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Case Series

Understanding air leak in COVID-19 patients: case series

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ABSTRACT

Around one fifth of COVID-19 patients progress to develop acute respiratory distress syndrome. This cohort carries the highest morbidity and mortality, and the greatest treatment challenges. They are more likely to require mechanical ventilation. Thoracic air leak has been noted to be more prevalent in this group of patients. This study aims to explore the relationship between ventilator settings and the development of air leak as possible triggers, and the basic pathophysiological concepts behind its development, as well as preventive strategies. In this case series the data of all patients admitted with COVID-19 pneumonia to Khoula hospital intensive care unit (ICU) during the period from March 1st, 2020 to July 31st, 2021 were collected retrospectively and analyzed. Fourteen patients representing 7.1% out of the 196 ICU admissions had demonstrated one or more air leak manifestation. Male to female incidence was 3:1 and the mean age was 53 years. The 71.4% of these patients had received mechanical ventilation, 14.3% of them received continuous positive airway pressure (CPAP), and 14.3% just received oxygen supplementation via plain face mask. The average ventilation to air leak development time is around 7.6 days (95% CI: 1.9-13.4%). In conclusion, although the majority of the patients who had air leak were mechanically ventilated, the condition can develop in non-ventilated and even spontaneously breathing COVID-19 patients, and no specific ventilator measure could be blamed for its development. Lung-protective ventilation strategies and accurate timing for escalation of respiratory support are the mainstay for prevention.

Keywords: Air leak, Ventilation, COVID-19, Complications, Pneumothorax, Pneumomediastinum

INTRODUCTION

COVID-19 is the disease caused by a new coronavirus called SARS-CoV-2. WHO first learned of this new virus on 31 December 2019, following a report of a cluster of cases of 'viral pneumonia' in Wuhan, People's Republic of China. The disease symptomatology involves a wide range of symptoms, the commonest of which are fever, dry cough, and fatigue. Severe disease causes shortness of breath that may result in hypoxemia and might require oxygen supplementation or assisted ventilation.

During this COVID-19 era and the associated surge in assisted ventilation, whether invasive or non-invasive, large number of cases were reported having thoracic air leak syndrome.[1]

Air leak syndrome is a clinical phenomenon that occurs when air leaks from a normally air-containing space into a space that does not normally contain air. This results in compression of some distensible organs interfering with their normal physiological functions and giving rise to respiratory distress or hemodynamic instability which may be life-threatening. It can involve the thoracic and peritoneal spaces. The thoracic air leak syndrome includes interstitial/ subcutaneous emphysema, pneumothorax, and pneumomediastinum. This phenomenon is linked to multiple etiological factors but

no reasonable connection could be affirmed to mechanical ventilation as a stand-alone causative etiology.[1]

In this case series we, retrospectively, analyzed the ventilator parameters of COVID-19 patients admitted to the intensive care unit and developed thoracic air leak during the period from March 2020 to July 2021.

The aim of this case series is to explain our understanding of the pathophysiological mechanism behind the air leak in COVID-19 patients and the suggested ventilation strategy to prevent, or minimize, its development.

CASE SERIES

Case 1

A male, 25 years old, with no significant past medical history was admitted with history of fever and shortness of breath for 3 days secondary to COVID pneumonia. His initial oxygen saturation was 85%. Following a brief trial of oxygen supplementation via a face mask he was intubated and ventilated when his oxygen saturation dropped to 80%. Two days following initiation of mechanical ventilation a routine follow up chest Xray revealed mild to moderate subcutaneous emphysema. Conservative approach was followed and later follow up did not show any increase in the emphysema. Five days later he went into sudden bradycardia and could not be revived.

Case 2

Male aged 79 years old with a past medical history significant for hypertension, ischemic heart disease and hypercholesterolemia transferred from the field hospital intubated and ventilated due to COVID pneumonia. On the twenty third's day after intubation developed a left side pneumothorax. He was managed by intercostal tube drainage that was removed 2 days after extubation.

Case 3

Male, 65 years old, known diabetic, hypertensive with ischemic heart disease, developed unilateral left side pneumothorax 15 days after intubation and initiation of mechanical ventilation for severe COVID pneumonia. Intercostal tube drainage was introduced however, the patient died 13 days later secondary to renal and circulatory failure.

Case 4

Female, 74 years old, with history of hypertension and depression developed a combination of pneumothorax, pneumomediastinum, and subcutaneous emphysema one day after intubation and initiation of mechanical ventilation due to COVID pneumonia. Bilateral intercostal drainage tubes were inserted immediately. Follow up image showed resolution of the air leak but the patient died one week later.

Case 5

Fifty-five years old male with COVID pneumonia and no significant past medical history developed the combination of pneumothorax, pneumomediastinum and subcutaneous emphysema one day after intubation and mechanical ventilation. Managed with intercostal tube drainage but failed to pick up saturation despite 100% FiO_2, died one day later.

Case 6

Female, 71 years old, known to have hypertension, diabetes mellitus, hyperlipidemia, and gout, admitted with shortness of breath and low oxygen saturation due to COVID pneumonia. Managed with CPAP. Three days later she developed unilateral pneumothorax and pneumomediastinum and underwent intercostal tube drainage. Next day she went into sudden cardiac arrest and could not be revived.

Case 7

Diabetic and hypertensive 48 years old male patient positive for COVID infection developed subcutaneous emphysema 12 days after intubation and mechanical ventilation. He was managed conservatively and the emphysema resolved in 4 days. Unfortunately, the patient died 28 days later suffering multiorgan failure.

Case 8

Male, 49 years old, with no significant past medical history, COVID positive status, developed unilateral pneumothorax 5 days post intubation which required an intercostal tube drainage. The patient required inotropic support and had expired 13 days after intubation.

Case 9

Female, 40 years old, with past history significant for diabetes mellitus and bronchial asthma, admitted in her third week post-partum with severe COVID pneumonia. She required intubation and ventilation however, twenty-three days after intubation she developed a unilateral pneumothorax necessitating an intercostal tube drainage. She had improved gradually and successfully extubated 2 weeks later.

Case 10

A male of 44 years age and no comorbidities was admitted for relatively low oxygen saturation (92%) secondary to severe COVID pneumonia. He was maintained on CPAP. Four days later his follow up chest Xray was significant for a unilateral pneumothorax that

required an intercostal tube drainage. He died 5 days later due to massive pulmonary embolus.

Case 11

Male, 43 years old, with no significant past medical history admitted for shortness of breath and low oxygen saturation secondary to COVD pneumonia. He developed bilateral pneumothorax one day after intubated and ventilation. Intercostal tube drainage performed but the patient went into severe bradycardia and could not be revived.

Case 12

Forty-three years old male patient admitted with shortness of breath, low oxygen saturation (90%), and cough secondary to COVID infection. He was managed with oxygen support via face mask. The next day a chest Xray revealed subcutaneous emphysema which was treated expectantly. The emphysema resolved within the next 3 days and patient was ultimately discharged home.

Case 13

Male, 34 years old, with no known comorbidities, admitted with COVID pneumonia. He was maintaining 97% saturation on room air so only low flow oxygen supplementation was offered through face mask. After 3 days he developed a unilateral pneumothorax and intercostal drainage tube was inserted. Two days later his condition deteriorated and was intubated and ventilated but did not survive more than 1 day.

Case 14

A male, aged 54 years, known diabetic and hypertensive was admitted with severe COVID pneumonia. As the oxygen saturation was very low (80%) he was intubated and ventilated.

The next day, a follow up chest Xray revealed pneumomediastinum and subcutaneous emphysema which were approached conservatively. The patient progressed well to extubation and home discharge.

Table 1: Clinical data of mechanically-ventilated patients who develop air leak.

Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Initial SpO_2%	80	95	95	95	82	94	93	92	80	85
FiO_2%	95	40	80	80	100	65	80	45	100	100
PEEP	15	8	12	8	8	6	5	6	7	8
Tidal volume	300	480	400	290	350	450	280	400	410	500
Peak pressure	16	20	28	36	25	20	38	24	28	34
Plateau pressure	38	20	25	35	22	18	36	23	26	32
Ventilation mode	P SIMV	APV/ SIMV	P SIMV	P SIMV	APV/SIMV	P SIMV	P SIMV	P SIMV	P SIMV	P SIMV
Air leak type	SE	PNX	PNX, PMS, SE	PNX, PMS, SE	PNX, PMS, SE	SE	PNX	PNX	PNX	SE, PMS
Vent. days before air leak develop	2	23	15	1	1	12	5	30	1	1
Management of air leak	Cons-ervative	ICD	ICD	ICD	ICD	Cons-ervative	ICD	ICD	ICD	Cons-ervative
Outcome	Died	Resolved	Died	Died	Died	Died	Died	Resolved	Died	Resolved

SE: subcutaneous emphysema, PNX: pneumothorax, PMS: penumomediastinum, ICD: intercostal drainage.

DISCUSSION

The COVID-19 pandemic presented the world to a puzzling lethal illness. Albeit the causative organism was recognized at an earlier stage of the pandemic, the disease symptomatology and pathophysiology remained obscure for a considerable time. This had reflected as chaotic treatment strategies. The medical community was very eager to any lighting at the end of the tunnel during the initial stages of the pandemic. Therefore, earlier scientific papers published about the disease were met with unprecedented welcome. With time; a better understanding of the disease developed and more scientifically-relevant preventive and therapeutic strategies emerged. The discovery and roll over of vaccines was the game-changer which is currently bringing the disease under partial control but complete control still remains a target to be achieved.

The greatest treatment challenges were specially encountered in managing patients with severe disease and adult respiratory distress syndrome who require multi-organ support in an intensive care unit as this cohort carries the highest risks of morbidity and mortality.[2] The

mechanical ventilation strategies and maneuvers; being a corner stone in the management of these cases; are critical.

Some conditions complicate the ventilation of COVID-19 patients. Air leak is a major complication of mechanical ventilation.[2] High-pressure settings cause air spill into the perivascular interstitium consequently altering the critical pressure gradient between the alveoli and the interstitial space prompting alveolus burst and escape of air into mediastinal, pericardial and pleural cavities. The resultant disturbance of the trans-pulmonary pressure causes diminished lung volume and reduced airflow which jeopardizes effective oxygenation and gas exchange along with carbon dioxide retention.[3] The incidence of air leak manifestations in COVID patients was estimated as 1%; which increases to 15% in mechanically ventilated patients.[4] In our series the incidence in mechanically ventilated patients was 5%. This may be attributed to the lung-protective ventilation strategies being used. None of the ventilator parameters was shown in multiple regression analysis to be related to the development of this complication in this group of patients (Figure 1).

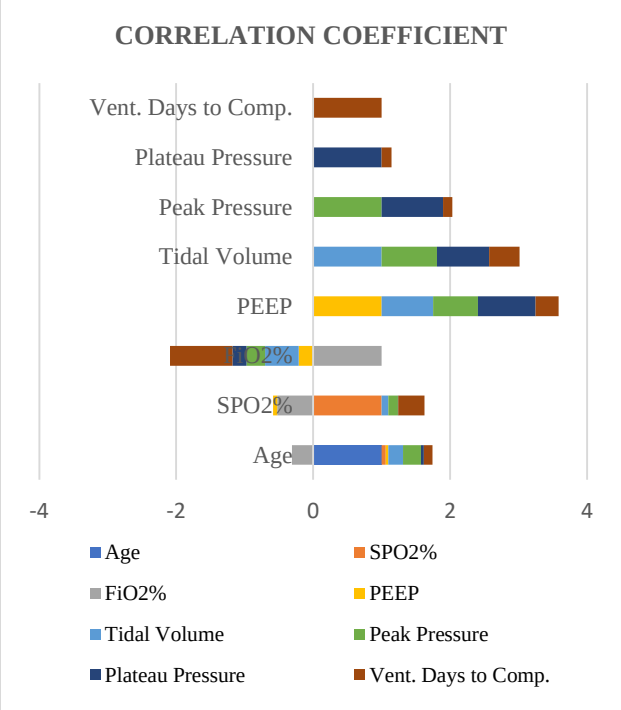

Figure 1: The correlation coefficient between the ventilator parameters and the development of air leak.

Around 20% of COVID 19 disease patients develop a clinical picture of acute respiratory distress syndrome (ARDS) which account for most of the morbidity and mortality.[5] The acute respiratory distress syndrome (ARDS) is a syndrome of non-hydrostatic pulmonary edema and hypoxemia with high morbidity and mortality: was originally described in 1967 by the Ashbaugh, Thomas L. Petty and coworkers.[6] Etiology is variable including sepsis, pneumonia, trauma, and others. The best early description of the pathological characteristics of ARDS was given by Bachofen and Weibel in 1977.[7] They divided it into acute, subacute and chronic phases corresponding to a time scale of 1-6 days, 7-14 days, and >14 days; respectively. The acute phase is characterized by interstitial and alveolar edema while the consequent phases comprise attempts of repair with fibroblasts infiltration and collagen deposition resulting in varying degrees of fibrosis.

The pathogenesis of the protein-rich edema is believed to involve epithelial and endothelial lung injury, neutrophils, monocytes, pro-inflammatory markers, and pro-coagulant factors.[7]

The most important therapeutic intervention for ARDS is mechanical ventilation (MV). However, standard MV has been linked to worsening of the acute lung injury and ARDS. The first evidence for this came from Brazil in 1998 in the study published by Amato & colleagues and was confirmed by the multicenter National Heart, Lung and Blood Institute–supported ARDS Network clinical trial in 2000.[8,9] This work had established the basis for the lung protective ventilation strategies.

Currently, the lung protective ventilation is recommended as the treatment of choice for ARDS. It comprises of a tidal volume of 4-8 ml/kg of predicted body weight and to maintain plateau pressure of <30 cm H_2O, with permissive hypercapnia.[10]

It was proposed that early COVID-19 is characterized by low elastance, recruitability and increased dead space, which progress later to a phenotype of greater elastance and recruitability comparable to the classic ARDS as the disease worsens, and may end in irreversible lung fibrosis in more severe cases.[5] It is worth noting that 10 out of the 14 patients who develop air leak manifestations in our setting had ultimately died which gives an indication of their COVID-19 disease severity.

The fibrotic lung is unique in extracellular matrix composition heterogeneity even between different regions in the same lung.[11,12] This is also true in lung fibrosis induced by severe COVID-19 infection.[13,14] The resultant differences in elasticity and distensibility between various parts of the lung causes what resembles a “Squishy ball” appearance.[11] Barotrauma may end in air leak secondary to over distension of some parts that exceeds the elasticity limits. Bronchopleural fistula may also develop manifesting as continuous air leak despite drainage of pleural cavity.[14] The lung-protective ventilation strategy may be fundamental in preventing this incidence. This also applies to recovered COVID-19 patients undergoing surgical procedure requiring general anesthesia in the early post infection period.[15]

Air leak had also occurred in COVID 19 patients who did not receive mechanical ventilation. We are reporting four

such cases in this series. Two of these patients had received non-invasive ventilation in the form of continuous positive airway pressure (CPAP). The other two patients had only respiratory support in the form of high flow oxygen via face mask.

There is scarce clinical and experimental evidence that intense spontaneous breathing effort during non-invasive ventilation can induce "self-inflicted lung injury" in patients with acute hypoxic respiratory failure and ARDS without COVID-19.[16,17] In patients with COVID-19, increased spontaneous breathing effort is associated with increased inspiratory pressure and volume and increased transpulmonary pressure, which can cause barotrauma and air leaks.[16,18]

There are also reports of self-inflicted lung injury that caused air leaks in COVID-19 patients with spontaneous breathing.[19,20] The computational modeling study performed by Liam weaver and colleagues concluded that trans-pulmonary and pleural pressure swings, and levels of driving pressure, lung strain and mechanical power which precipitate lung injury in mechanically ventilated patients can also develop in spontaneously breathing COVID-19 patients with hypoxemia.[21]

CONCLUSION

Manifestations of air leaks have been observed in all forms of respiratory support in patients with COVID-19. Mechanical ventilation has the highest incidence. There are no specific ventilator configuration parameters that are directly related to the onset of the condition. Prevention can be achieved by using mechanical ventilation in a timely manner in non-invasively assisted individuals to reduce the progression of self-inflicted lung injury, and to apply lung protective ventilation strategies to invasively assisted individuals.

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