

Rishik Vashisht, MD

Department of Critical Care,
Respiratory Institute, Cleveland Clinic

Abhijit Duggal, MD, MPH, MSc

Department of Critical Care, Respiratory Institute, Cleveland Clinic

Respiratory failure in patients infected with SARS-CoV-2

Posted April 18, 2020

■ ABSTRACT

The management of patients with COVID-19-induced acute respiratory distress syndrome focuses on identifying the causes for respiratory failure and on following best practices for supportive care with oxygen supplementation and mechanical ventilation. In this patient population, appropriate measures need to be taken to prevent the spread of the coronavirus. Nearly 90% of COVID-19 patients admitted to the ICU need mechanical ventilation and most of these develop severe ARDS, which causes high morbidity and mortality. These patients need to be managed according to guidelines for the low-tidal-volume lung-protective ventilation. Practitioners also need to evaluate for other potential causes of respiratory failure.

Treatment for coronavirus disease 2019 (COVID-19)-induced acute respiratory distress syndrome (ARDS) must be based on best practices and guidelines, as for ARDS due to other causes. Other possible reasons for respiratory failure need to be considered in the care of these patients. At present, no specific therapies have been proven to be beneficial, and supportive care based on oxygen supplementation and mechanical ventilation, when needed, is the cornerstone of therapy.

A minority of infected patients. In the current global pandemic of severe acute respiratory syndrome coronavirus (SARS-CoV-2), about 5% to 10% of infected patients need to be admitted to the intensive care unit (ICU), most often because of severe and rapidly evolving hypoxemia.^{1,2} Their most common diagnosis is COVID-19 pneumonia, presenting with fever, fatigue, dry cough, myalgia, and dyspnea. Up to 88%

of COVID-19 patients who are admitted to the ICU need mechanical ventilation,² and most mechanically ventilated patients go on to develop severe ARDS.³

■ MANAGEMENT OF ACUTE RESPIRATORY FAILURE

Oxygen per high-flow nasal cannula. Patients with COVID-19 pneumonia who have rapidly escalating oxygen requirements should be moved to an ICU and should receive supplemental oxygen through a high-flow nasal cannula to maintain oxygen saturation between 92% and 96%.⁴

A high-flow nasal cannula is recommended over noninvasive positive-pressure ventilation (NIPPV), which has a very high failure rate in ARDS patients and is associated with poor outcomes. NIPPV may aggravate lung injury in these patients due to large swings in transpulmonary pressures and tidal volumes. Also of concern is that NIPPV generates aerosols that can spread the virus to other patients and to healthcare providers.⁴

Low threshold for intubation. In view of the rapidly fulminant progression of this disease, intubation should not be delayed while trying other, unproven therapies. Delay in intubation is associated with worse outcomes in viral pneumonia, so if adequate oxygenation is not achieved with a high-flow nasal cannula, intubation should not be delayed for a trial of NIPPV.

We do not recommend awake prone positioning. Although cases have been reported in which patients avoided intubation by being placed in the prone position, there is insufficient evidence in support its efficacy or safety. Further, trying awake prone positioning may delay necessary intubation and lead to poor outcomes.

■ MANAGEMENT OF ARDS

Once intubated, patients need to be managed according to the low-tidal-volume lung-protective ventilation strategy tested in the Acute Respiratory Distress

The statements and opinions expressed in COVID-19 Curbside Consults are based on experience and the available literature as of the date posted. While we try to regularly update this content, any offered recommendations cannot be substituted for the clinical judgment of clinicians caring for individual patients.

doi:10.3949/ccjm.87a.ccc025

TABLE 1
A high-PEEP, low F_{iO_2} strategy

F_{iO_2}	PEEP
0.3	5
0.3	8
0.3	10
0.3	12
0.3	14
0.4	16
0.4	16
0.5	18
0.5	18
0.5–0.8	20
0.8	22
0.9	22
1.0	22
1.0	24

Use a minimum positive end-expiratory pressure (PEEP) of 5 cm H₂O. Consider using incremental combinations of fraction of inspired oxygen F_{iO_2} and PEEP as shown to achieve PaO₂ of 5–80 mm Hg or SpO₂ 88%–95%.

From the Acute Respiratory Distress Syndrome Network, reference 6.

Syndrome Network study⁵ and recommended by the Surviving Sepsis Campaign COVID-19 panel.⁴

Low tidal volumes: 4 to 8 mL per kg of predicted body weight.⁴

Plateau pressures: lower than 30 cm H₂O.⁴

High PEEP. COVID-19-associated ARDS responds dramatically to a high positive end-expiratory pressure (PEEP) strategy, with recruitment of the lung parenchyma. A modified high-PEEP strategy (Table 1)⁶ should be considered. These patients should be placed on high PEEP,⁴ and the fraction of inspired oxygen (F_{iO_2}) should be reduced quickly once they are clinically stable. PEEP down-titration needs to be very slow, as there is a high risk of decruitment in these patients.

Conservative fluid management. Other ARDS trials have clearly demonstrated better outcomes with conservative fluid management.⁷ Therefore, for patients who are not in shock, a net negative fluid balance using the Fluid and Catheter Treatment Trial Lite protocol⁸ should be attempted (Table 2).

Consider early prone position ventilation for patients with moderate to severe ARDS (PaO₂-FiO₂ ratio less than 150, on FiO₂ 0.6 or greater), in view of the recruitability of the lung parenchyma.⁴

Consider neuromuscular blocking agents only

for ventilator dyssynchrony despite optimal use of sedation. Consider boluses of neuromuscular blocking agents as the initial treatment of choice instead of continuous infusions to help with synchrony.⁴

Recruitment maneuvers have little or no role, according to current evidence and expert opinion.

Consider extracorporeal membrane oxygenation as a rescue intervention for refractory hypoxemia.⁴

We do not suggest corticosteroids for management of COVID-19 ARDS.

Start appropriate antibiotics if secondary infection is suspected. Based on early experience, ARDS due to COVID-19 behaves like ARDS due to other viruses, with an average duration of mechanical ventilation of around 2 weeks. This prolonged duration of mechanical ventilation puts patients at risk for developing secondary bacterial pneumonias.

■ TWO PHASES OF COVID-19 PNEUMONIA?

Gattinoni et al⁹ hypothesize that COVID-19 pneumonia has two distinct phases of respiratory failure. The initial phase, “type L,” is characterized by *low* elastance or normal compliance, *low* ventilation-to-perfusion ratio, *low* lung weight, and *low* lung recruitability. With continued inflammation, the alveolar capillary membrane permeability increases, leading to increased interstitial edema, increased lung weight, and dependent atelectasis. They describe this phase as “type H,” or typical ARDS. It is characterized by *high* elastance, *high* right-to-left shunt, increased lung weight, and *high* recruitability.

Some suggest treating the early (type L) phase with low PEEP and a less-restrictive tidal volume strategy. However, in the absence of any evidence, we suggest that mechanically ventilated patients should continue to be managed with low-tidal-volume and high-PEEP strategies.

■ TO AVOID SPREADING THE VIRUS WHEN CARING FOR VENTILATED PATIENTS

Mechanical ventilation and other care for patients with acute respiratory failure is associated with a higher risk of nosocomial transmission. Therefore, caregivers should keep the following in mind.

Minimize unnecessary disconnection of the endotracheal tube to avoid derecruitment and unnecessary release of the virus into the environment.

Adhere to personal protective equipment protocols.

Keep fittings tight. Ventilator circuits need to have tight seals to prevent aerosolization.

Place ventilator and intravenous line monitors

outside the room to allow frequent ventilator adjustments while simultaneously decreasing the risk of exposure to staff.

Provide other general supportive care such as sedation, delirium prevention, and infection surveillance based on standard ICU practice and protocols.

■ CONSIDER OTHER CAUSES OF RESPIRATORY FAILURE

Asthma, COPD exacerbations. Like most other viral infections, COVID-19 pneumonia can lead to exacerbations of both chronic obstructive pulmonary disease (COPD) and asthma.¹⁰ SARS-CoV-2 infections can trigger an inflammatory reaction leading to these exacerbations, which need to be managed with corticosteroids and bronchodilators based on best practice guidelines for the underlying disease processes.

Pulmonary embolism. Initial observational data have suggested abnormal coagulation patterns in COVID-19 patients. One study found that up to 31% of patients with COVID-19 infection who required ICU care had thrombotic complications, with pulmonary embolism being the prominent diagnosis.¹¹

We suggest checking D-dimer at admission and every other day.

- If the initial D-dimer value is less than 3,000 ng/mL we suggest standard thromboprophylaxis.
- If the initial D-dimer value is higher than 3,000 ng/mL, we suggest point-of-care ultrasonography to assess for thrombotic events. If no thrombosis is detected, consider thromboprophylaxis in a higher dose.

Heart failure. COVID-19 patients who otherwise have minimal lung involvement could potentially present with dyspnea and hypoxemia that may be triggered by pulmonary embolism and right heart failure.

Myocarditis. SARS-CoV-2 infections have also been linked to myocarditis as a result of direct myocardial injury leading to severe heart failure exacerbations and cardiogenic shock. These patients can present with signs and symptoms ranging from mild dyspnea to acute pulmonary edema or even sudden cardiac death. Cardiac involvement can be seen in up to 25% of cases; therefore, we suggest following serial troponin measurements on presentation.

TABLE 2
Simplified conservative fluid management protocol (Fluid and Catheter Treatment Trial Lite)

Central venous pressure, mm Hg (recommended)	Pulmonary artery occlusion pressure, mm Hg (optional)	Mean arterial pressure \geq and off vasopressors \geq 12 hour	
		Urine output < 0.5 mL/kg/hr	Urine output \geq 0.5 mL/kg/hr
> 8	> 12	Furosemide ^a ; reassess in 1 hour	Furosemide ^a ; reassess in 4 hours
4–8	8–12	Give fluid bolus; reassess in 1 hour	Furosemide ^a ; reassess in 4 hours
< 4	< 8	Give fluid bolus; reassess in 1 hour	No intervention; reassess in 4 hours

^aRecommended furosemide dosing: begin with 20-mg bolus or 3-mg/hour infusion or last known effective dose. Double each subsequent dose until goal achieved (oliguria reversal or intravascular pressure target) or a maximum infusion rate of 24 mg/hour or a 160-mg bolus is reached. Do not exceed 620 mg/day. Also, if patient has heart failure, consider treatment with dobutamine.

From reference 8.

■ REFERENCES

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; 323(13):1239-1242. doi:10.1001/jama.2020.2648
2. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA* April 2020. doi:10.1001/jama.2020.5394
3. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; 382(8):727-733. doi:10.1056/NEJMoa2001017
4. Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Read Online Crit Care Med | Soc Crit Care Med* 9000; Online First. https://journals.lww.com/ccmjournal/Fulltext/onlinefirst/Surviving_Sepsis_Campaign_Guidelines_on_the.95707.aspx.
5. Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; 342(18):1301-1308. doi:10.1056/NEJM200005043421801
6. ARDS Clinical Network. Prospective randomized, multi-center trial of higher end-expiratory lung volume/lower FiO2 versus lower end-expiratory lung volume/higher FiO2 ventilation in acute lung injury and acute respiratory distress syndrome. Assessment of Low Tidal Volume and Elevated End-Expiratory Volume to Obviate Lung Injury (ALVEOLI) active research protocol. July 20, 1999. http://www.ardsnet.org/files/alveoliV1_1999-07-20.pdf. Accessed April 17, 2020.
7. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wiedemann HP, Wheeler AP, Bernard GR, et al. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 2006; 354(24):2564-2575. doi:10.1056/NEJMoa062200
8. Grissom CK, Hirshberg EL, Dickerson JB, et al. Fluid management with a simplified conservative protocol for the acute respiratory distress syndrome. *Crit Care Med* 2015; 43(2):288-295. doi:10.1097/CCM.0000000000000715

-
9. **Gattinoni L, Chiumello D, Caironi P, et al.** COVID-19 pneumonia: different respiratory treatment for different phenotype? *Intensive Care Med* 2020. doi:10.1007/s00134-020-06033-2
 10. **Hewitt R, Farne H, Ritchie A, Luke E, Johnston SL, Mallia P.** The role of viral infections in exacerbations of chronic obstructive pulmonary disease and asthma. *Ther Adv Respir Dis* 2016; 10(2):158-174. doi:10.1177/1753465815618113
 11. **Klok FA, Kruip MJHA, Meer NJM Van Der, et al.** Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res* 2020; (xxx):1-3. doi:10.1016/j.thromres.2020.04.013