**RESEARCH ARTICLE** / *Araştırma Makalesi*

# Radiological Features and Outcomes of COVID-19 Associated ARDS Patients with Barotrauma

## Barotravma Saptanan COVID-19 İlişkili ARDS Hastalarının Radyolojik Özellikleri ve Sonlanımları

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Geliş Tarihi / Received : **04.08.2022** Kabul Tarihi / Accepted: **24.12.2022** Çevrimiçi / Online: **16.03.2023**

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Cite this article/Atıf
**Gonderen K., Yildirim M., Yildirim F., Simsek M., Radiological Features and Outcomes of COVID-19 Associated ARDS Patients with Barotrauma. Sakarya Med J 2023 ;13(1):35-40 DOI: 10.31832/smj.1151067**

**Abstract**

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| Introduction | Barotrauma developing spontaneously or associated with positive pressure ventilation is reported more frequently in patients with novel coronavirus 2019 (COVID-19). In this study, we aimed to determine the frequency of barotrauma in critically-ill patients with COVID-19 associated acute respiratory distress syndrome (ARDS) who received invasive mechanical ventilation (IMV), (non-invasive mechanical ventilation NIMV) or high flow nasal oxygen therapy (HFNO) and reveal clinical features, radiological findings and outcomes of these patients. |
| Materials and Methods | In this two-center study, the patients who followed up in the ICU due to COVID-19 were retrospectively investigated. Barotrauma findings were determined as pneumothorax, pneumomomediastinum, pneumopericardium and subcutaneous emphysema. |
| Results | Barotrauma was detected in 29 (4.4%) of 660 patients. Nineteen (65.5%) patients had pneumothorax, 5 (17.2%) patients had pneumomediastinum, 5 (17.2%) patients had subcutaneous emphysema; 18 (62.1%) patients underwent tube thoracostomy, 11 (37.9%) patients were followed conservatively. When barotrauma developed, 17 (58.6%) patients were receiving IMV, 11 (37.9%) patients were receiving NIMV, and 1 (3.4%) patient was receiving HFNO. The mean length of stay in the ICU was 15.3±10.8 days, 19 (65.5%) of the patients died. |
| Conclusion | Barotrauma is not uncommon in COVID-19 ARDS patients; It is a complication that can increase mortality and length of stay in ICU. |
| Keywords | COVID-19, ARDS, barotrauma, intensive care unit |

**Öz**

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| *Amaç* | *Spontan veya pozitif basınçlı ventilasyona bağlı gelişen barotravmanın Coronavirus 2019 (COVID-19) hastalarında diğer hastalara göre daha sık olduğu bildirilmiştir. Bu çalışmada yoğun bakım ünitesinde; invaziv mekanik ventilasyon (İMV), non-invaziv mekanik ventilasyon (NİMV) ya da yüksek akışlı nazal oksijen tedavisi (YANO) alan COVİD-19 ilişkili akut solunum distres sendromu (ARDS) hastalarında barotravma insidansının tespit edilmesi ve bu hastaların klinik, radyolojik özellikleri ve sonlanımlarının ortaya koyulması amaçlanmıştır.* |
| *Yöntem ve Gereçler* | *Bu iki merkezli çalışmada, yoğun bakım ünitesinde COVİD-19 ilişkili ARDS nedeniyle izlenen ve İMV, NİMV ve YANO tedavisi alan hastalar retrospektif olarak incelendi. Barotravma bulguları pnömotoraks, pnömomediastinum, pnömoperikardiyum ve subkütan amfizem olarak belirlendi.* |
| *Bulgular* | *Toplam 660 hastanın 29'unda (%4,4) barotravma tespit edildi. Barotavma izlenen hastaların 19'unda(%65,5) pnömotoraks, 5'inde (%17,2) pnömomediastinum ve 5'inde (%17,2) subkutan amfizem tespit edildi. Onsekiz (%62,1) hastaya tedavi amaçlı tüp torakostomi uygulanırken, 11 (%37,9) hasta konservatif olarak izlendi. Barotravma saptandığı anda 17 (%58,6) hasta İMV, 11 (%37,9) hasta NİMV ve 1 (%3,4) hasta YANO tedavisi almaktaydı. Barotravma izlenen 29 hastanın ortalama yoğun bakım yatış süresi 15,3±10,8 gün idi ve 19 (%65,5) hasta kaybedildi.* |
| *Sonuç* | *Barotravma, COVİD-19 ilişkili ARDS hastalarında nadir olmayan ve yoğun bakım yatış süresi ve mortaliteyi artırabilecek bir durum olarak tespit edildi.* |
| *Anahtar Kelimeler* | *COVİD-19, ARDS, barotravma, yoğun bakım* |

## INTRODUCTION

Physiologically, spontaneous breathing is negative pressure breathing whereas the patients on mechanical ventilation (MV) invasively or non-invasively are ventilated with positive pressure. Barotrauma is a common complication of positive pressure ventilation which is not physiological.[1] High transpulmonary pressure caused by invasive and noninvasive mechanical ventilation (IMV an NIMV) can lead extraalveolar air leakage where it is not normally found in patients receiving MV. Barotrauma which can also be a manifestation of ventilator induced lung injury (VILI) may result in severe conditions such as pneumothorax, pneumomediastinum, pneumopericardium and subcutaneous emphysema.[2] Barotrauma has not been observed commonly in patients with acute respiratory failure due to viral pneumonia. However; it has been reported to be frequent in patients with Coronavirus Disease 2019 (COVID-19) related acute respiratory distress syndrome (ARDS).[3-5] In COVID-19 associated ARDS patients who receive IMV; the incidence of barotrauma have found 17-33%.[6-7] Although the pathopysiological basis of susceptibility to barotrauma in COVID-19 patients still remains unclear; rupture of alveoli secondary to severe diffuse alveolar damage in those patients seems major underlying proposing pathophysiological mechanism. Because it has been shown that barotrauma develops in spontaneously breathing COVID 19 patients.[8]

In our study, we aimed to determine the frequency of barotrauma in critically-ill patients with COVID-19 associated ARDS who received IMV, NIMV or high flow nasal oxygen therapy (HFNO). We also aimed to reveal clinical features, radiological findings and results of these patients.

## MATERIALS and METHODS

### Patients selection and data collection

Patients who admitted to University of Health Sciences Kütahya Training and Research Hospital and Diskapi Yildirim Beyazit Training and Research Hospital COVID-19 intensive care units (ICUs) between 1st July 2020 – 15th January 2021 were retrospectively analysed. Patients who was tested positive for SARS-CoV-2 based on real-time reverse transcriptase polymerase chain reaction (RT-PCR) from a nasopharyngeal swab and had the diagnosis of ARDS were included in study. Clinical features, radiological findings and outcomes of patients who received IMV, NIMV or HFNO during ICU stay were recorded. To determine barotrauma; the signs of subcutaneous emphysema, pneumomediastinum, pneumothorax and pneumopericardium at chest computed tomography (CT) scans and X-ray graphies were observed. Patients' airway pressures ((plateau pressure (Pplat), peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP)) at the day of barotrauma, barotrauma signs and treatments were noted.

Patients' demographic data (age, gender), comorbidities, Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) score and partial pressure of arterial oxygen/fraction of inspired oxygen ratios (PaO2/FiO2) on ICU admission, presence and severity of ARDS defined by Berlin criteria[9] were recorded. Type L and type H phenotypes of COVID-19 associated ARDS for each patients were determined based on previous definition.[10] Lung protective MV and open lung strategy were performed in patients who received IMV. ARDSnet PEEP – FiO2 table[11] was applied for PEEP titration and transpulmonary pressure could not be measured due to lack of esophageal manometry. The follow up strategy to detect barotrauma in both centers was same. Daily chest X-ray scan was performed in patients who had severe ARDS and chest imaging was performed for all patients whose clinical condition detoriorated and airway pressures increased. Chest imagings were analysed by two experienced intensive care specialists in both of the centers.

Official permission was obtained from the Turkish Ministry of Health for this retrospective study (Number:2020_11_19T14_17_48) and Instutional Review

Board of our tertiary hospital was approved the study.

Statistical analysis was performed using SPSS Statistics (Version 17.0, SPSS Inc). The normal distribution of the data was tested using the Shapiro-Wilk test. Continuous variables were shown as mean±standard deviation or median (25th and 75th percentiles) depending on data distribution. Categorical variables are expressed as numbers (%). Level of statistical significance was considered as $p<0.05$.

## RESULTS

A total of 660 COVID-19 associated ARDS patients admitted to two ICUs during the study period. Among 660 patients; 175 (26.5%), 450 (68.1%), 35 (5.3%) were received IMV, both NIMV and HFNO, only HFNO respectively. Twenty nine (4.4%) patients had barotrauma (subcutaneous emphysema, pneumomediastinum, pneumothorax) signs at chest X-ray graphies (n=10) and chest computed tomography (CT) scans (n=19). Barotrauma frequency in our two centers were similar [4.8% (21/436) vs 3.6% (8/224); p=0.04]. The mean age of patients with barotrauma was 68.8±12.6 and 23 of 29 patients (79.3%) were male. Thirteen patients (44.8%) were ex-smoker, 10 (34.5) patients had a history of chronic obstructive pulmonary disease (COPD) and 5 (17.2%) patients had bullo or emphysema at chest CT scan on ICU admission. Mean APACHE II score and median SOFA score on admission were 19.1±6.6 and 4 [IQR= 3-10], respectively. On ICU admission, twenty three (79.3%) patients had severe ARDS, while 5 (17.2%) and 1 (3.4%) patients had moderate and mild ARDS, respectively. In terms of COVID-19 associated ARDS phenotypes, 8 (27.6%) patients had the signs of L type, whereas 21 (72.4%) patients had H type (Table). Subcutanous emphysema, pneumothorax, pneumomediastinum were observed in 5 (17.2%), 19 (65.5%), 5 (17.2%) patients, respectively. Four (13.8%) patients had both subcutanous emphysema and pneumothorax. Tube thoracostomy was performed in 18 (62.1%) patients, while 11 (37.9%) patients are treated conservatively. At the day of barotrauma; 17 (58.6%), 11 (37.9%) and 1 (3.4%) patients were receiving IMV, NIMV and HFNO respectively. In the patients who received IMV, mean PIP and Pplat at the day of barotrauma were 47.6±9.3 and 33.8±6.7 cmH2O and Pplat of 12 (70.6%) patients were higher than 30 cmH2O. Mean length of ICU stay in patients with barotrauma was 15.3±10.8 days and 19 (65.5%) patients deceased (Table).

**Table:** General Characteristics and Outcomes of Patients with Barotrauma

| **Characteristics** | **n=29 (%)** |
|---|---|
| Age (mean±SD) | 68.9±12.9 |
| **Gender** | |
| Male | 23 (79.3) |
| Female | 6 (20.7) |
| APACHE II (mean±SD) | 19.1±6.6 |
| SOFA (median [25-75]) | 4 [3-10] |
| **Smoking status** | |
| Ex-smoker | 13 (44.8) |
| None | 16 (55.2) |
| **Comorbidities** | |
| Coronary artery diseases | 13 (44.8) |
| Hypertension | 16 (55.2) |
| Diabetes mellitus | 12 (41.4) |
| Arrhythmia | 10 (34.5) |
| COPD/Asthma | 10 (34,5) |
| Chronic kidney disease | 2 (6.9) |
| **ARDS Type** | |
| L Type | 8 (27.6) |
| H Type | 21 (72.4) |
| ARDS Severity | |
| Mild | 1 (3.4) |
| Moderate | 5 (17.2) |
| Severe | 23 (79.2) |
| **Thoracic Computed Tomography Findings on ICU Admission** | |
| Bilateral involvement | 27 (93.1) |
| Bulla/emphysema | 5 (17.2) |
| **Barotrauma diagnosis with:** | |
| Chest X-ray | 19 (65.5) |
| **Barotrauma types** | |
| Pneumothorax | 19 (65.5) |
| Subcutaneous emphysema | 5 (17.2) |

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|---|---|
| Pneumomediastinum | 5 (17.2) |

| **Characteristics** | **n=29 (%)** |
|---|---|
| **Barotrauma treatment modalities** | |
| Chest tube | 15 (51.7) |
| Conservative medical follow-up | 9 (31.0) |
| Subcutaneous intraket placement | 5 (17.2) |
| **Respiratory support at the day of barotrauma** | |
| Non-invasive mechanical ventilation | 11 (37.9) |
| Invasive mechanical ventilation | 17 (58.6) |
| High-flow nasal oxygen therapy | 1 (3.4) |
| **Mechanical ventilation mode at the day of barotrauma (n=17)** | |
| Assiste/Control Ventilation (ACV) | 14 (48.3) |
| Synchronized Intermitant Mandatory Ventilation (SIMV) | 3 (10.3) |
| **Airway pressures at the day of barotrauma (n=17)** | |
| Plateau pressure (mean±SD)(cmH20) | 33.8±6.7 |
| Peak airway pressure (mean±SD)(cmH20) | 47.6±9.3 |
| PEEP (mean±SD)(cmH20) | 10±2 |
| **ICU Outcomes** | |
| Exitus | 14 (48.3) |
| Discharged to the ward | 15 (51.7) |
| Lenght of ICU Stay (mean±SD) (days) | 15.3±10.8 |
| SD:standard derivation, APACHE II:Acute Physiology and Chronic Health Evaluation, SOFA:Sequential Organ Failure Assessment, COPD: chronic obstructive pulmonary disease, ARDS:Acute Respiratory Distress Syndrome, ICU:intesive care unit, PEEP:positive end expiratory pressure | |

In figure 1a and 1b, pneumomediastinum and subcutanous emphysema at chest X ray graphies were shown in two patients who received NIMV and in figure 1c, pneumothorax was shown in a patient who were performed IMV. Subcutanous emphysema and pneumomediastinum were depicted in two patients' chest CT scans in figure 2a-2b.

## DISCUSSION

In our two-center study barotrauma frequency was 4.4%. Our study showed that NIMV and HFNO may create a predisposition to barotrauma in COVID-19 associated ARDS patients, as well as IMV. We also observed elevated Pplat in patients with barotrauma.

The determined barotrauma frequency in our large cohort of patients with COVID-19 associated ARDS was lower than reported previous studies.[3,4,12]

Barotrauma prevelance in critically-ill patients during SARS ve Middle East Respiratory Syndrome (MERS-CoV) epidemics were reported 12% and 34%, respectively.[13,14] The reported incidence of barotrauma in patients with COVID-19 varies between 1% to 40%, and there is uncertainty regarding its influence on mortality.[15-17] In our study barotrauma frequency was 4.4% and it may be associated with lower number of patients in the previous studies.

Pathophysiology of spontaneus barotrauma in ARDS have been attributed Macklin phenomenon.[5] Macklin MT and Macklin CC defined the pressure gradiant between alveoli and interstitium of lungs.[18] Released alveolar air from alveolar rupture centripetally dissects through the pulmonary interstitium along the bronchovascular sheaths toward the pulmonary hila and into the mediastinum and subcutanous space which has the lowest resistance.[19] When mediastinal pleura ruptures, pleural space fills with free air and results in pneumothorax. The clinical affects of these cases are ranged from asymptomatic illness to severe life-threatining conditions.[20] In a previous study by McGuinees et al.[12], researchers investigated barotrauma frequency in patients who underwent IMV and determined that barotrauma prevelance in COVID-19 patients was higher than those without COVID-19 (24% vs 1%, p<0.001). They observed barotrauma in 89 (15%) of 601 patients and reported barotrauma as an independent risk factor for mortality (Odds Ratio:2.2; p=0.03). Similar to our findings pneumothorax was the most common barotrauma sign. Relationship and underlying mechanism between COVID-19 and barotrauma are still remaining unclear. Radiological changes including airspace opacities, consolidations and reticulary pattern are common in COVID-19 cases.[21] However; cavitation, cyste formation and bullae during COVID-19 course have been oberved

by previous case reports.[22-24]

In our study, we observed barotrauma frequency %9.7 in the patients with COVID-19 associated ARDS who received IMV. In the previous McGuinees et al's study[12] which reported higher barotrauma frequency than our study, there was no data on patients' disease severity or airway pressures. Therefore, it is not applicable to compare results of these two studies. In another recent study investigators evaluated occurence of pneumomediastinum, pneumothorax and subcutanous emphysema during COVID-19 course. They reported that 11 of 1648 (0.7%) hospitalized patients had pneumomediastinum in the absence of MV and all patients were non-smokers without any risk factor for these complications and 8 of their 11 patients deceased.[25] These findings suggests there may be a link between these complications and COVID-19 associated lung infection.

Although the incidence of barotrauma in patients receiving NIMV is lower than patients receiving IMV, predisposing lung pathologies such as ARDS, COPD, asthma increased the risk of barotaruma during NIMV. In a previous study by Martinelli et al. analysed 62 hospitalized COVID-19 patients with pneumothorax and only 3 of patients (4.8%) were receiving NIMV at the day of pneumothorax.[15] In our study, 11 of 29 patients (37.9%) with barotrauma was receiving NIMV at the day of barotrauma. There may be some factors leading these different results. In our study we analysed our ICU patients while in Martinelli et al' study they investigated hospitalized patients not critically ill patients. Diagnosing barotrauma in ICU setting is more likely due to advanced monitorization and more common use of chest imaging. Moreover, ICU patients may be more prone to barotrauma because of their more severe respiratory failure and ARDS.

Our study is important, because there is limited data on COVID-19 and barotrauma in COVID-19 associated ARDS patients in ICU settings and our study has data of two different centers. On the other hand, our study has some limitations. Firstly, our study includes small number of patients with barotrauma. Secondly, we were not able to perform chest CT scan for all our patients who are suspected with barotrauma. Therefore frequency of barotrauma might be detected lower than it is. Finally, due to its retrospective nature temporal bias and data veracity are major concerns.

## CONCLUSION

Barotrauma is not an uncommon condition in patients with COVID-19 associated ARDS and it is a serious complication that can increase mortality and prolong length of stay in ICU.

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