Review Article :

COVID-19, Pulmonary Involvement and Ventilatory Support Strategy

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Abstract

The new coronavirus COVID-19 (SARS-CoV-2) has spread quickly throughout the world and become a threat in many aspects. Although governments and health agencies have dedicated strategic plan, yet the number of new confirmed cases continues to rise. The virus is affecting primarily the respiratory system causing respiratory failure that led to Acute Respiratory Distress Syndrome (ARDS) in some cases. Till now, the scientists and health care professionals are working to use the best evidence and knowledge to fight this pandemic. Current respiratory management is supportive including oxygen therapy and mechanical ventilation. This review aims to summarize the available evidence in regard the management of respiratory system impact of COVID-19 disease.

Keywords:

COVID-19, ARDS, Ventilatory Support Strategies, hyperinflammation, Oxygen Therapy

Introduction

In late December 2019, a worldwide pandemic of a novel coronavirus disease (later known as COVID-19) began in Wuhan, China. [1] Although the exact viral dynamics of this disease remain unclear, some reports have shown that COVID-19 might have originated from bats or pangolins. [2] Early case reports showed that patients with COVID-19 presented with fever, dry cough, fatigue, nasal congestion, sore throat, and diarrhea. [1,3,4] As of December 30th, 2021, there were over 284 million confirmed cases of COVID-19 worldwide. In Saudi Arabia, 554,665 cases of COVID-19 have been confirmed since the first case was reported on March 2, 2020.[5,6] Approximately 222 countries had confirmed cases, [5] million deaths worldwide, and USA had the highest number of deaths by just over 822 thousand, with a fatality rate approximating 1.5%.[5]

The transmission of COVID-19 has been found to occur via droplets, although one

study showed there is some likelihood of transmission through aerosols. [7,8] Patients with severe COVID-19 develop acute respiratory distress syndrome (ARDS) necessitating intensive care unit (ICU) admission and mechanical ventilation. [1] Previous COVID-19 reports have shown that the median amount of time between hospital admission and onset of ARDS was nine days (IQR: 8–14) [1]. Among 1,099 confirmed COVID-19 patients in China, 454 (41.3%) required oxygen therapy, [25] (2.3%) required invasive mechanical ventilation, and 56 (5.1%) required non-invasive mechanical ventilation. [3] Unpublished data from February 29 to March 10, 2020, showed that the rate of patients requiring oxygen therapy more than doubled in a center in Italy, and one-third of these patients deteriorated to the point of needing mechanical ventilation. [9]

The pathophysiology of COVID-19 is not yet entirely understood, as are the previously identified coronaviruses, including the severe acute respiratory syndrome-related coronavirus (SARS-CoV-1) and the Middle East respiratory syndrome-related coronavirus (MERS-CoV). [1] However, the inflammatory cytokines involved in COVID-19 are associated with pulmonary inflammation and disease severity, contributing to ARDS progression and mortality. [1] A laboratory examination showed that a cytokine storm, marked by increased interleukin (IL)-1B and TNFa levels, is associated with the severity of the disease. In contrast, a recent correlation study determined that COVID-19 (SARS-CoV-2) infection is responsible for multi-organ injury rather than inflammatory response. [10] Another study of 150 COVID-19 patients illustrated that non-survivor patients have higher ferritin and IL-6 levels than survivor patients ($P< 0.001$), suggesting that hyperinflammation is strongly related to mortality. [11]

According to expert observations, hypoxemic patients with COVID-19 have presented to emergency rooms (ERs) with two different phenotypes: low lung elastance and high lung elastance. [12] The low elastance phenotype is characterized by normal lung compliance with normal tidal volume, ventilation/perfusion mismatch due to hypoxemic vasoconstriction, and chest Computerized Tomography (CT) densities in pleural cavities and along lung fissures. Patients with the low elastance phenotype display hypoxemia without dyspnea, low carbon dioxide levels due to normal compliance, and high tidal and minute volumes. The high elastance phenotype is characterized by increased pulmonary edema, decreased tidal volume, ventilation/perfusion mismatch due to atelectasis, and bilateral lung infil-

tration. Hypoxemic patients with the high elastance phenotype have similar presentations to severe ARDS patients, with bilateral opacities and low lung compliance. [12] To date, no reports have found any patients to have developed both phenotypes. These two types of COVID-19 patients require different management; thus, it is highly important to determine the phenotypes of COVID-19 patients using presented manifestation and CT.

OxygenTherapy/Bronchodilation Treatment

According to preliminary data in China among 1099 patients, approximately 40% of COVID-19 cases in December 2019 required oxygen (O2) therapy. [3] Later, in January 2020, a study in China reported that 65% of enrolled patients required oxygen supplements. [4] Increased FiO2 could reverse hypoxemia (normally, 21% of oxygen is require to achieve normal oxygenation level in the blood with oxygen saturation >95%), especially for non-dyspneic patients (low elastance phenotype). [12] Many oxygen devices are available to support oxygenation and can be utilized to deliver multiple fractions of inspired oxygen. All these devices disperse exhaled air to variant distances (ranging from 0.1 to 1 meter). [13] According to a previous study of SARS-CoV-1, O2 therapy is a significant risk factor for the spread of infections ($P < 0.05$).14 The association of SARS-CoV-1 infection spread with jet nebulizer use is controversial. COVID-19 patients with coexistent obstructive respiratory disease, such as asthma or chronic obstructive pulmonary disease (COPD), often require nebulized bronchodilators; these patients are also likely to exhibit coughing during treatment, thus producing aerosol droplets. [14]

Prone Positioning Prior to Mechanical Ventilation

Prone positioning is one of the treatment strategies for severely hypoxemic patients with ARDS. [15] Previous case studies of ARDS have reported increases in arterial partial pressure of oxygen by 47–53 mmHg after prone positioning. [16] Moreover, randomized control trials (RCTs) and meta-analyses have demonstrated mortality reduction after early application of prone positioning in intubated patients with severe ARDS. [17] To date, prone positioning has only been recommended for severely hypoxemic intubated patients. A recent multicenter observational study in China evaluated prone positioning combined with either non-invasive ventilation (NIV) or high flow nasal cannula (HFNC). 18 Twenty patients diagnosed with ARDS after contracting influenza or pneumonia were included in this observational study. [18] Although this study was small, the use of

prone positioning with HFNC or NIV was shown be a beneficial strategy to improve oxygenation if tolerated by hypoxemic COVID-19 patients. A case series of six non-infectious ARDS patients in Mexico also produced similar findings. 19 To our knowledge, only one ongoing randomized clinical trial has evaluated prone positioning in non-intubated patients. [20]

Non-Invasive Ventilation (NIV)

NIV is an important supportive modality that can be implemented early in acute respiratory failure (ARF) and ARDS to prevent intubation. [21] In China, observational studies of COVID-19 have found the use of NIV to reverse ARF in severe patients. Specifically, small studies have shown oxygenation improvement and intubation reduction in refractory severe patients with COVID-19. [3,9] Further, an inspiratory positive airway pressure (IPAP) of 12 ± 2 cmH2O and an expiratory positive airway pressure (EPAP) of 7 ± 2 cmH2O yielded a positive response in a retrospective study of 20 patients with ARF secondary to SARS-CoV-1. [22] However, evidence concerning NIV treatment for SARS-CoV-1 or MERS-CoV is limited. [22,23] In addition to the failure rate and lack of RCTs on this subject, the 2017 European Thoracic Society (ERS)/ATS NIV guidelines could not support using NIV during a viral pandemic due to the risk of passing infection to healthcare workers (HCWs). [24] It is notable that the high failure rate of NIV in patients with hypoxic respiratory failure might be due to a lack of team experience, NIV interface intolerance, copious secretions, or patient-ventilator desynchronies. [25] It is still unclear whether NIV might super-spread nosocomial infections, and given the current situation, it is likely that the number of patients will outpace the current invasive ventilator capacities of most ICUs. [26] Thus, it is still necessary to strictly control the medical environment during NIV treatment and to always be cautious of the risk of cross-infection to HCWs. The latest expert recommendations for infection prevention and control measures during NIV utilization have advised the use of dual-limb NIV devices with expiratory high-efficiency particulate air filters (HEPAs). [9]

Invasive Ventilation Strategies

COVID-19 patients who develop ARDS (high elastance phenotype) usually present with progressive hypoxemia, respiratory distress, and hypercapnia, warranting intubation and invasive mechanical ventilation. [1,3,4,27,28] The ARDS guidelines for mechanical ventilation are updated regularly with new evidence and new technologies. [29] According to the ARDS network proto-

col, the use of low tidal volume (<6 ml/kg ideal body weight) and low plateau pressure ventilation (<30 cmH2O) is strongly recommended to prevent ventilator-induced lung injury. [29] This standard could be applied for patients with the high elastance phenotype, considering their decreased lung compliance. In contrast, patients with low elastance could be ventilated at a normal tidal volume (6–8 ml/kg) due to their normal lung compliance. Driving pressure—plateau pressure minus positive end-expiratory pressure (PEEP)—is currently considered to be a better predictor of patient outcomes than tidal volume or plateau pressure alone. 30 To date, no RCT has confirmed the optimal target driving pressure. However, it has been recommended to keep driving pressure as low as 15 cmH2O. [30] Moreover, the optimal PEEP is still a controversial subject. Previous studies have demonstrated three methods (ARDSnetwork PEEP/FiO2 table, lower inflection point of pressure-volume loop, and esophageal pressure) of setting the optimal PEEP in ARDS patients. [31-34] Setting the PEEP above the lower inflection point of a pressure-volume curve or through esophageal pressure guidance has produced better outcomes than the traditional ARDSnetwork PEEP/FiO2 strategy. [32,34] More importantly, high PEEPs should not be used in patients with the low elastance phenotype, as they could impact hemodynamics. Furthermore, recent ARDS guidelines have strongly recommended prone positioning for 12 hours per day in patients with moderate to severe ARDS (P/F ratio < 150 mmHg) due to the highly positive outcomes produced by this practice. [15,29] Finally, it should be noted that endotracheal intubation of infected patients with SARS-CoV-1 has been found to result in cross-infection of HCWs. [35] Therefore, it is imperative that clinicians act with caution and adhere to infection prevention and control measures while providing care for COVID-19 patients.

Clinical Implications and Conclusions

Despite all efforts, the pathogenesis of the COVID-19 is not yet well understood, and the number of new cases continues to rise. This review provides strong evidence in support of the management of symptomatic COVID-19 patients with respiratory system impact. Further research and RCTs are needed to review expert recommendations on this pandemic.

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Declaration of Conflicting Interests

The authors declare that there is no financial conflict of interest.

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