Managing Critically Ill Adults with COVID-19

About the Guideline

- This guideline provides recommendations on the management of patients with severe or critical COVID-19 in the ICU.
- The target users of this guideline are frontline clinicians, allied health professionals, and policymakers involved in the care of patients with COVID-19 in the intensive care unit (ICU).
- A panel of 43 experts from 14 countries reviewed the literature and identified relevant and recent evidence on supportive care for COVID-19 patients in the ICU.
- Recommendations were generated based on the balance between benefit and harm, resource and cost implications, equity, and feasibility.

Overview

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of a rapidly spreading illness, Coronavirus Disease 2019 (COVID-19).
- 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
      - SpO2 less than 90% on room air
  - Critical COVID-19
    - ARDS or respiratory failure requiring ventilation, sepsis or septic shock
- Recommendations are organized based on five topics:
  1. Infection control
  2. Laboratory diagnosis and specimens
  3. Hemodynamic support
  4. Ventilatory support
  5. COVID-19 therapy

Key Clinical Considerations

Infection control

- Current data points to significant burden of infection among healthcare workers.
- Risk of patient-to-patient transmission in the ICU is currently unknown.
- Adherence to infection control precautions is paramount.
- Infection control policies and procedures already in place at healthcare institutions should be followed; the recommendations in this guideline should serve as considerations rather than a requirement to change policies.
Aerosol-generating procedures

- **Best Practice Statement:** For healthcare workers performing aerosol-generating procedures on patients with COVID-19 in the ICU, the *recommendation* is to use fitted respirator masks (N95 respirators, FFP2, or equivalent), as opposed to surgical/medical masks, in addition to other personal protective equipment (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles).

- Aerosol-generating procedures include:
  - endotracheal intubation
  - bronchoscopy
  - open suctioning
  - administration of nebulized treatment
  - manual ventilation before intubation
  - physical proning of the patient
  - disconnecting the patient from the ventilator
  - non-invasive positive pressure ventilation
  - tracheostomy
  - cardiopulmonary resuscitation

Use of negative pressure rooms

- **Best Practice Statement:** The *recommendation* is to perform aerosol-generating procedures on ICU patients with COVID-19 in a negative pressure room.

- Negative pressure rooms are intended to prevent the spread of contagious airborne pathogens from room to room and avoid the accidental release of pathogens into a larger space and open facility.

- When not feasible, a portable high-efficiency particulate air (HEPA) filter should be used.

- The presence of unnecessary staff in the room should be avoided.

Usual care of nonventilated patients

- **Weak recommendation:** For healthcare workers providing usual care for non-ventilated COVID-19 patients, the *suggestion* is to use surgical/medical masks, as opposed to respirator masks, in addition to other personal protective equipment (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles).

Non-aerosol-generating procedures on ventilated (closed-circuit) patients

- **Weak recommendation:** For healthcare workers who are performing non-aerosol-generating procedures on mechanically ventilated (closed circuit) patients with COVID-19, the *suggestion* is to use surgical/medical masks, as opposed to respirator masks, in addition to other personal protective equipment (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles).

Endotracheal intubation
• Techniques that can reduce the number of attempts at endotracheal intubation and the duration of the procedure and minimize the proximity between the operator and the patient should be prioritized.

• **Best Practice Statement:** For COVID-19 patients requiring endotracheal intubation, the *recommendation* is that endotracheal intubation be performed by the healthcare worker who is most experienced with airway management in order to minimize the number of attempts and risk of transmission.

• Weak recommendation: For healthcare workers performing endotracheal intubation on patients with COVID-19, the *suggestion* is to use video-guided laryngoscopy, over direct laryngoscopy, if available.

**Laboratory diagnosis and specimens**

• Every critically ill patient arriving with evidence of respiratory infection should be considered potentially infected with SARS-CoV-2.

• Diagnostic challenges exist due to an extended incubation period (approximately two weeks) that includes a prolonged interval (approximately five days) of viral shedding prior to the onset of symptoms.

• The duration of asymptomatic shedding varies and may also differ based on the anatomic level (upper versus lower) of the infection in the respiratory system.

• A single negative swab from the upper airway does not rule out SARS-CoV-2 infection; repeated sampling from multiple sites, including the lower airway, will increase diagnostic yield.

• A positive test for another respiratory virus does not rule out COVID-19 and should not delay testing if there is a high suspicion of COVID-19.

• A single positive swab confirms the diagnosis of COVID-19.

**Intubated and mechanically ventilated adults with suspicion of COVID-19**

• Weak recommendation: For diagnostic testing, the *suggestion* is to obtain lower respiratory tract samples in preference to upper respiratory tract (nasopharyngeal or oropharyngeal).

• Weak recommendation: Regarding lower respiratory samples, the *suggestion* is to obtain endotracheal aspirates in preference to bronchial wash or bronchoalveolar lavage samples.

**Hemodynamic support**

• The incidence of shock in adult patients with COVID-19 may reach 20-35% among patients in the ICU.

**Fluid therapy**

• Weak recommendation: In adults with COVID-19 and shock, the *suggestion* is to use dynamic parameters, skin temperature, capillary refilling time, and/or serum lactate measurement over static parameters in order to assess fluid responsiveness.
  o Dynamic parameters include stroke volume variation, pulse pressure variation, and stroke volume change with passive leg raise or fluid challenge.
  o Static parameters include central venous pressure and mean arterial pressure (MAP).
• Weak recommendation: For the acute resuscitation of adults with COVID-19, the suggestion is to use a conservative over a liberal fluid strategy.
• Weak recommendation: For the acute resuscitation of adults with COVID-19 and shock, the recommendation is to use crystalloids over colloids.
• Weak recommendation: For the acute resuscitation of adults with COVID-19 and shock, the suggestion is to use buffered/balanced crystalloids over unbalanced crystalloids.
• Strong recommendation: For the acute resuscitation of adults with COVID-19 and shock, the recommendation is against using hydroxyethyl starches.
• Weak recommendation: For the acute resuscitation of adults with COVID-19 and shock, the suggestion is against using gelatins.
• Weak recommendation: For the acute resuscitation of adults with COVID-19 and shock, the suggestion is against using dextans.
• Weak recommendation: For the acute resuscitation of adults with COVID-19 and shock, the suggestion is against the routine use of albumin for initial resuscitation.

Vasoactive agents
• Weak recommendation: For adults with COVID-19 and shock, the suggestion is to use norepinephrine as the first line vasoactive agent, over other agents.
• Weak recommendation: If norepinephrine is not available, the suggestion is to use either vasopressin or epinephrine as the first line vasoactive agent, over other vasoactive agents for adults with COVID-19 and shock.
  o The decision between vasopressin and epinephrine may be based on availability and contraindications to the two agents.
    ▪ With vasopressin, digital ischemia may be a concern.
    ▪ With epinephrine, tachycardia and excess lactate production may be concerns.
• Strong recommendation: For adults with COVID-19 and shock, the recommendation is against using dopamine if norepinephrine is available.
  o This recommendation is based on increased harm, including increased risk of mortality, in patients treated with dopamine.
• Weak recommendation: For adults with COVID-19 and shock, the suggestion is to add vasopressin as a second line agent, over titrating norepinephrine dose, if target MAP cannot be achieved by norepinephrine alone.
• Weak recommendation: For adults with COVID-19 and shock, the suggestion is to titrate vasoactive agents to target a MAP of 60-65 mmHg, rather than higher MAP targets.
• Weak recommendation: For adults with COVID-19 and shock with evidence of cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation and norepinephrine, the suggestion is to add dobutamine, over increasing norepinephrine dose.
  o It is also suggested to add dobutamine, over no treatment, in these patients; this is based on physiological rationale.

Ventilatory support
The true incidence of hypoxic respiratory failure in patients with COVID-19 is unclear, however about 14% will develop severe disease requiring oxygen therapy and 5% will require ICU admission and mechanical ventilation.

In another study, 67% of critically ill COVID-19 patients had ARDS, 63.5% received high flow nasal cannula (HFNC), 56% required invasive mechanical ventilation, and 42% received non-invasive positive pressure ventilation (NIPPV).

**Oxygen therapy**

- A reasonable SPO$_2$ range for patients on oxygen therapy is 92% to 96%.
  - Strong recommendation: In adults with COVID-19, the suggestion is to start supplemental oxygen if the peripheral SPO$_2$ is less than 92%, and the recommendation is to start supplemental oxygen if the SPO2 is less than 90%.
  - Strong recommendation: In adults with COVID-19 and acute hypoxemic respiratory failure on oxygen, the recommendation is that SPO$_2$ be maintained no higher than 96%.

- Weak recommendation: For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the suggestion is to use HFNC over conventional oxygen therapy.

- Weak recommendation: For adults with COVID-19 and acute hypoxemic respiratory failure, the suggestion is to use HFNC over NIPPV.
  - There is evidence for decreased risk of intubation with HFNC compared with NIPPV in acute respiratory failure.
  - Some studies suggest that NIPPV may carry a greater risk of nosocomial infection of healthcare providers.

- Weak recommendation: In adults with COVID-19 and acute hypoxemic respiratory failure, if HFNC is not available and there is no urgent indication for endotracheal intubation, the suggestion is a trial of NIPPV with close monitoring and short interval assessment for worsening of respiratory failure.

**Best Practice Statement:** In adults with COVID-19 receiving NIPPV or HFNC, the recommendation is for close monitoring for worsening of respiratory status and early intubation in a controlled setting if worsening occurs.
  - Limited experience with NIPPV in pandemics suggests a high failure rate.
  - When resources become stretched, if there is insufficient ability to provide invasive ventilation, a moderate chance of success with NIPPV may justify its use.

**Invasive mechanical ventilation**

- Strong recommendation: In mechanically ventilated adults with COVID-19 and ARDS, the recommendation is to use low tidal volume (Vt) ventilation (Vt 4-8 mL/kg of predicted body weight) over higher tidal volumes (Vt greater than 8 mL/kg).
  - The panel of experts believes that COVID-19 patients should be managed as others with acute respiratory failure in the ICU.
Low Vt ventilation is one of the main strategies to minimize ventilator-induced lung injury (VILI).

- The ARDSNet study protocol set the initial Vt at 6 mL/kg which can be increased to 8 mL/kg if the patient is double triggering or if inspiratory airway pressure decreases below PEEP.

**Strong recommendation:** For mechanically ventilated adults with COVID-19 and ARDS, the **recommendation** is targeting plateau pressures (Pplat) of less than 30 cm H₂O.

- Pplat limitation is a lung protective strategy to minimize VILI.
- The ARDSNet study protocol set the initial Vt at 6 mL/kg, and then measured Pplat (after a 0.5 second inspiratory pause). If the Pplat was greater than 30 cmH₂O, Vt could be reduced in 1 mL/kg (to 4 mL/kg) steps until Pplat was within range.

**Strong recommendation:** For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, the **suggestion** is to use a higher PEEP strategy over a lower PEEP strategy.

- PEEP increases and sustains alveolar recruitment, which improves oxygenation.
- If using a higher PEEP strategy (i.e. PEEP greater than 10 cm H₂O), monitor patients for barotrauma.

**Weak recommendation:** For mechanically ventilated adult patients with COVID-19 and ARDS, the **suggestion** is to use a conservative fluid strategy over a liberal fluid strategy.

- Limited data show that cardiac failure, alone or with respiratory failure, caused 40% of COVID-19 deaths.

**Weak recommendation:** For mechanically ventilated adult patients with COVID-19 and moderate to severe ARDS, the **suggestion** is to use prone ventilation for 12 to 16 hours, over no prone ventilation.

- The progression of radiographic features in a series of COVID-19 patients suggests a role for prone ventilation.
- Theoretically, prone positioning decreases ventral alveolar distention and dorsal alveolar collapse.
- A protocol for proning should be used.
- Clinicians should be aware of the following complications:
  - Pressure sores
  - Vascular line and endotracheal tube displacement
  - Facial edema
  - Transient hemodynamic instability
  - Corneal abrasions
  - Brachial plexus injury
  - Hemodialysis vascular flow issues

- Absolute contraindications for prone ventilation are:
  - Unstable spine
  - Open abdomen or open chest
- Enteral nutrition (via nasogastric or nasoduodenal tube) can be continued during proning.
• Weak recommendation: For mechanically ventilated adult patients with COVID-19 and moderate to severe ARDS, the suggestion is to use intermittent boluses of neuromuscular blocking agents (NMBA) as needed, over continuous NMBA infusion.

• Weak recommendation: In the event of persistent ventilator dyssynchrony, the need for ongoing deep sedation, prone ventilation, or persistently high plateau pressures, for mechanically ventilated adult patients with COVID-19 and moderate to severe ARDS, the suggestion is to use a continuous NMBA infusion for up to 48 hours.

• Weak recommendation: For mechanically ventilated adult patients with COVID-19 and ARDS, the recommendation is against routine use of inhaled nitric oxide.

• Weak recommendation: For mechanically ventilated adult patients with COVID-19, severe ARDS, and hypoxemia despite optimizing ventilation and other rescue strategies, the suggestion is a trial of inhaled pulmonary vasodilator as a rescue therapy; treatment should be tapered off if there is no rapid improvement in oxygenation.

• Weak recommendation: For mechanically ventilated adult patients with COVID-19 and hypoxemia despite optimizing ventilation, the suggestion is to use recruitment maneuvers (RM) over not using RM.
  o Strong recommendation: If RM are used, the recommendation is against using staircase (incremental PEEP).
  o Monitor patients closely for severe desaturation, hypotension, or barotrauma.
  o Stop RMs if they lead to patient deterioration.

• Weak recommendation: For mechanically ventilated adult patients with COVID-19 and refractory hypoxemia despite optimizing ventilation, use of rescue therapies, and proning, the suggestion is to use venovenous (VV) extracorporeal membrane oxygenation (ECMO) if available, or referring patient to an ECMO center.
  o ECMO is a resource intensive technique and remains a limited resource; its use should be reserved for carefully selected patients.

COVID-19 therapy

• Strong recommendation: For adults with severe or critical COVID-19, the recommendation is against using hydroxychloroquine.

• Strong recommendation: For adults with severe or critical COVID-19, the recommendation is to use a short course of systemic corticosteroids.

• Weak recommendation: For adults with severe or critical COVID-19 who are considered for systemic corticosteroids, the suggestion is to use dexamethasone. If dexamethasone is not available, other corticosteroids equivalent to 6 mg daily of dexamethasone may be used for up to 10 days.

• Weak recommendation: For adults with severe COVID-19 who do not require mechanical ventilation, the suggestion is to use IV remdesivir, which should be started within 72 hours of positive PCR or antigen test.

• Weak recommendation: For adults undergoing mechanical ventilation for critical COVID-19, the suggestion is against starting IV remdesivir.

• Weak recommendation: For critically ill adults with COVID-19 and fever, the suggestion is to use acetaminophen or paracetamol for temperature control.
• Weak recommendation: For critically ill adults with COVID-19, the *suggestion* is against routine use of standard IV immunoglobulin.

• Weak recommendation: For adults with severe or critical COVID-19, the *suggestion* is against the use of convalescent plasma outside of clinical trials.

• Strong recommendation: For adults with severe or critical COVID-19, the *recommendation* is to use pharmacologic VTE prophylaxis.

• Weak recommendation: For adults with severe or critical COVID-19 and no evidence of VTE, the *suggestion* is against the routine use of therapeutic anticoagulation outside of clinical trials.

References:
