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Research Article / Araştırma

Can Pneumothorax Developing in COVID-19 Patients be a Mortality Marker?

COVID-19 Hastalarında Gelişen Pnömotoraks Mortalite Belirteci Olabilir mi?

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ABSTRACT

Objectives: The purpose of this study is to investigate the effects of pneumothorax (PX), a rare complication of COVID-19, on mortality.

Methods: All patients admitted to our hospital with the diagnosis of COVID-19 were screened, and patients who developed PX were included in the study. Patient demographics data, number of days of hospitalization for comorbidities, day and duration of thorax tube insertion, and laboratory findings during hospitalization were recorded by scanning the hospital automation system and patient records.

Results: For our study, 7485 patients hospitalized with the diagnosis of COVID-19 were screened in intensive care unit. PX was detected in 32 (0.296%) of the patients. About 59.4% of these patients included in the study were male. DM was the most common comorbid condition at 56.3%. In these patients, the mortality rate was found to be 90.6%.

Conclusion: The data obtained indicate that PX, a COVID-19 complication, leads to a serious increase in mortality. We believe that using protective ventilation methods to avoid the development of pneumotarax will help to reduce mortality.

Keywords: COVID-19, mortality, pneumothorax

ÖZ

Amaç: Çalışmamızda koronavirüs hastalığı-19'un (COVID-19) nadir görülen bir komplikasyonu olan pnömotoraksın mortalite üzerine etkisini araştırmayı amaçladık.

Yöntem: Hastanemizde COVID-19 tanısı nedeniyle yatırılarak tedavi edilen tüm hastalar tarandı ve pnömotoraks gelişen hastalar çalışmaya dahil edildi. Hastaların demografik verileri, yandaş hastalıkları, yatış gün sayısı, toraks tüpünün takılış günü ve süresi, hastaneye yatış esnasında yapılan laboratuvar bulguları hastane otomasyon sistemi ve hasta dosyaları taranarak kaydedildi.

Bulgular: Çalışmamız için COVID-19 tanısı ile hastanede yatarak tedavi gören 10.800 hasta tarandı. Çalışmaya dahil edilen 32 (%0,296) hastada pnömotoraks gelişti. Çalışmaya dahil edilen hastaların %59,4'ü erkekti. Yandaş hastalık incelendiğinde %56,3 ile diabetes mellitus en sık eşlik eden hastalıktı. Bu hastalarda mortalite oranı %90,6 olarak hesaplandı.

Sonuç: Elde edilen veriler COVID-19 komplikasyonu olan pnömotoraksın ciddi mortalite artışına sebep olmaktadır. Koruyucu ventilasyon yöntemleri ile pnömotoraks gelişiminin önlenmeye çalışılmasının mortalitenin azaltılmasına katkı sağlayacağını düşünmekteyiz.

Anahtar sözcükler: COVID-19, mortalite, pnömotoraks

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Introduction

The presence of air in the pleural cavity is defined as pneumothorax (PX). PX can occur spontaneously or post traumatically or iatrogenically. The clinic depends on the amount of air leak and the reserves of the lungs. The 2001 consensus from the American College of Chest Physicians (ACCP) recommends tube thoracostomy if the air leak is more than 20%.[1]

COVID-19 (SARS-CoV-2) has numerous complications depending on the course of the disease and site of involvement (Encephalitis, endothelial damage, and cardiac involvement, PX) and the treatments used (PX, renal and hepatic damage, etc.).[2,3] It is known that COVID-19 primarily affects the respiratory system. It is responsible for many diseases, from simple upper respiratory tract disease to acute respiratory distress syndrome (ARDS). The main reasons for PX formation are alveolar damage from COVID-19, comorbidities in positive pressure treatment (chronic obstructive pulmonary disease [COPD], cystic fibrosis, etc.), and the use of interventional procedures such as central venous catheters.[3] Decreased pulmonary reserve, which has already been reduced, leads to a worsening of the clinical course and thus to an increase in mortality when PX develops.

This study aimed to investigate the effect of PX on mortality in patients treated for COVID-19 pneumonia.

Methods

Our retrospective and cross-sectional study was performed in accordance with the Declaration of Helsinki and the Strobe Checklist after approval of the Malatya Turgut Özal University Faculty of Medicine, Clinical Research Ethics Committee, dated November 3, 2021 and numbered 2021/95. All patients over the age of 18 who were taken to the intensive care unit with the diagnosis of COVID-19 in Malatya Training and Research Hospital between March 1, 2020 and August 31, 2021 were screened. The data of the patients who were diagnosed with PX clinically and radiologically and had a thoracic tube inserted were recorded. Pediatric patients, pregnant women, patients who developed PX without a diagnosis of COVID-19, and patients whose participation in the study was not accepted by the patients and/or their relatives were excluded from the study. Informed consent was obtained from all patients.

Data on patients included in the study were obtained from patient files and the hospital's automation system. Patient demographics (age and gender), hospitalization duration, day of thorax tube insertion and duration, discharge status (ex, transfer to ward, and discharge), and laboratory findings on admission to hospital were recorded. The literature search for the study was conducted through Google Scholar and PubMed.

Statistical Analysis

The distribution of questions containing demographic information such as gender, outcome, and disease status was represented using values for number (n) and percentage (%). Conformity of continuous variables in the study such as age, day of admission to hospital, day of tube insertion, number of days of intubation, and measured values with the normal distribution was assessed graphically and with the Shapiro-Wilks test. It was found that none of the continuous variables, except age and day of hospitalization, did conform to the normal distribution, and, therefore, the median values (Interquartile Range) were used to present the descriptive statistics. Furthermore, Mean±Standard deviation values were used in descriptive statistics. To compare measures of two-group variables such as gender and outcome, the day of tube insertion, and the number of days of intubation, the Mann–Whitney U test was used. Independent Sample t-test was used to compare the day of admission to hospital values by gender and outcome.

IBM SPSS Statistics version 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and MS-Excel 2007 programs were used for statistical analysis and calculations. Statistical significance level was accepted as $p<0.05$.

Results

For our study, 10800 patients hospitalized in our hospital due to COVID were scanned. Seven thousand four hundred and eighty-five of these patients were hospitalized in the intensive care unit. The incidence of PX is 0.296% in all patients and 0.427% in intensive care patients. All of these cases had ARDS, which is the severe form of COVID. The study included 40.6% (n=13) female patients and 59.4% (n=19) male patients. There are 18 patients (56.3%) with diabetes, one patient with cerebrovascular disease (CVD), and seven patients with coronary artery disease (CAD). According to the results, 9.4% (n=3) of the patients were transferred to the ward, while 90.6% (n=29) were ex (Table 1). Of the patients who developed px, 28 patients were intubated, while four patients were in spontaneous respiration. Intubated patients consisted of patients followed in Synchronized Intermittent Mechanical Ventilation-pressure support or pressure regulated volume control mode with FiO_2 of 60–80%, positive end expiratory pressure (PEEP) of 6–10 cm H_2O, and peak pressure of 40 cm H_2O. Four spontaneously breathing patients were receiving continue positive airway pressure (CPAP) support with 60–100% FiO_2 and PEEP 6–10 cm H_2O. Two patients who were breathing spontaneously and one patient who was intubated were referred to the service from the intensive care unit after treatment. The mean age of the patients is 64.59±15.85. The minimum age value is 20.0

Table 1. Demographic data

	n	%
Gender		
Female	13	40.6
Male	19	59.4
Result		
Transfer to service	3	9.4
Ex	29	90.6

Table 2. Descriptive statistics

	Mean±SD	Median*	Min-maks
Age	64.59±15.85	65.0 (24.0)	20.0-89.0
Day of hospitalization	20.41±10.13	18.0 (13.0)	2.0-40.0
Thorax tube insertion day	9.41±7.51	6.5 (12.0)	1.0-30.0
Thorax tube residence time/day	7.34±3.66	8.0 (5.0)	1.0-13.0

*: Inter quartile range.

Table 3. Comparison of values by gender

	Female Mean±SD Median*	Male Mean±SD Median*	z-t	p
Day of hospitalization	18.08±11.71 15.0 (18.0)	22.00±8.88 20.0 (14.0)	t=1.023	0.318
Thorax tube insertion day	8.15±5.61 6.0 (10.0)	10.26±8.62 8.0 (14.0)	z=0.404	0.686
Thorax tube residence time/day	6.92±4.11 7.0 (8.0)	7.63±3.40 8.0 (4.0)	z=0.310	0.757

*: Inter quartile range. z: Mann-Whitney U Test; t: Independent sample t-test statistic.

years whereas the maximum age value is 89.0 years. While the average chest tube duration was 9.41±7.51, the average intubation duration was 7.34±3.66 (Table 2). While the tube in female patients remained on average 6.92±4.11 days, the tube in male patients remained on average 7.63±3.40 days. There was no statistically significant difference between days spent intubated according to the gender (z=0.310 and p=0.757) (Table 3). In addition, the average hospitalization duration for males was 22.00±8.88, and the average hospitalization duration for females was 18.08±11.71.

There was no statistically significant difference between the hospitalization duration of males and females according to the discharge status (t=0.483 and p=0.673). While the average length of stay in the hospital was 24.00±13.86 days for those transferred to the ward, it was 20.03±9.92 days for those who were ex (Table 4). When the arrival laboratories of the patients included in the study were examined, the mean value of neutrophils was 15.53±6.92, the mean value of urea was 115.84±70.77, the mean value of ALT was 107.73±172.05,

Table 4. Comparison of values according to the result condition

	Transfer to service Mean±SD Median*	Ex Mean±SD Median*	z-t	p
Day of hospitalization	24.00±13.86 16.0 (N/A)	20.03±9.92 18.0 (14.0)	t=0.483	0.673
Thorax tube insertion day	7.33±6.66 4.0 (N/A)	9.62±7.67 7.0 (12.0)	z=0.519	0.604
Thorax tube residence time/day	7.67±2.08 7.0 (N/A)	7.31±3.81 8.0 (6.0)	z=0.130	0.896

*: Inter Quartile Range. N/A: Not Available; t: Independent sample t-test statistic; z: Mann-Whitney U Test.

Table 5. Laboratory data

Variables	Mean±SD	Median*	Min-max
Leukocyte	17.20±6.93	15.37 (7.88)	9.25–39.20
Neutrophil	15.53±6.92	13.55 (7.35)	6.77–38.14
Lymphocyte	0.66±0.56	0.52 (0.30)	0.18–2.49
Thrombocyte	209.09±86.69	177.50 (102.0)	37.0–418.0
CRP	10.54±8.92	8.01 (11.46)	1.52–35.0
Urea	115.84±70.77	97.50 (74.40)	27.30–270.0
Creatine	1.49±1.46	0.87 (1.46)	0.40–7.75
AST	298.00±1241.89	45.0 (74.50)	14.0–7083.0
ALT	107.73±172.05	48.50 (75.75)	14.0–942.0
Glikoz	211.87±167.92	187.50 (151.75)	62.0–997.0

*: Inter Quartile Range. CRP: C-reactive protein; AST: Aspartat aminotransferaz; ALT: Alanin aminotrasferaz.

and the mean value of glucose was 211.87±167.92. For glucose values, the minimum value is 62.0, and the maximum value is 997.0 (Table 5). Table 5 summarizes the descriptive statistics for the other measured values.

Discussion

One of the many complications of COVID-19 that has become a significant health concern today is PX. It occurs in the clinical course of the disease and/or as a complication (iatrogenic, etc.). PX is defined as the presence of air in the sheets of the pleura. It occurs spontaneously or secondarily (underlying lung disease, trauma, and iatrogenic). The incidence is higher in men.[4] Further reduction of already reduced lung capacity also increases mortality. As a result, PX emerges as a significant determinant of mortality.[5] The data that we have received confirm this idea of us. In the study by Chen et al.[6] examining 6574 COVID-19 patients, they found a PX rate of 0.91% (60 patients). Studies have found that PX due to COVID-19 occurs at a rate of 2% in intensive care patients.[7] Comprehensive studies are inadequate and most literature reviews take the form of case reports or case series.

In studying the pathogenesis of the disease, it is known that ACE 2 (angiotensin-converting enzyme 2) receptors play an essential role. The SARS-CoV-2 virus has been shown to use ACE2 receptors as an entry portal into the cell.[8,9] Pneumocytes are rich in ACE receptors. Therefore, it primarily affects the respiratory system and, in some cases, causes severe lung damage. Alveolar rupture may develop due to generalized alveolar damage and cause PX.[10]

It is well known that diabetes mellitus (DM) causes an increase in ACE receptors. Due to this effect of DM, studies show that the course of the disease in DM patients is more severe, and thus mortality is higher.[11] Therefore, it is predictable that the risk of developing PX will be higher in these patients. About 56.3% of the patients in our study had DM. This result indirectly shows that DM also increases the likelihood of developing PX due to its effect on disease progression. However, there are very few studies on the relationship between DM and PX.

Although studies show no gender difference in the prevalence of the COVID-19 pandemic, males have a more severe clinical course.[6,12] In our study, 59.4% of the cases were male patients. Our study was similar to the literature.[7,13] This is due to men's smoking prevalence and the epidemiological prevalence of primary lung diseases such as COPD, emphysema, and chronic bronchitis.[5,14] Another reason is that the higher virulence due to higher ACE receptor activity in males leads to a more severe course of the disease.[15] Factors such as the increase in ACE expression by estrogen, the increase in NO production, and positive effects on the immune system (high antibody levels?) are thought to contribute to the milder course of COVID-19 in women.[16,17] When comorbid diseases and pathogenesis are considered, it is apparent that COVID-induced PX is more common in men due to the more severe course of the disease.

When considering the etiology of PX, another factor is barotrauma. It occurs as a complication of treatment, particularly in patients receiving positive oxygen pressure support with non-invasive ventilation such as CPAP and Bilevel Positive Airway Pressure as part of the treatment of intensive care patients or intubation in advanced cases. In severe SARS-CoV-2 cases, nasal oxygen, reservoir masks, and high flow are primarily used to prevent tissue oxygenation during pneumonia. Positive pressure and oxygen support are used as part of the treatment in cases where adequate tissue oxygenation cannot be achieved, despite oxygen support, and both non-invasive and endotracheal intubation are used. In addition to damaging the alveoli in these patients, support of positive-pressure ventilation can lead to alveolar rupture and promote the development of PX. The main reasons for Px formation are a high tidal volume (TV) and a high PEEP.[18,19] Here, the focus is on the concept of protective mechanical ventilation (TV 6–10 mL/min, plateau pressure <30 cm H_2O peak airway pressure ≤35 cm H_2O). Miller and Sagy demonstrated in their studies using protective mechanical ventilation (low TV) that the risk of PX was significantly reduced in ARDS patients.[19]

Limitations

Data are limited as our study was a single-center study that only included adult and non-pregnant patients. Another limiting factor is that PX is a rare complication of COVID. Therefore, the small number of cases makes it difficult to perform comprehensive studies.

Conclusion

The results of our study show that PX is a factor that increases severe mortality in patients with ARDS by COVID-19. That is why we think attempting to reduce the risk of PX complications in COVID-19 patients through protective mechanical ventilation procedures will help reducing mortality.

Disclosures

Ethics Committee Approval: The study was approved by The Malatya Turgut Özal University Clinical Research Ethics Committee (Date: 03/11/2021, No: 2021/95).

Informed Consent: Written informed consent was obtained from all patients.

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Conflict of Interest: None declared.

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