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.

<u>Intubated and mechanically ventilated adults with suspicion of COVID-19</u>

- 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.

<u>Fluid therapy</u>

- 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.
    - Dynamic parameters include stroke volume variation, pulse pressure variation, and stroke volume change with passive leg raise or fluid challenge.
    - 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 dextrans.
- 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.
    - 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.
    - 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.
    - 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.
- No recommendations:
    - The use of helmet NIPPV compared with mask NIPPV
    - The use of awake prone positioning in nonintubated adults with severe COVID-19

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 H_2O.
  - 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 cmH_2O, 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 H_2O), 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.
    - Strong recommendation: If RM are used, the *recommendation* is against using staircase (incremental PEEP).
    - Monitor patients closely for severe desaturation, hypotension, or barotrauma.
    - 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.
    - 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:

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