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Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

ABSTRACT

Background: The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of a rapidly spreading illness, Coronavirus Disease 2019 (COVID-19), affecting thousands of people around the world. Urgent guidance for clinicians caring for the sickest of these patients is needed.

Methods: We formed a panel of 36 experts from 12 countries. All panel members completed the World Health Organization conflict of interest disclosure form. The panel proposed 53 questions that are relevant to the management of COVID-19 in the ICU. We searched the literature for direct and indirect evidence on the management of COVID-19 in critically ill patients in the ICU. We identified relevant and recent systematic reviews on most questions relating to supportive care. We assessed the certainty in the evidence using the *Grading of Recommendations, Assessment, Development and Evaluation* (GRADE) approach, then generated recommendations based on the balance between benefit and harm, resource and cost implications, equity, and feasibility. Recommendations were either strong or weak, or in the form of best practice recommendations.

Results: The Surviving Sepsis Campaign COVID-19 panel issued 54 statements, of which 4 are best practice statements, 9 are strong recommendations, and 35 are weak recommendations. No recommendation was provided for 6 questions. The topics were: 1) infection control, 2) laboratory diagnosis and specimens, 3) hemodynamic support, 4) ventilatory support, and 5) COVID-19 therapy.

Conclusion: The Surviving Sepsis Campaign COVID-19 panel issued several recommendations to help support healthcare workers caring for critically ill ICU patients with COVID-19. When available, we will provide new evidence in further releases of these guidelines.

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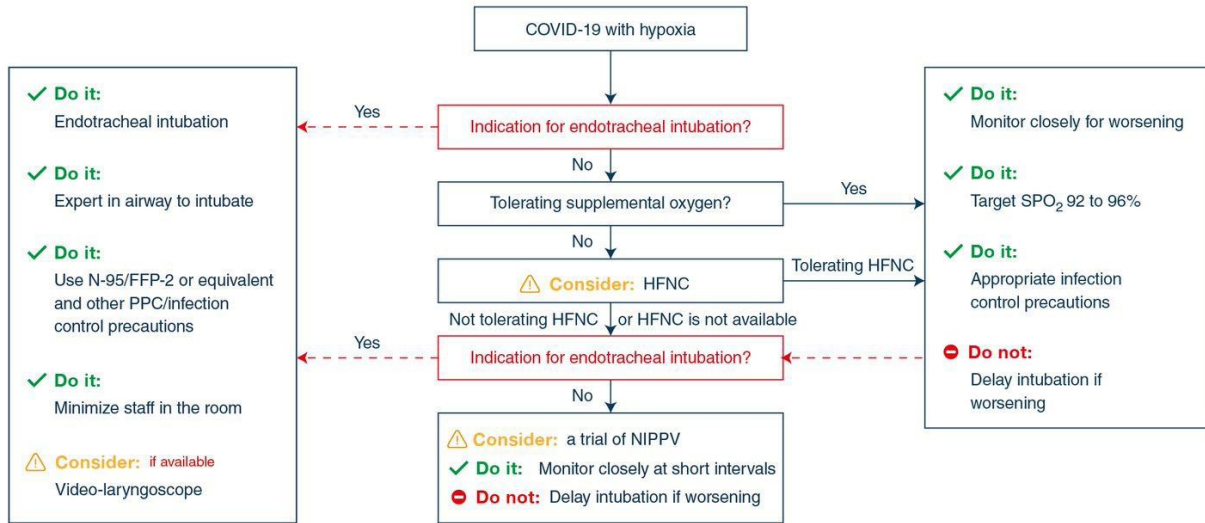


Figure 2.

| COVID-19 with mild ARDS | COVID-19 with Mod to Severe ARDS | Rescue/Adjunctive therapy |
|---|---|---|
| <p>✓ Do: Vt 4-8 ml/kg and P_{plat} < 30 cm H₂O</p> | <p>⚠ CONSIDER: Higher PEEP</p> | <p>❓ Uncertain: Antivirals, chloroquine, anti-IL6</p> |
| <p>✓ Do: Investigate for bacterial infection</p> | <p>⚠ CONSIDER: NMBA boluses to facilitate ventilation targets</p> | <p>⚠ CONSIDER: if proning, high P_{plt}, asynchrony NMBA infusion for 24 h</p> |
| <p>✓ Do: Target SPO2 92% - 96%</p> | <p>⚠ CONSIDER: if PEEP responsive Traditional Recruitment maneuvers</p> | <p>⚠ CONSIDER: Prone ventilation 12-16 h</p> |
| <p>⚠ CONSIDER: Conservative fluid strategy</p> | <p>⚠ CONSIDER: Prone ventilation 12-16 h</p> | <p>⚠ CONSIDER: STOP if no quick response A trial of inhaled Nitric Oxide</p> |
| <p>⚠ CONSIDER: Empiric antibiotics</p> | <p>⚠ CONSIDER: if proning, high P_{plt}, asynchrony NMBA infusion for 24 h</p> | <p>⚠ CONSIDER: follow local criteria for ECMO V-V ECMO or referral to ECMO center</p> |
| <p>❓ Uncertain: Systematic corticosteroids</p> | <p>🚫 Don't do: Staircase Recruitment maneuvers</p> | |
| | <p>⚠ CONSIDER: Short course of systemic corticosteroids</p> | |
| | <p>❓ Uncertain: Antivirals, chloroquine, anti-IL6</p> | |

Figure 3.

Table 1. Implications of different recommendations to key stakeholders

| Recommendation | Meaning | Implications to patients | Implications to clinicians | Implications to policymakers |
|---|--|---|--|--|
| Strong recommendation or Best practice statement | Must do or Must avoid | Almost all individuals in this situation would want the recommended intervention, and only a small proportion would not want it | Most individuals should receive the recommended course of action | Can be adapted as policy in most situations, including the use as performance indicators |
| Weak recommendation | Consider doing or Consider avoiding | The majority of individuals in this situation would want the recommended intervention, but many would not | Different choices are likely to be appropriate for different patients, and the recommendation should be tailored to the individual patient's circumstances. Such as patients', family's, or substitute decision maker's values and preferences | Policies will likely be variable |

Table 2. Recommendations and statements

| | Recommendation | Strength |
|-----|--|-------------------------|
| | Infection Control and Testing: | |
| 1 | For healthcare workers performing aerosol-generating procedures* on patients with COVID-19 in the ICU, we recommend using 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) | Best practice statement |
| 2 | We recommend performing aerosol-generating procedures on ICU patients with COVID-19 in a negative pressure room. | Best practice statement |
| 3 | For healthcare workers providing usual care for non-ventilated COVID-19 patients, we suggest using 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). | Weak |
| 4 | For healthcare workers who are performing non-aerosol-generating procedures on mechanically ventilated (closed circuit) patients with COVID-19, we suggest using 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). | Weak |
| 5 | For healthcare workers performing endotracheal intubation on patients with COVID-19, we suggest using video-guided laryngoscopy, over direct laryngoscopy, if available. | Weak |
| 6 | For COVID-19 patients requiring endotracheal intubation , we recommend 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. | Best practice statement |
| 7.1 | For intubated and mechanically ventilated adults with suspicion of COVID-19: For diagnostic testing, we suggest obtaining lower respiratory tract samples in preference to upper respiratory tract (nasopharyngeal or oropharyngeal) samples. | Weak |
| 7.2 | For intubated and mechanically ventilated adults with suspicion of COVID-19: With regard to lower respiratory samples, we suggest obtaining endotracheal aspirates in preference to bronchial wash or bronchoalveolar lavage samples. | Weak |
| | Hemodynamics: | |
| 8 | In adults with COVID-19 and shock , we suggest using dynamic parameters skin temperature, capillary refilling time, and/or serum lactate measurement over static parameters in order to assess fluid responsiveness. | Weak |
| 9 | For the acute resuscitation of adults with COVID-19 and shock , we suggest using a conservative over a liberal fluid strategy. | Weak |
| 10 | For the acute resuscitation of adults with COVID-19 and shock , we recommend using crystalloids over colloids. | Weak |
| 11 | For the acute resuscitation of adults with COVID-19 and shock , we suggest using buffered/balanced crystalloids over unbalanced crystalloids. | Weak |

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| 12 | For the acute resuscitation of adults with COVID-19 and shock , we recommend against using hydroxyethyl starches. | Strong |
| 13 | For the acute resuscitation of adults with COVID-19 and shock , we suggest against using gelatins. | Weak |
| 14 | For the acute resuscitation of adults with COVID-19 and shock , we suggest against using dextrans. | Weak |
| 15 | For the acute resuscitation of adults with COVID-19 and shock , we suggest against the routine use of albumin for initial resuscitation. | Weak |
| 16 | For adults with COVID-19 and shock , we suggest using norepinephrine as the first-line vasoactive agent, over other agents. | Weak |
| 17 | If norepinephrine is not available, we suggest using either vasopressin or epinephrine as the first-line vasoactive agent, over other vasoactive agents, for adults with COVID-19 and shock . | Weak |
| 18 | For adults with COVID-19 and shock , we recommend against using dopamine if norepinephrine is available. | Strong |
| 19 | For adults with COVID-19 and shock , we suggest adding vasopressin as a second-line agent, over titrating norepinephrine dose, if target mean arterial pressure (MAP) cannot be achieved by norepinephrine alone. | Weak |
| 20 | For adults with COVID-19 and shock , we suggest titrating vasoactive agents to target a MAP of 60-65 mmHg, rather than higher MAP targets. | Weak |
| 21 | For adults with COVID-19 and shock with evidence of cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation and norepinephrine , we suggest adding dobutamine, over increasing norepinephrine dose. | Weak |
| 22 | For adults with COVID-19 and refractory shock , we suggest using low-dose corticosteroid therapy ("shock-reversal"); over no corticosteroid. Remark: A typical corticosteroid regimen in septic shock is intravenous hydrocortisone 200 mg per day administered either as an infusion or intermittent doses. | Weak |
| Ventilation | | |
| 23 | In adults with COVID-19, we suggest starting supplemental oxygen if the peripheral oxygen saturation (SPO ₂) is < 92%, and recommend starting supplemental oxygen if SPO ₂ is < 90% | Weak Strong |
| 24 | In adults with COVID-19 and acute hypoxemic respiratory failure on oxygen , we recommend that SPO ₂ be maintained no higher than 96%. | Strong |
| 25 | For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, we suggest using HFNC over conventional oxygen therapy. | Weak |
| 26 | In adults with COVID-19 and acute hypoxemic respiratory failure , we suggest using HFNC over NIPPV. | Weak |
| 27 | In adults with COVID-19 and acute hypoxemic respiratory failure , if HFNC is not available and there is no urgent indication for endotracheal intubation, we suggest a trial of NIPPV with close monitoring and short-interval assessment for worsening of respiratory failure. | Weak |
| 28 | We were not able to make a recommendation regarding the use of helmet NIPPV compared with mask NIPPV. It is an option, but we are not certain about its safety or efficacy in COVID-19. | No recommendation |

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| 29 | In adults with COVID-19 receiving NIPPV or HFNC, we recommend close monitoring for worsening of respiratory status, and early intubation in a controlled setting if worsening occurs. | Best practice statement |
| 30 | In mechanically ventilated adults with COVID-19 and ARDS, we recommend using low tidal volume (Vt) ventilation (Vt 4-8 mL/kg of predicted body weight), over higher tidal volumes (Vt>8 mL/kg). | Strong |
| 31 | For mechanically ventilated adults with COVID-19 and ARDS , we recommend targeting plateau pressures (Pplat) of < 30 cm H ₂ O. | Strong |
| 32 | For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, we suggest using a higher PEEP strategy, over a lower PEEP strategy. Remarks: If using a higher PEEP strategy (i.e., PEEP > 10 cm H ₂ O), clinicians should monitor patients for barotrauma. | Strong |
| 33 | For mechanically ventilated adults with COVID-19 and ARDS, we suggest using a conservative fluid strategy over a liberal fluid strategy. | Weak |
| 34 | For mechanically ventilated adults with COVID-19 and moderate to severe ARDS , we suggest prone ventilation for 12 to 16 hours , over no prone ventilation. | Weak |
| 35.1 | For mechanically ventilated adults with COVID-19 and moderate to severe ARDS : We suggest using, as needed, intermittent boluses of neuromuscular blocking agents (NMBA), over continuous NMBA infusion, to facilitate protective lung ventilation. | Weak |
| 35.2 | In the event of persistent ventilator dyssynchrony, the need for ongoing deep sedation, prone ventilation, or persistently high plateau pressures, we suggest using a continuous NMBA infusion for up to 48 hours. | Weak |
| 36 | In mechanically ventilated adults with COVID-19 ARDS, we recommend against the routine use of inhaled nitric oxide. | Weak |
| 37 | In mechanically ventilated adults with COVID-19, severe ARDS and hypoxemia despite optimizing ventilation and other rescue strategies, we suggest a trial of inhaled pulmonary vasodilator as a rescue therapy; if no rapid improvement in oxygenation is observed, the treatment should be tapered off. | Weak |
| 38 | For mechanically ventilated adults with COVID-19 and hypoxemia despite optimizing ventilation, we suggest using recruitment maneuvers, over not using recruitment maneuvers. | Weak |
| 39 | If recruitment maneuvers are used, we recommend against using staircase (incremental PEEP) recruitment maneuvers. | Strong |
| 40 | In mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimizing ventilation, use of rescue therapies, and proning, we suggest using venovenous (VV) ECMO if available, or referring the patient to an ECMO center. Remark: Due to the resource-intensive nature of ECMO, and the need for experienced centers and healthcare workers, and infrastructure, ECMO should only be considered in carefully selected patients with COVID-19 and severe ARDS. | Weak |
| Therapy | | |
| 41 | In mechanically ventilated adults with COVID-19 and respiratory failure (without ARDS), we suggest against the routine use of systemic corticosteroids. | Weak |
| 42 | In mechanically ventilated adults with COVID-19 and ARDS , we suggest using systemic corticosteroids, over not using corticosteroids. | Weak |

| | | |
|------|---|-------------------|
| | <p>Remark: The majority of our panel support a weak recommendation (i.e. suggestion) to use steroids in the sickest patients with COVID-19 and ARDS. However, because of the very low-quality evidence, some experts on the panel preferred not to issue a recommendation until higher quality direct evidence is available.</p> | |
| 43 | <p>In mechanically ventilated patients with COVID-19 and respiratory failure, we suggest using empiric antimicrobials/antibacterial agents, over no antimicrobials.</p> <p>Remark: if the treating team initiates empiric antimicrobials, they should assess for de-escalation daily, and re-evaluate the duration of therapy and spectrum of coverage based on the microbiology results and the patient’s clinical status.</p> | Weak |
| 44 | <p>For critically ill adults with COVID-19 who develop fever, we suggest using acetaminophen/paracetamol for temperature control, over no treatment.</p> | Weak |
| 45 | <p>In critically ill adults with COVID-19, we suggest against the routine use of standard intravenous immunoglobulins (IVIG).</p> | Weak |
| 46 | <p>In critically ill adults with COVID-19, we suggest against the routine use of convalescent plasma.</p> | Weak |
| 47.1 | <p>In critically ill adults with COVID-19: we suggest against the routine use of lopinavir/ritonavir.</p> | Weak |
| 47.2 | <p>There is insufficient evidence to issue a recommendation on the use of other antiviral agents in critically ill adults with COVID-19.</p> | No recommendation |
| 48 | <p>There is insufficient evidence to issue a recommendation on the use of recombinant rIFNs, alone or in combination with antivirals, in critically ill adults with COVID-19.</p> | No recommendation |
| 49 | <p>There is insufficient evidence to issue a recommendation on the use of chloroquine or hydroxychloroquine in critically ill adults with COVID-19.</p> | No recommendation |
| 50 | <p>There is insufficient evidence to issue a recommendation on the use of tocilizumab in critically ill adults with COVID-19.</p> | No recommendation |