]. In this study, mild ARDS was not associated with pneumothorax, but moderate and severe were associated. Pneumothorax with severe ARDS was required surgical treatment. Left pneumothorax was more related with non-surgical methods, and right pneumothorax with surgical methods. Surgical treatment was more associated with hospital stays.

#### 5.CONCLUSION

According to this study, Covid-19 are more often in males and over 60 years of ages in patients admitted to intensive-care unit. Hypertension and chronic obstructive pulmonary disease are related

with pneumothorax. Multifocal involvements of the lung are related with pneumothorax. Mild ARDS is not related with pneumothorax, but moderate and severe ARDS are related. Pneumothorax with severe ARDS is require surgical treatment. Pneumothorax is related with mortality in Covid-19.

## ETHICAL APPROVAL

Republic of Turkey Ministry of Health 2020/12-10T13\_04\_00 numbered and Gaziantep University Medical Ethics Committee 2021/16 numbered approval have been received.

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