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COVID-19-Related life-threatening complications: pneumothorax, pneumo mediastinum and subcutaneous emphysema

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Abstract

Complications of COVID-19-related pneumothorax, subcutaneous emphysema, and pneumomediastinum are frequently observed in moderate and severe pneumonia cases. The aim of this study is to determine the incidence and potential risk factors of life-threatening complications such as pneumothorax, pneumomediastinum, and subcutaneous emphysema that develop in patients received in the tertiary ICUs of our hospital, which serves as a pandemic hospital and to analyze their relationship with mortality. Patients' demographic characteristics, comorbid diseases, length of hospital stay, day and duration of thoracic tube placement, discharge status, and hospitalization laboratory findings were recorded, and the relationship of these parameters with mortality due to pneumothorax, subcutaneous emphysema, and pneumomediastinum were investigated. Of these patients, 33 had pneumothorax, 12 had pneumomediastinum, and 28 had subcutaneous emphysema. Male and female patients were equally represented, and mortality rates were similar. While the rate of pneumothorax in the study patients was 2.21 %, the rate of all life-threatening sequelae such as pneumothorax, pneumomediastinum, and subcutaneous emphysema was 4.7 %, with a high mortality rate (90 %) in 70 patients with these complications. Patients diagnosed with COVID-19 pneumonia should be constantly monitored for life-threatening complications such as pneumothorax, pneumomediastinum, and subcutaneous emphysema during their long-term follow-up.

Keywords: *Covid-19, pneumothorax, pneumomediastinum, subcutaneous emphysema, intensive care unit*

Introduction

The new coronavirus, which was first detected in Wuhan, China in December 2019 and identified as severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), continued to increase worldwide, and it led to the declaration of the COVID-19 pandemic on March 11, 2020 [1].

To ensure adequate oxygenation in patients admitted to the intensive care unit (ICU) due to coronavirus disease, non-invasive or invasive mechanical ventilation support is used. Therefore, pneumothorax is common in these patients [2]. Complications of COVID-19-related pneumothorax (PNX), pneumomediastinum (PM), and subcutaneous emphysema (SCE) are frequently observed in moderate and severe pneumonia cases [3]. In the etiology of PNX, PM and SCE developing based on COVID-19, alveolar destruction and spontaneous alveolar rupture caused

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by destructive damage in the lung parenchyma, as well as alveolar damage and rupture due to positive pressure air given by respiratory support devices have been demonstrated [2,4]. In the literature, PNX, PM and SCE complications due to alveolar damage caused by COVID-19 pneumonia have been included in the form of case reports [5-8]. These studies include either combining multicenter cases or single-center case reports [9]. In COVID-19 pneumonia patients followed in ICU, PNX, PM, and SCE are more common complications, unlike the definitions made in the initial stages of the pandemic [10]. The aim of this study is to determine the incidence and potential risk factors of life-threatening complications such as pneumothorax, pneumo-mediastinum, and subcutaneous emphysema that develop in patients hospitalized in the tertiary ICU of our hospital, which serves as a pandemic hospital, and to analyze their relationship with mortality.

Materials and Methods

Our retrospective cross-sectional study was carried out in accordance with the Declaration of Helsinki and the Strobe Checklist after the approval of the X University Faculty of Medicine Clinical Research Ethics Committee dated 30.12.2021 and numbered 2021/119. The written informed consent form was not obtained due to the retrospective type of study. We were able to attain vast patient potential and experience since our hospital functioned actively as a pandemic hospital. The files of 1490 patients over the age of 18 who were diagnosed with COVID -19 and hospitalized in our hospital's 3rd Stage intensive care units between March 2020 and April 2022 were scanned for the study. The diagnosis of all patients was confirmed in laboratory and radiologically. Patients who had pneumothorax, pneumomediastinum, or subcutaneous emphysema without a COVID-19 diagnosis were not included in the study.

Data on the patients included in the study were obtained from patient files and the hospital's automation system. Patients' demographic characteristics (age, gender), comorbid diseases, length of hospital stay, day and duration of thoracic tube placement, discharge status, and laboratory findings on admission to the intensive care unit (CRP, WBC, lactate, CK, D-dimer) were recorded, and the relationship of these parameters with mortality due to pneumothorax, pneumomediastinum, and subcutaneous emphysema was examined. No data could be reached regarding smoking.

Statistical Analysis

Data analysis was done with SPSS (Statistical Program in Social Sciences) 21 package program. Shapiro Wilk Test was used to determine whether the data were fit for normal distribution. The level of significance was taken as $p< 0.05$. Non-parametric test methods were used when the variables did not have a normal distribution ($p>0.05$). Chi-square analysis was performed in the analysis of categorical data. Pairwise group comparisons were made through Mann-Whitney U test.

Results

The study included 70 patients (33 of 70 patients had pneumothorax, 12 had pneumo-mediastinum, and 28 had subcutaneous emphysema) who were diagnosed with COVID-19 pneumonia and had complications such as PNX, PM, and SCE while being followed up on and treated in the ICU. Both pneumothorax and pneumomediastinum were observed in two of these patients. Additionally, 1 patient had pneumothorax and subcutaneous emphysema. Of the 70 patients included in the study, 90% died. In the study, the mean age of the patients who died was 65.65±12.57, while the mean age of the survivors was 50.43±23.29, with similar mortality rates. Non-survivors (31-94) were older than those discharged (19-89) and the mortality rate by gender was slightly higher in females however, no significant difference was found between demographic data and mortality ($p>0.05$) (Table1).

The most common comorbidities in our intensive care unit patients were heart diseases, respiratory issues, and diabetes. When the relationship of comorbid diseases with mortality was evaluated, the presence of comorbid disease was associated with increased mortality in these patient groups ($p<0.05$) (Table2).

In our study, in accordance with the literature, PNX developed in 2.21% of the patients followed up in the ICU. In addition, the rate of development of complications such as PNX, PM and SCE related to COVID-19 was higher in our patients followed up in the ICU (4.7%), and the effects of these complications on mortality were similar ($p>0.05$) (Table 3).

Invasive mechanical ventilation (IMV) support was also provided to 66 (94.3%) of 70 patients. 63 (95.4%) patients who underwent IMV support died. 33 patients developed pneumothorax, 23 patients subcutaneous emphysema, and 10 patients pneumomediastinum. There were only 4 patients who underwent NIV. The solely complication was subcutaneous emphysema. 4 (5.7%) patients who did not undergo IMV were discharged. It was observed that the mortality rate was higher in patients who were provided with IMV support. This was statistically significant ($p=0.001$).

When the patients who underwent tube thoracostomy were examined, we observed that tube thoracostomy was applied to 18 of 20 right pneumothorax cases and 7 of 8 left pneumothorax cases. Tube thoracostomy was administered to 5 cases with bilaterally due to bilateral pneumothorax. In addition, 2 patients who underwent tube thoracostomy had both pneumothorax and pneumomediastinum. Finally, tube thoracostomy was performed in 5 patients with accompanying subcutaneous emphysema.

It was observed that the length of hospital stay, ICU stay (days) and the day of insertion of the thoracic tube did not affect the mortality rate in all patients. This was also not significant ($p>0.05$). When the effect of laboratory values on mortality is evaluated,it was observed that high levels of CRP (C-reaktif protein) was associated with increased mortality ($p<0.05$) (Table 4).

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Table 1. Comparison of groups by age and gender

	Groups	Nonsurvivors		Survivors		p values
		n	%	n	%	
Gender	Female	33	52.4	2	28.6	0.225
	Male	30	47.6	5	71.4	
	Groups	**Mean±SD**		**Median (Minimum-Maximum)**		**p values**
Age (years)	Nonsurvivors	65.65 ± 12.57		65 (31-94)		0.054
	Survivors	50.43 ± 23.29		46 (19-89)		

Chi-squareTest value ($\chi 2$), SD; standard deviation, Mann Whitney test, $p<0.05$

Table 2. Comparison of comorbid diseases and mortality

	Groups	n / %	Groups		Total	p Values
			Nonsurvivors	Survivors		
Cardiac diseases	No	n	23	6	29	**0.011***
		%	36.5%	85.7%	41.4%	
	Yes	n	40	1	41	
		%	63.5%	14.3%	58.6%	
Respiratory diseases	No	n	43	7	50	0.025*
		%	68.3%	100.0%	71.4%	
	Yes	n	20	0	20	
		%	31.7%	0.0%	28.6%	
Other comorbid diseases	No	n	47	7	54	0.049*
		%	74.6%	100.0%	77.1%	
	Yes	n	16	0	16	
		%	25.4%	0.0%	22.9%	
Diabetes Mellitus	No	n	29	6	35	0.037*
		%	46.0%	85.7%	50.0%	
	Yes	n	34	1	35	
		%	54.0%	14.3%	50.0%	

Chi-squareTest value ($\chi 2$), *$p<0.05$

Table 3. Relationship between type of complications and mortality

	Groups	n / %	Groups		Groups	p Values
			Nonsurvivors	Survivors		
Pneumothorax	No	n	34	3	37	0.416
		%	54.0%	42.9%	52.9%	
	Right	n	18	2	20	
		%	28.6%	28.6%	28.6%	
	Left	n	7	1	8	
		%	11.1%	14.3%	11.4%	
	Bilateral	n	4	1	5	
		%	6.3%	14.3%	7.1%	
Pneumomediastinum	No	n	54	4	58	0.088
		%	85.7%	57.1%	82.9%	
	Yes	n	9	3	12	
		%	14.3%	42.9%	17.1%	
Subcutaneous emphysema	No	n	36	6	42	0.119
		%	57.1%	85.7%	60.0%	
	Yes	n	27	1	28	
		%	42.9%	14.3%	40.0%	

Chi-squareTest value ($x2$), *$p<0.05$

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Table 4. Analysis of variables in terms of mortality

	Nonsurvivors			Survivors			
	Mean±SD	Minimum	Maximum	Mean±SD	Minimum	Maximum	p Values
Day of thorax tube insertion	7.25±13.32	1.00	85.00	8.57±14.71	1.00	37.00	0.885
Number of days of hospital stay	22.51±13.57	3.00	88.00	27.00±22.92	6.00	57.00	0.875
Number of days of stay in intensive care	20.02±13.03	2.00	86.00	21.71±20.10	4.00	53.00	0.652
	11.94±7.65	0.77	33.77	5.12±5.60	1.52	17.19	0.015
WBC (10^3/µL)	14.60±6.72	4.08	39.19	11.28±5.43	5.00	22.29	0.147
Lactate (mmol/L)	2.86±2.59	0.90	18.00	3.49±3.46	1.10	11.00	0.875
D-dimer (mg/dL)	4.39±7.57	0.01	31.80	1.11±1.33	0.12	3.99	0.111

	Yes, No (n,%)		Nonsurvivors	Survivors	Total	p Values
Endotracheal intubation	Yes	n, %	63 (100%)	3 (42.9%)	66 (94.3)	0.001*
	No	n, %	0 (0.0%)	4 (57.1%)	4 (5.7%)	

Mann Whitney test, * Chi-square Test, p<0.05

Discussion

COVID-19 disease can progress from asymptomatic illness to severe respiratory failure and even death. In retrospective studies on COVID-19 patients, it has been shown that PNX may occur in 1-2% of hospitalized patients, and 1% of patients who died from infection [10-12]. In our study, in accordance with the literature, PNX developed in 2.21% of the patients followed up in the ICU. The development of PNX has been documented in the literature to be a significant prognostic marker in COVID-19 positive patients, and in one study, 86.3 % of patients with pneumothorax were lost [2]. According to the literature, the presence of PNX in patients with COVID-19 disease causes a considerable increase in the risk of mortality, as demonstrated in our study. In addition, the rate of development of complications such as PNX, PM and SCE related to COVID-19 was higher in our patients followed up in the ICU (4.7%). In one study, the rate of PNX/SCE development was defined as 9.6% [10]. Many studies have demonstrated that these problems increase mortality [13,14]. In our study, 70 patients with these problems also had a high mortality rate (90%). In studies conducted, individuals with life-threatening complications such as PNX, PM, and SCE had similar 28-day survival rates [9]. The fact that the mortality rates were similar in our analysis and no significant difference was found validates the conclusions of this large patient series study.

The number of male and female patients in our study was equal, and the mortality rates were similar, but there are publications in which males had a more severe clinical course [9]. In a multicenter trial conducted in England, PNX and PM found in patients under 70 years of age did not alter COVID-19-related survival; however, PNX and PM seen in patients over 70 years of age were demonstrated to be more fatal [9].

In the present study, the mean age of the patients who died (65.65±12.57) was higher than the mean age of the survivors (50.43±23.29), and patients over the age of 65 were more likely to die from PNX and PM.

In a study, the most common comorbid diseases were found to be hypertension, obesity, and diabetes [15,16]. Similarly, pulmonary problems, heart diseases, and diabetes were the most common comorbidities in our ICU patients. The effects of these diseases, which are known to increase mortality, on survival were similar.

NIV and IMV are utilized as a part of treatment in intensive care patients when adequate tissue oxygenation cannot be achieved despite oxygen support. As a result, PNX, PM, and SCE may develop in patients, exacerbating the current scenario. The reduced survival rates observed in IMV patients were consistent with our findings [15,17].

While moderate episodes may heal spontaneously with watchful monitoring, oxygen support, and analgesia, alveolar damage and alveolar rupture can occur more easily in individuals with severe respiratory failure, such as our patients, and frequently necessitate chest tube drainage [10]. At the same time, high PEEP and CPAP applied to this patient group may also cause of PNX development. Tube thoracostomy was performed by a thoracic surgeon in our PNX cases with severe respiratory failure. It has been shown in studies that when PNX develops, tube thoracostomy is an adequate treatment option in most cases [18]. In a study of 124 cases, right pneumothorax was found in 82 (66.1%) patients (2). In our study, right pneumothorax developed more frequently (60.6%). In line with the literature, right pneumothorax developed more commonly in our study, and tube thoracostomy was performed on all patients with an indication. Furthermore, since there is a risk of aerosol in such applications, practitioners should use protective equipment and

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take precautions to limit this risk [13]. However, as the already reduced lung capacity in COVID-19 patients is further reduced in the presence of PNX, it is more fatal, and tube thoracostomy in the intensive care unit did not impact mortality, despite being used in our COVID-19 patients with PNX.

The first laboratory results at admission revealed that most patients had normal WBC with a drop in lymphocyte and eosinophil counts in a study that examined the clinical aspects of 140 patients with a mean age of 57 years [19]. Dynamic changes in biomarker levels can help predict the course, prognosis, and outcome of the disease [20]. Serial follow-up tests (starting at >3 days) revealed a further decline in eosinophil and lymphocyte counts, which were positively correlated with disease severity, and high D-dimer, CRP, and procalcitonin levels were associated with a severe disease course [19]. In another study, it was found that high WBC levels checked in the early period had a substantial effect on prognosis, although no statistically significant association exists between CRP and WBC levels and mortality [2]. In our study, WBC levels were within normal ranges in laboratory findings obtained at the time of admission to the intensive care unit, and we believe that high CRP level are associated with the severity of COVID-19 pneumonia.

Limitations

Only COVID-19-positive patients admitted to ICU were included in the study. Suspected but undiagnosed cases were excluded from the study. The study was conducted in a single center and retrospectively.

Conclusion

PNX, PM, and SCE cases have been reported, in addition to many other clinical pictures mentioned in the literature during the COVID-19 infection process. These studies appear in the form of multicentre case reports or single-centre case reports. With 70 patients, our study is one of the most comprehensive ever conducted in a single centre. We believe that patients with COVID-19 pneumonia should be closely monitored in terms of these life-threatening complications in intensive care follow-ups, and that more comprehensive studies on prognostic factors in this regard should be conducted.

Conflict of interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical approval

Ethics Committee Approval: This study was approved by Ethics committee of Malatya Turgut Ozal University, (Approval No: 2021/119).

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