Case Report: Barotrauma in COVID-19 Case Series

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Abstract. Severe acute respiratory syndrome coronavirus 2 can cause pulmonary complications, such as increased risk of barotrauma (BT), but its prevalence and risk factors are not known. In this case series, the course of BT and its related risk factors were discussed in patients with COVID-19 who were admitted to the intensive care unit. Medical records of the patients with COVID-19 and BT and hospitalized in the intensive care unit for 5 months were extracted. The course of BT and its possible associated risk factors are descriptively presented. Among 103 patients with COVID-19 who were intubated, 13 patients (12.6%) had BT. One patient developed BT before intubation. All patients with BT were male. Half of them developed BT in the first 5 days of intubation. Eight patients (61.53%) had a positive culture for *Klebsiella pneumoniae*. Nine patients (69.9%) died. High positive end-expiratory pressure, coinfection with bacterial pneumonia, and history of lung disease may affect BT incidence. The treatment team should increase their upervision on the ventilator setting, especially in the first week of intubation.

INTRODUCTION

On March 11, 2020, the World Health Organization (WHO) declared the novel coronavirus, namely severe acute respiratory syndrome coronavirus 2 disease, as a pandemic and global health emergency.¹ The disease rapidly spread worldwide, causing more than 16 million infections and more than 600,000 reported deaths by July 31, 2020.² This disease has very different manifestations at hospital admission, including fever, cough, and dyspnea. Abdominal pain, myalgia, diarrhea, sore throat, fatigue, and loss of smell are other possible symptoms.³ A positive polymerase chain reaction test for the virus on samples from nasopharyngeal swabs is a definitive diagnostic test for COVID-19. This test has high specificity but results in false negatives in some cases.⁴

About 15% of patients with COVID-19 infection develop moderate to severe forms that require hospitalization and respiratory support, and about 5% require intensive care unit (ICU) care and supportive treatments, such as intubation and ventilation.^{4,5} The most common complication in patients with COVID-19 is pneumonia, but other complications may also occur, such as acute respiratory distress syndrome (ARDS), sepsis, septic shock, and multiple organ failure.⁶ The WHO guidelines recommend immediate use of mechanical ventilation in patients with hypoxia, hypercapnia, respiratory fatigue, and disturbed level of consciousness.⁶ Different lung-protective strategies have been expressed in the ventilator settings of ARSD patients to reduce the mortality rate. Mechanical ventilation also has many complications, such as barotrauma (BT), which can increase mortality. High positive end-expiratory pressure (PEEP) with overdistention of the alveoli can lead to alveolar rupture and cause BT.7 Barotrauma has many different presentations, including pneumothorax, subcutaneous emphysema, pneumoperitoneum, pneumomediastinum or pneumopericardium, air embolization, tension lung cysts, and hyperinflated left lower lobe.⁸

In this case series, we investigated patients with COVID-19 infection who were facing one of the complications of BT (e.g., pneumothorax, pneumomediastinum, or subcutaneous emphysema) during hospitalization with or without intubation.

The predisposing factors, side effects, and mortality rates were discussed.

METHODS

This retrospective case series was performed at Khorshid Hospital in Isfahan, Iran. This hospital is one of the most important centers for the treatment of patients with COVID-19 in Iran. Patients who were admitted to the ICU from February 22, 2020 to July 5, 2020 and who had evidence of BT were included in the study. This evidence was corroborated by a chest X-ray or computed tomography (CT) scan. The COVID-19 diagnoses of all the patients in the study were confirmed by reverse-transcription polymerase chain reaction on specimens from nasopharyngeal swabs. Intubated patients were treated with the volume mode of ventilator following the ARDS guideline network.^{9,10} In our setting, treatment of the patients included conservative and corticosteroid therapy (based on inflammatory factors and the patient's general condition), and no specific antiviral therapy was used. Demographic characteristics, laboratory tests, respiratory conditions, mechanical ventilator settings, and disease progression and outcomes were extracted from the medical the files of the patients.

RESULTS

During the 5 months since the outbreak of the coronavirus and the hospitalization of 2,154 patients at Khorshid Hospital, 256 patients (11.9%) were admitted to the ICU; of them, 103 patients (40%) were intubated. Thirteen patients (12.6%) developed BT (one patient was intubated after BT). All patients were male. Some characteristics of the patients are presented in Table 1. Mean age was 57.9 ± 16.7 years in the BT group and 69.3 ± 15.2 years in the other intubated patients. Four patients in the BT group (31%) and 10 patients (11%) in the non-BT group had chronic lung disease. Lactate dehydrogenase levels were 946 \pm 733 µ/L in the non-BT group was and 1.027 \pm 354 µ/L in the BT group. Klebsiella pneumonia was grown in the endotracheal tube culture of eight patients (61.53%). In the endotracheal tube culture of other patients, Acinetobacter baumannii and Staphylococcus aureus were grown. The mean duration of hospital stay was 27.3 ± 8.2 days in patients with BT and 13.7 ± 8.2 days in other intubated patients.

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TABLE 1 Demographic findings of patients who experience barotrauma

Demographics	Values
Age (mean ± SD)	57.9 ± 16.72
Sex, N (%)	
Male	13 (100)
Female	0 (0)
Comorbid condition, N (%)	
Obesity	2 (15.38)
Overweight	8 (61.53)
DM	3 (23.07)
HTN	2 (15.38)
Chronic lung disease	3 (23.07)
CKD	1 (7.69)
IHD	1 (7.69)
Cancer	1 (7.69)

CKD = chronic kidney disease; DM = diabetes mellitus; HTN = hypertension; IHD = ischemic heart disease

All the patients had the ARDS criteria, including sudden onset of symptoms within 7 days, bilateral alveolar infiltration, severe progressive hypoxemia in the absence of cardiogenic pulmonary edema symptoms, and a PaO₂/FiO₂ ratio of < 300. Based on the severity classification of ARDS, one patient had mild ARDS, four patients (30.76%) had moderate ARDS, and eight patients (61.53%) had severe ARDS. Based on the types of BT, eight patients (61.53%) developed subcutaneous emphysema, and four patients (30.76%) developed multiple type involvement (Table 2). One patient developed pneumothorax before intubation. In intubated patients on the day of BT onset, nine patients (75%) had a PEEP between 5 and 10 cm H₂O, and three patients (25%) had a PEEP > 10 cm H_2O . Details of the severity of ARDS and PEEP are shown in Table 2.

In BT patients, the average time between hospitalization and intubation was about 8.2 days, the average time between intubation and BT was about 5.6 days, and the average time between BT to death was about 8.1 days (Table 3). Four patients (30.7%) were discharged, and nine patients died (69.9%). Details of the type of BT and the time of its occurrence are shown in Figure 1.

DISCUSSION

Barotrauma caused by mechanical ventilation is a potentially fatal complication reported in 15% of intubated patients.^{11,12} It is more common in patients with an underlying lung disease, such as chronic obstructive pulmonary disease or ARDS.¹³ The knowledge of the complications of the COVID-19 disease has been increasing over the past year. In COVID-19 patients with severe involvement of the lung parenchyma, pulmonary compliance is reduced due to pathological changes such as edema, vascular congestion, and inflammation.¹⁴ As a result, it is possible that overinflation and high PEEP in such hypoplastic and fibrotic lungs can lead to alveolar rupture and BT.¹⁵ We show the barotrauma event on a CT scan of one patient in Figure 2.

In the present study, 12.6% of the developed BT. Reports on the prevalence of BT in COVID-19 patients have been reported differently. McGuinness et al.¹⁶ compared the prevalence of BT in intubated COVID-19 patients and those with ARDS for other reasons. They reported that the prevalence of BT was 15% in patients with COVID-19 and 10% in other patients, and this complication was more common in young people with COVID-19. In a systematic study, Salehi et al.¹⁷ evaluated CT scans from 3,647 patients with COVID-19, which were published in 37 papers. In this study, pneumothorax was described as an atypical finding in COVID-19 patients, with a low prevalence in CT scan findings. During the past year, cases of BT in COVID-19 patients have been reported in various forms (pneumothorax, pneumomediastinum, and subcutaneous emphysema). Some cases that have attracted the attention of researchers are BT as the first presentation of COVID-19 in the inflammatory phase,¹⁸ BT in COVID patients without noninvasive or invasive mechanical ventilation,¹⁹ and BT in patients without underlying lung disease.²⁰ Because in some reports BT increased mortality in intubated patients,^{20,21} the authors recommend early imaging to diagnose and treat the complications of COVID-19 pneumonia, such as pneumothorax and subcutaneous emphysema.22

All the patients with BT in this study were male. Several reports have shown that more men are infected with COVID-19 than women.^{23,24} More mortality and morbidity have also been reported in men.^{25,26} Similar to the present results, in another case series of BT in COVID-19, the prevalence of BT was higher in men.^{11,27} Bwire et al.²⁸ explained the biological differences in the immune system between men and women and stated that women are more resistant to COVID-19 infection than men due to different sex hormones and the higher expression of coronavirus receptors (angiotensin converting enzyme 2) in men. Tracheal culture revealed Klebsiella pneumonia in 61% of patients and Acinetobacter baumannii in 15% of patients. Bacterial pneumonia superimposed on COVID-19 may predispose patients to BT. Diaz et al.¹² reported that Pneumocystis jiroveci pneumonia is one of the risk factors for BT.

Only one of the patients had BT without mechanical ventilation. Although most studies have reported BT in mechanically ventilated patients, like other viral pneumonia, pneumothorax has been reported in nonintubated COVID-19 patients.^{18,19,27}

Severity of ARDS and barotraumas finding and associated PEEP									
Patient characteristics	N (%)	Subcutaneous emphysema	Pneumothorax	Pneumomediastinum ± pneumothorax ± subcutaneous emphysema*	Subcutaneous emphysema + pneumothorax				
ARDS severity									
Mild	1 (7.69)	0	0	0	1				
Moderate	4 (30.76)	4	0	0	0				
Severe	8 (61.53)	4	1	2	1				
PEEP	,								
5–10	9 (75)	7	1	1	0				
> 10	3 (25)	1	0	1	1				

TABLE 2

ARDS = acute respiratory distress syndrome; PEEP = positive end expiratory pressure.

One patient developed pneumothorax before intubation.

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TABLE 3 nterval (as days) between admission, mechanical ventilation, and barotrauma/death

	Days				
Patient data	0–5	5–10	10–15	>15	
Admission to mechanical ventilation					
N (%)	3 (23.07)	6 (46.15)	3 (23.07)	1 (7.69)	
Mean (range)		8.23	(0–16)	· · ·	
Mechanical ventilation to Barotraumas					
N (%)	6 (50)	4 (33.33)	1 (8.33)	1 (8.33)	
Mean (range)		5.6 (D–18)	· · · ·	
Barotraumas to death					
N (%)	3 (33.33)	2 (22.22)	3 (33.33)	1 (11.11)	
Mean (range)		, í í 8.1 (⁻	1–23)	,	
Barotraumas to discharge					
N (%)	0	0	0	4 (33.3)	
Mean (range)	24 (15–32)				

Udi et al.¹¹ compared ventilator settings in patients with and without BT. They reported that there may not be a direct association between BT and mechanical parameters of the ventilator. Although higher airway pressures in mechanical ventilation are expected to be associated with a higher risk of BT, and some studies have reported this,²⁹ in most studies, similar to the present study, this association has not been found.^{30,31} It seems that other factors, such as pulmonary compliance, the severity of pneumonitis, patient respiratory effort, coinfection, etc., affect this complication.

In our patients, BT occurred most often (50%) in the first 5 days. Abdallat et al.³² reported that the median time between intubation and BT was 3.5 days, and in the case series by

Lassence et al.³³ it was 4 days. Therefore, it is recommended that more attention be paid to this complication at this time.

CONCLUSION

In this article, BT was investigated as a less-reported complication of COVID-19 infection. It seems that middleaged men are more susceptible to this complication, especially in the first 5 days after intubation. According to the present findings, a high PEEP in mechanical ventilation, coinfection with bacterial pneumonia, and a history of chronic lung disease may have considerable effects on BT incidence. This complication leads to longer hospital stays for patients,



FIGURE 1. Type of barotrauma and the interval of its occurrence of it in each patient. This figure appears in color at www.ajtmh.org.



FIGURE 2. Barotruma events. The patients is a 68-year-old man with history of diabetes who developed bilateral pneumothorax, pneumomediastinum, and subcutaneous emphysema.

but it does not necessarily increase mortality. It is recommended that low pressure be used to adjust the ventilator, the ventilator be adjusted on a daily basis according to the patient's condition, and examination for subcutaneous emphysema be performed, especially in the first week of intubation.

Limitation. Because this is a retrospective study and CT scans were not performed on all the intubated patients, mild cases of BT were not diagnosed. The present data are related to overt BT. This is a case series and the demographic data, characteristics, and outcomes of the two groups could not be compared.

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REFERENCES

 Salzberger B, Glück T, Ehrenstein B, 2020.Successful containment of COVID-19: the WHO-Report on the COVID-19 outbreak in China. New York, NY: Springer.

- Roser M, Ritchie H, Ortiz-Ospina E, Hasell J, 2020.Coronavirus disease (COVID-19)–Statistics and research. *Our World in Data* (In press).
- Stokes EK et al., 2020. Coronavirus disease 2019 case surveillance— United States, January 22–May 30, 2020. Morbidity and Mortality Weekly Report 69: 759.
- Richardson S et al., 2020. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 323: 2052–2059.
- Wang D et al., 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 323: 1061–1069.
- WHO, 2020. Clinical Management of Severe Acute Respiratory Infection (SARI) when COVID-19 Disease is Suspected: Interim Guidance, 13 March 2020. Geneva, Switzerland: World Health Organization.
- Brower R et al., 2004. National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. Higher versus lower positive endexpiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med 351: 327–336.
- 8. Ioannidis G et al., 2015. Barotrauma and pneumothorax. *J Thorac Dis 7 (Suppl 1):* S38.
- 9. Ferrando C et al., 2020. Clinical features, ventilatory management, and outcome of ARDS caused by COVID-19 are similar to other causes of ARDS. *Intensive Care Med* 46: 2200–2211.
- Raoof S, Nava S, Carpati C, Hill NS, How I, 2020. Do it: high flow, non-invasive ventilation and awake (non-intubation) proning in COVID-19 patients with respiratory failure. *Chest* 158: 1992–2002.
- Udi J et al., 2021. Incidence of barotrauma in patients with COVID-19 pneumonia during prolonged invasive mechanical ventilation–a case-control study. *J Intensive Care Med 36:* 477–483.
- 12. Diaz R, Heller D, 2020. *Barotrauma and Mechanical Ventilation.* Treasure Island, FL: Stat-Pearls Publishing.
- Sassoon CS, Light RW, O'Hara VS, Moritz TE, 1992. latrogenic pneumothorax: etiology and morbidity. *Respiration.* 59: 215–220.
- Alhazzani W, Møller M, Arabi Y, Loeb M, Gong M, Fan E, Du B, 2020. Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Intensive Care Med* 1–34.
- Aiolfi A et al., 2020. Management of persistent pneumothorax with thoracoscopy and blebs resection in COVID-19 patients. *Ann Thorac Surg 110:* e413–e415.
- McGuinness G et al., 2020. Increased incidence of barotrauma in patients with COVID-19 on invasive mechanical ventilation. *Radiology* 297: E252–E262.
- Salehi S, Åbedi A, Balakrishnan S, Gholamrezanezhad A, 2020. Coronavirus disease 2019 (COVID-19) imaging reporting and data system (COVID-RADS) and common lexicon: a proposal based on the imaging data of 37 studies. *Eur Radiol 30:* 4930–4942.
- Ucpinar BA, Sahin C, Yanc U, 2020. Spontaneous pneumothorax and subcutaneous emphysema in COVID-19 patient: case report. J Infect Public Health 13: 887–889.
- Wang W, Gao R, Zheng Y, Jiang L, 2020.COVID-19 with spontaneous pneumothorax, pneumomediastinum and subcutaneous emphysema. J Travel Med 27: taaa062.
- Aydın S, Öz G, Dumanlı A, Balcı A, Gencer A. 2020. A case of spontaneous pneumothorax in COVID-19 pneumonia. J Surg Res 3: 96–101.
- Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G, 2020. Real estimates of mortality following COVID-19 infection. *Lancet Infect Dis* 20: 773.
- Sun R, Liu H, Wang X, 2020. Mediastinal emphysema, giant bulla, and pneumothorax developed during the course of COVID-19 pneumonia. *Korean J Radiol 21*: 541.
- Martinelli AW et al., 2020. COVID-19 and pneumothorax: a multicentre retrospective case series. *Eur Respir J* 56: 2002697.
- Conti P, Younes A, 2020. Coronavirus COV-19/SARS-CoV-2 affects women less than men: clinical response to viral infection. *J Biol Regul Homeost Agents* 34: 339–343.

- Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN, 2020. Cardiovascular disease, drug therapy, and mortality in COVID-19. *N Engl J Med 382:* e102.
- Sami R et al., 2020. A one-year hospital-based prospective COVID-19 open-cohort in the eastern Mediterranean region: the Khorshid COVID Cohort (KCC) study. *medRxiv*.
- Vega JML, Gordo MLP, Tascón AD, Vélez SO, 2020. Pneumomediastinum and spontaneous pneumothorax as an extrapulmonary complication of COVID-19 disease. *Emerg Radiol* (In press).
- 28. Bwire GM, 2020. Coronavirus: why men are more vulnerable to COVID-19 than women? *SN Compr Clin Med* 1–4.
- Eisner M, Thompson B, Schoenfeld D, Anzueto A, Matthay M, 2002. Acute Respiratory Distress Syndrome Network. Airway pressures and early barotrauma in patients with acute lung

injury and acute respiratory distress syndrome. *Am J Respir Crit Care Med* 165: 978–982.

- Weg JG et al., 1998. The relation of pneumothorax and other air leaks to mortality in the acute respiratory distress syndrome. *N Engl J Med 338*: 341–346.
- Anzueto A et al., 2004. Incidence, risk factors and outcome of barotrauma in mechanically ventilated patients. *Intensive Care Med* 30: 612–619.
- Abdallat M, Khalil M, Al-Awwa G, Kothuru R, La Punzina C, 2020. Barotrauma in COVID-19 patients. *Journal of Lung Health and Diseases 4*.
- de Lassence A et al., 2006. Pneumothorax in the intensive care unit: incidence, risk factors, and outcome. *Anesthesiology 104:* 5–13.