Managing COVID-19 ARDS in Adults

Patients with severe COVID-19 pneumonia develop acute hypoxemic respiratory failure. While severely hypoxic COVID-19 patients meet the criteria for typical acute respiratory distress syndrome (ARDS), COVID-19 ARDS has unique characteristics. Unlike typical ARDS, COVID-19 ARDS may respond to steroids (Hornby, 2020), venous thromboembolism is more common, and there may be subtypes with differing lung compliance. It is important to note the key differences between the management of COVID-19 ARDS versus typical ARDS. The treatment of COVID-19 ARDS includes antiviral, anti-inflammatory, and anticoagulant medications in addition to end-organ support, where the treatment of typical ARDS focuses on of control of the primary etiology (infection, trauma, aspiration, etc.) and end-organ support. COVID-19 ARDS diagnosis and treatment guidelines are outlined below.

COVID-19 in the ICU: Definitions

Severe COVID-19

Signs of pneumonia (fever, cough, dyspnea, tachypnea) plus one of the following:

- Respiratory rate greater than 30 breaths/minute
- Severe respiratory distress
- SpO_2 less than 90% on room air

Critical COVID-19

- Profound acute hypoxic respiratory failure from ARDS is the dominant finding usually requiring ventilation.
- Hypercapnia is rare unless associated with chronic obstructive pulmonary disease or narcotic overdose
- Fevers can wax and wane
- May present with other COVID-19 complications (e.g., sepsis, septic shock, dehydration/hypovolemia, stroke/systemic thromboembolism, arrhythmia, heart failure)

The Berlin Definition of ARDS

The Berlin definition of ARDS specify the following three criteria must be met:

- Timing within one week of clinical insult
- Presence of bilateral opacities not fully explained by effusions, lobar/lung collapse or nodules
- Respiratory failure not explained by heart failure or volume overload (Matthay, 2021).

The severity of the ARDS is defined by the degree of hypoxemia, the ratio of partial pressure of oxygen in arterial blood (PaO_2) to the fraction of inspiratory oxygen concentration (FiO_2) (PaO_2/FiO_2). ARDS can be classified as mild, moderate, or severe based on the Berlin definition of ARDS (Ranieri et al., 2012).

Berlin Definition of ARDS (Ranieri et al., 2012)	
ARDS Severity	**PaO_2/FiO_2 Ratio**
Mild	200-300
Moderate	100-200
Severe	<100
**on positive end-expiratory pressure (PEEP) ≥ 5 cm H2O*	

It is important to remember that certain variables may impact the PaO_2/FiO_2 ratio, including:

- Chest x-ray severity
- Respiratory system compliance
- Positive end-expiratory pressure (PEEP)
- Corrected expired volume/minute

Interventions for COVID-19 ARDS

Intubation Management

*Perfusion is equally as important as ventilation, and patients who are mechanically ventilated for COVID-19 ARDS often require prolonged ventilation periods for two weeks or more.

- Intubate and extubate in a negative pressure room; staff should don appropriate personal protective equipment (PPE), preferably Powered Air Purifying Respirators (PAPRs); minimize number of staff in room.
- Use a low tidal volume (Vt) strategy; Vt 4-8 mL/kg of predicted body weight (most common 6 mL/kg).
- Target plateau pressure of less than 30 cm H_2O; higher levels significantly increase the risk of barotrauma.
    - If plateau pressure is greater than 30 cm H_2O, decrease PEEP or decrease Vt.
- Use FiO_2, PEEP, and Vt to oxygenate the blood and ventilate the patient.
    - In mild ARDS, can start with lower PEEP.
    - In moderate to severe ARDS, consider higher PEEP strategy (10 cm H_2O or greater).
- Maintain SpO_2 no higher than 96% to avoid oxygen toxicity
- Assess patient response to low tidal volume ventilation within the first four hours of ventilation. Consider obtaining an arterial blood gas to measure PaO_2:FiO_2 ratio.
    - If PaO_2:FiO_2 is greater than or equal to 150 mm Hg continue low tidal volume ventilation
    - If PaO_2:FiO_2 less than 150 mm Hg consider pronating patient if possible.
- Consider alternative modes of ventilation, such as pressure-limited modes or volume targeted pressure-controlled ventilation (remember, compliant lungs need less pressure).
- Use recruitment maneuvers; avoid using staircase (incremental PEEP) recruitment maneuvers.
- Early proning for mechanically ventilated adults with COVID-19 ARDS
    - Consider proning for 12-16 hours/day and repeat daily until no longer needed or there is no response.
    - If improvement is seen with prone sessions, consider weaning FiO_2 and PEEP.
    - Watch for hemodynamic and ventilation/perfusion instability for 1st hour post-proning and placing patient supine.

    - Proning results take longer to see than typical ARDS; results are more due to redistribution of perfusion and gravitational forces (Gattinoni et al., 2020)
    - Put cables and intravenous lines on one side, when possible.
    - If available, use a proning team (an experienced group of critical care nurses and respiratory therapists). Some facilities require a critical care or anesthesia provider to be nearby in case of disruption of the endotracheal tube.
- Inhaled pulmonary vasodilator therapy (e.g., inhaled nitric oxide)
    - For patients who remain hypoxemic despite optimizing ventilation and other rescue strategies.
    - Utilized as a trial of rescue therapy.
    - Has been shown to provide a modest, transient improvement in oxygenation without any improvement in mortality or duration of ventilation.
    - If no rapid improvement in oxygenation, taper the treatment.
- Sedation
    - When proning, patients may require additional sedation to tolerate the prone position.
    - If patients continue to have ventilator dyssynchony despite optimizing ventilator settings and sedation, consider using a neuromuscular blocking agent.
- Patients decompensate quickly, especially during weaning; use a very, very slow weaning process even if patient appears comfortable on low pressure support (PS) settings.
- COVID-19 is associated with a hypercoagulable state; if using continuous renal replacement therapy (CRRT), consider frequent boluses of heparin or an infusion pre-circuit.
- Consider tracheostomy if the patient is anticipated to be on the ventilator for over 14 days and if oxygen requirements allow. This is a highly aerosolized procedure so perform it in a negative pressure room.
- In mechanically ventilated patients with COVID-19 and refractory hypoxemia despite optimizing ventilation, use of rescue therapies, and proning, attempt veno-venous extracorporeal membrane oxygenation (ECMO), if available, or refer the patient to an ECMO center. ECMO should only be considered for select patients with COVID-19 and severe ARDS.

Pharmacotherapy (Alhazzani et al., 2021; NIH, 2021)

- Strong recommendations
    - Use a short course of systemic corticosteroids and start early in disease course (within 14 days of onset). Conversely, avoid corticosteroids in patients who have persistent ARDS beyond 14 days, as their use may increase mortality in this setting.
    - Administer pharmacologic venous thromboembolism (VTE) prophylaxis; if the patient develops a deep vein thrombosis (DVT), place on therapeutic anticoagulation unless there are contraindications. Intermediate anticoagulation dosing is not recommended except in a clinical trial.
- Moderate recommendations
    - For patients on oxygen and considered for corticosteroids, use dexamethasone over other corticosteroids; if dexamethasone is unavailable, can use prednisone, methylprednisolone, or hydrocortisone.

  - Evaluate hospitalized patients on supplemental oxygen with rapidly increasing oxygen needs for emergency authorization use of baricitinib or tociluzimab; do not use the two drugs together except in a clinical trial.
  - Evaluate hospitalized patients requiring oxygen for remdesivir therapy.
  - Consider a trial of epoprostenol nebulized therapy for intubated and mechanically ventilated patients who continue to be hypoxic despite other interventions (Sonti et al., 2021).
  - For adults with severe or critical COVID-19, it is suggested that convalescent plasma not be used outside of clinical trials.
- Weak recommendation
  - If the patient is in septic shock, use a conservative versus liberal resuscitation therapy with a buffered crystalloid solution.

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