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Pulmonary Barotrauma in COVID-19 Patients With ARDS on Invasive and Non-Invasive Positive Pressure Ventilation

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Abstract

Background: We experienced a high incidence of pulmonary barotrauma among patients with coronavirus disease-2019 (COVID-19) associated acute respiratory distress syndrome (ARDS) at our institution. In current study, we sought to evaluate the incidence, clinical outcomes, and characteristics of barotrauma among COVID-19 patients receiving invasive and non-invasive positive pressure ventilation. **Methodology:** This retrospective cohort study included adult patients diagnosed with COVID-19 pneumonia and requiring oxygen support or positive airway pressure for ARDS who presented to our tertiary-care center from March through November, 2020. **Results:** A total of 353 patients met our inclusion criteria, of which 232 patients who required heated high-flow nasal cannula, continuous or bilevel positive airway pressure were assigned to non-invasive group. The remaining 121 patients required invasive mechanical ventilation and were assigned to invasive group. Of the total 353 patients, 32 patients (65.6% males) with a mean age of 63 $\pm$ 11 years developed barotrauma in the form of subcutaneous emphysema, pneumothorax, or pneumomediastinum. The incidence of barotrauma was 4.74% (11/232) and 17.35% (21/121) in the non-invasive group and invasive group, respectively. The median length of hospital stay was 22 (15.7 −33.0) days with an overall mortality of 62.5% (n = 20). **Conclusions:** Patients with COVID-19 ARDS have a high incidence of barotrauma. Pulmonary barotrauma should be considered in patients with COVID-19 pneumonia who exhibit worsening of their respiratory disease as it is likely associated with a high mortality risk. Utilizing lung-protective ventilation strategies may reduce the risk of barotrauma.

Keywords

COVID-19, pulmonary barotrauma, mechanical ventilation, acute respiratory distress syndrome, pneumothorax, pneumomediastinum

Introduction

Barotrauma is the tissue damage occurring as a consequence of the pressure gradient between an unvented body cavity and the surrounding air/fluid interface or across a tissue-plane.[1] The manifestations of pulmonary barotrauma can range from subcutaneous emphysema (SE) to spontaneous pneumothorax (PTX) and pneumomediastinum (PM). Although uncommonly associated with viral pneumonia, a higher incidence of barotrauma associated with coronavirus disease-2019 (COVID-19) is being observed.[2-4] Based on currently available evidence, the incidence of barotrauma among COVID-19 patients requiring invasive mechanical ventilation ranges from 9%-32%.[5-9] In this study, we sought to investigate the incidence of barotrauma among COVID-19 patients requiring invasive and non-invasive positive pressure ventilation at our tertiary-care center and delineate their characteristics.

Methods

A retrospective chart review was conducted to elucidate the incidence of barotrauma and associated characteristics among patients with COVID-19 pneumonia and acute respiratory

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failure. In all the cases, a diagnosis of COVID-19 infection was confirmed with reverse transcriptase-polymerase chain reaction assays performed from the nasopharyngeal swab. We obtained medical records of adult patients with COVID-19 infection requiring oxygen support or positive airway pressure that were admitted to our institution between March and November 2020. A total of 1,073 records were screened, of which, 353 patients satisfied our pre-defined inclusion criteria and were evaluated for the occurrence of barotrauma on chest x-ray (CXR) or computed tomography (CT) scan. We searched for barotrauma using keywords—pneumothorax, subcutaneous emphysema, pneumopericardium, mediastinal emphysema, and pneumomediastinum in the patient charts. We used the following inclusion criteria: patients requiring non-invasive positive pressure ventilation (NIPPV) in the form of heated high-flow nasal cannula (HFNC) 15 to 70 L/min, continuous, or bilevel positive airway pressure were assigned to non-invasive group whereas patients receiving invasive mechanical ventilation (IMV) for respiratory failure secondary to COVID-19 pneumonia were assigned the invasive group. Patients who eventually required IMV were included in Invasive group regardless of the type of oxygen support received prior to intubation. We excluded patients requiring <15 L/min oxygen; on positive airway pressure for reasons other than respiratory failure such as sleep-apnea; intubated for trauma, surgery, or airway protection without COVID-19 pneumonia. Patients with traumatic or iatrogenic PTX, PM, and/or SE were not considered as barotrauma. The study was approved by the institutional review board and a full waiver of the informed consent was obtained. Access to the collected study data was only permitted to the study authors and was stored in a secure environment. Patients who met the criteria for barotrauma were studied in detail to collect information pertaining to their age, gender, body mass index (BMI), co-morbidities, smoking history, acute respiratory distress syndrome (ARDS) severity, ventilator, and NIPPV settings, intervention for barotrauma, mortality, and hospital length of stay (LOS). The patient characteristics were descriptively reported. All analyses were conducted in R (v4.0.2).

Table 1. Clinical Characteristics of Patients and Their Outcomes.[a]

Characteristic	Value
Age (years)	63 ± 11
Males—no. (%)	21 (65.6)
BMI—kg/m^2	30.7 ± 6.4
Co-morbidities (N = 32)	
• Hypertension—no. (%)	17 (53.1)
• Diabetes mellitus—no. (%)	13 (40.6)
• Congestive heart failure—no. (%)	1 (3.1)
• Coronary artery disease—no. (%)	6 (18.7)
• COPD—no. (%)	2 (6.2)
• Chronic kidney disease—no. (%)	3 (9.3)
• Smokers—no. (%)	8 (25)
CT evidence of emphysema/blebs/bullae/cysts—no. (%)	0 (0)
Type of Barotrauma (N = 32)	
• Subcutaneous emphysema—no. (%)	24 (75)
• Pneumomediastinum—no. (%)	21 (65.6)
• Pneumothorax—no. (%)	23 (71.8)
Location of Pneumothorax (N = 23)	
• Right—no. (%)	12 (52.2)
• Left—no. (%)	6 (26)
• Bilateral—no. (%)	5 (21.7)
Days from symptom onset to barotrauma	18.5 (14-24)
Days from hospital admission to barotrauma	11 (6-19)
Type of intervention used (N = 13)	
• Chest tube—no. (%)	12 (92.3)
• Blow holes—no. (%)	1 (7.7)
Type of ventilation prior to barotrauma (N = 32)	
• High-flow nasal canula—no. (%)	3 (9.3)
• CPAP/ BPAP—no. (%)	8 (25)
• Endotracheal intubation—no. (%)	21 (65.7)
Total length of stay (days)	22 (15.7-33.0)
Mortality (N = 20)	
• Non-invasive ventilation—no. (%)	16 (80)
• Invasive ventilation—no. (%)	4 (20)

Abbreviations: BMI, Basal Metabolic Index; COPD, chronic obstructive pulmonary disease; NIPPV, non-invasive positive pressure ventilation; CPAP, continuous positive airway pressure; BPAP, bilevel positive airway pressure; PEEP, positive end-expiratory pressure.

[a] The values are reported as numbers (%), mean ± SD, or median (interquartile range).

Results

A total of 353 patients met the inclusion criteria, of which 232 patients were allocated to the non-invasive group and 121 were allocated to the invasive group. In our study, there were 32 patients who developed at least one barotrauma event. The incidence of barotrauma was 4.74% (11/232) in the non-invasive group and 17.35% (21/121) in the invasive group. There were 68 barotrauma events observed in total. The most common type of barotrauma was SE (n = 24) followed by PTX (n = 23) and PM (n = 21). The mean age of our cohort was 63 ± 11 yrs with 65% patients being males (Table 1). The duration for the development of barotrauma was 18.5 (14-24) days from symptom onset and 11 (6-19) days from hospital admission. Interestingly, despite a high incidence of barotrauma, we did not observe CT-based evidence of emphysema, cysts, or bullae. The patients had a median hospital LOS of 22 (15.7-33.0) days with an overall mortality of 62.5% (n = 20).

Among patients in the invasive group, barotrauma occurred at 5 (3-8) days following intubation. The mean positive end-expiratory pressure (PEEP) was 16 cmH_2O and driving pressure, which is the difference between Plateau pressure (Pplat) and PEEP, was 15.3 cmH_2O as shown in Table 2. Among 34% (11/32) of patients who developed barotrauma in the non-invasive group, 3 patients received HFNC with peak flow rates between 40-70 L of oxygen/min, 4 patients were on CPAP with peak pressures between 10-14 cmH_2O, and 4 patients were on BPAP with peak inspiratory and expiratory pressures up to 12 and 6 cmH_2O, respectively.

Discussion

Barotrauma is a well-recognized complication of invasive mechanical ventilation (IMV).[10] Although barotrauma can occur in any patient receiving IMV, it is more frequently encountered in patients with ARDS.[10-12] The incidence of barotrauma in patients with ARDS on IMV varies from 4.8%-11%.[5,11-14] In our study, we found that the incidence of barotrauma among COVID-19 patients with ARDS requiring IMV was 17.35%. This closely resembles what previous studies on COVID-19 patients have reported (15%-40%) and is much higher than the reported values in patients with non-COVID-19 ARDS.[4,5,15] The incidence of barotrauma in patients on NIPPV in our study was 4.74%. We found that the literature on the incidence of barotrauma in COVID-19 patients with ARDS on NIPPV is scarce and mostly consists of individual case-based evidence.[16] Recently, a study published by Kahn et al reported this incidence to be 8% among their patient cohort.[9] Moreover, the risk of barotrauma on NIPPV, in general, is rare and the true incidence is unknown.[17] Although smoking is a known risk factor for barotrauma, only 25% of COVID-19 patients with barotrauma in our study were smokers.

Positive pressure ventilation is commonly utilized in the management of patients with ARDS, which improves oxygenation and survival.[18] The utilization of positive pressure predisposes an already diseased lung in ARDS to ventilator-associated lung injury (VALI). This can be in the form of macrobarotrauma (identified on imaging) and/or microbarotrauma, which is associated with diffuse lung injury and possibly the release of inflammatory mediators. Utilizing lung protective ventilation strategies such as low tidal volume (TV) of 4-8 ml/Kg ideal body weight, Pplat $\leq$30 cmH_2O, and a lower driving pressure (between 13 and 15 cmH_2O) is associated with reduced mortality in ARDS and has further shown to decrease VALI.[18-20] These strategies mitigate the alveolar overdistention and may limit the risk of barotrauma. However, in our study, around 40% of patients on IMV developed barotrauma despite an acceptable Pplat and driving pressure and all of our patients on IMV with barotrauma received a TV of <8 ml/Kg ideal body weight. Moreover, spontaneous PTX and PM in COVID-19 patients on room air has also been reported.[19-21] This raises a suspicion that barotrauma in COVID-19 is likely multifactorial.

Although less well understood, some reports suggest a perfusion-related compromise, disruption of pulmonary microvasculature secondary to thrombi, maladaptive immune response, and ischemic damage within the lung parenchyma in COVID-19 can predispose to diffuse alveolar damage and rupture.[5,16,22] Another concerning factor is patient self-inflicted lung injury (P-SILI), which can induce lung injury as a consequence of intense inspiratory efforts.[23,24] The idea has been backed-up by animal models that showed that high tidal volume generated by negative pressure ventilation resulted in pulmonary edema, in a manner similar to positive pressure ventilation.[25] In patients with ARDS and acute hypoxemic respiratory failure, respiratory drive is increased. The intense inspiratory efforts generated as a consequence predispose to lung injury due to uncontrolled swings in transpulmonary pressure, which, in turn, abnormally increases lung stress and causes inflation of big tidal volumes.[23] Alveolar rupture can lead to air-leak causing pulmonary interstitial emphysema, which can lead to PTX, PM, and SE.[16,26] This can be precipitated with an increase in intra-alveolar pressure due to any situation such as positive pressure ventilation, recruitment maneuver, coughing, or ventilator asynchrony.[15,20] Theoretically, disruption of type-II pneumocytes upon COVID-19 viral entry via ACE-2 receptors[27] may contribute to the development of pulmonary interstitial emphysema. This may also explain why hypertension and diabetes mellitus were the most common co-morbidities in our study among patients with barotrauma as the expression of ACE-2 receptors is increased in both hypertension and diabetes mellitus.[28] Barotrauma in COVID-19 is likely associated with a higher hospital LOS and mortality compared to those without barotrauma.[5,29] In a recent study, the total hospital LOS among COVID-19 patients with barotrauma was reported to be 25 (22-28) days, which was significantly greater ($P < 0.001$) than those without barotrauma with a mortality rate of 53%.[5] The authors also observed the median time from mechanical ventilation to barotrauma to be

Table 2. Clinical Characteristics of Patients Requiring Invasive Mechanical Ventilation.[a]

Characteristic	Value
Intubation to barotrauma among invasive ventilation group (days)	5 (3-8)
ARDS severity among invasive ventilation group (N = 21)	
• Mild—no. (%)	2 (9.5)
• Moderate—no. (%)	12 (57.1)
• Severe—no. (%)	7 (33.4)
Ventilatory settings prior to barotrauma event (N = 21)	
• Plateau pressure (cmH_2O)	29 (27-31)
• PEEP (cmH_2O)	16 (14-18)
• Driving pressure (cmH_2O)	15.3 ± 3.6
• Tidal volume per kg ideal body weight	6.18 ± 0.81
PEEP among invasive ventilation group (N = 21)	
• ≤ 10 cmH_2O	1 (4.7)
• 11-15 cmH_2O	5 (23.8)
• 16-20 cmH_2O	15 (71.4)
• >20 cmH_2O	0 (0)
Driving pressure among invasive ventilation group (N = 21)	
• <15 cmH_2O	9 (42.9)
• ≥ 15 cmH_2O	12 (57.1)

[a] The values are reported as numbers (%), mean ± SD, or median (interquartile range). For abbreviations, please refer to Table 1.

5.3 (0-25) days. Abdallat et al, similarly, reported this duration to be 3.5 (0-15) days.[29] Our findings, as well, lie in concordance to these previously reported values.

This study has certain noteworthy limitations such as its retrospective design and a relatively small sample size. Another limitation is the unavailability of a propensity-matched control group comprising non-COVID patients for across-group comparisons. Despite these, our study is one of the few studies that evaluates the incidence of barotrauma among COVID-19 patients over a follow-up period and adds valuable information to the medical literature. Patients with COVID-19 pneumonia may progress rapidly and develop worsening respiratory failure due to ARDS, which may make the identification of barotrauma challenging. Early imaging modalities such as CXR, CT scan, or lung ultrasound can assist in making a prompt diagnosis in such patients. The increased incidence of barotrauma during the COVID-19 pandemic also raises challenges in the management of PTX. There may be a higher risk of aerosolization of COVID-19 during the surgically placed thoracostomy tube. The percutaneous approach via Seldinger's technique using a guide-wire can be performed in lesser time and might help reduce the exposure to aerosolized COVID-19 virus. Around 38% of patients with barotrauma in our study received chest tubes, all of which were performed via the minimally invasive percutaneous approach.

Conclusion

Barotrauma in COVID-19 correlates with a worse prognosis and may be under-reported. We propose that further research is required as COVID-19 pneumonia may have a different underlying pathophysiology from typical pneumonia-induced ARDS predisposing patients to a higher risk of barotrauma. Pulmonary barotrauma should be considered in COVID-19 patients with worsening respiratory disease.

Authors' Note

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Declaration of Conflicting Interests

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