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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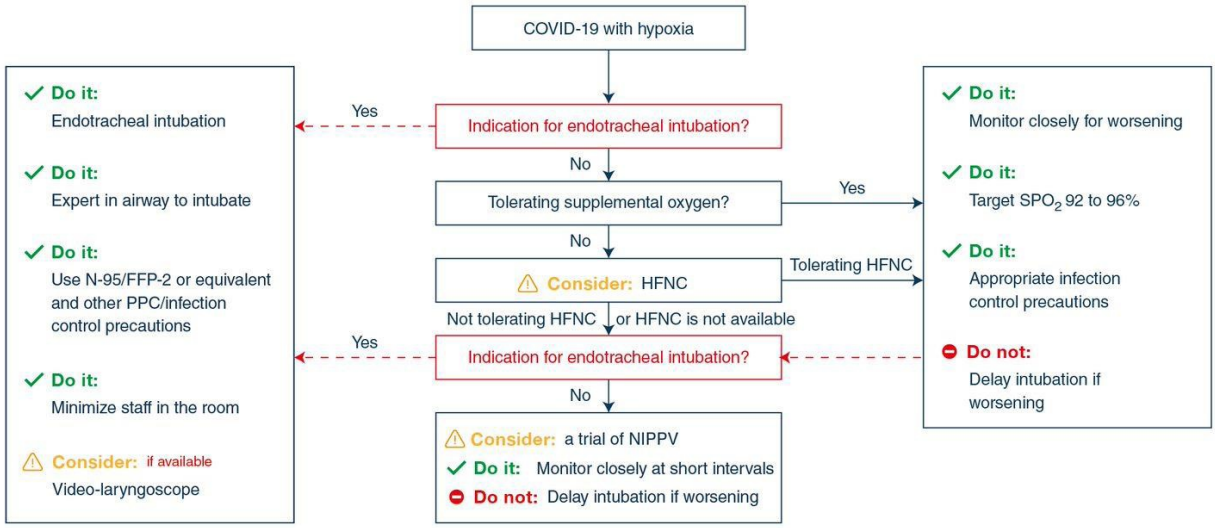

Figure 2.

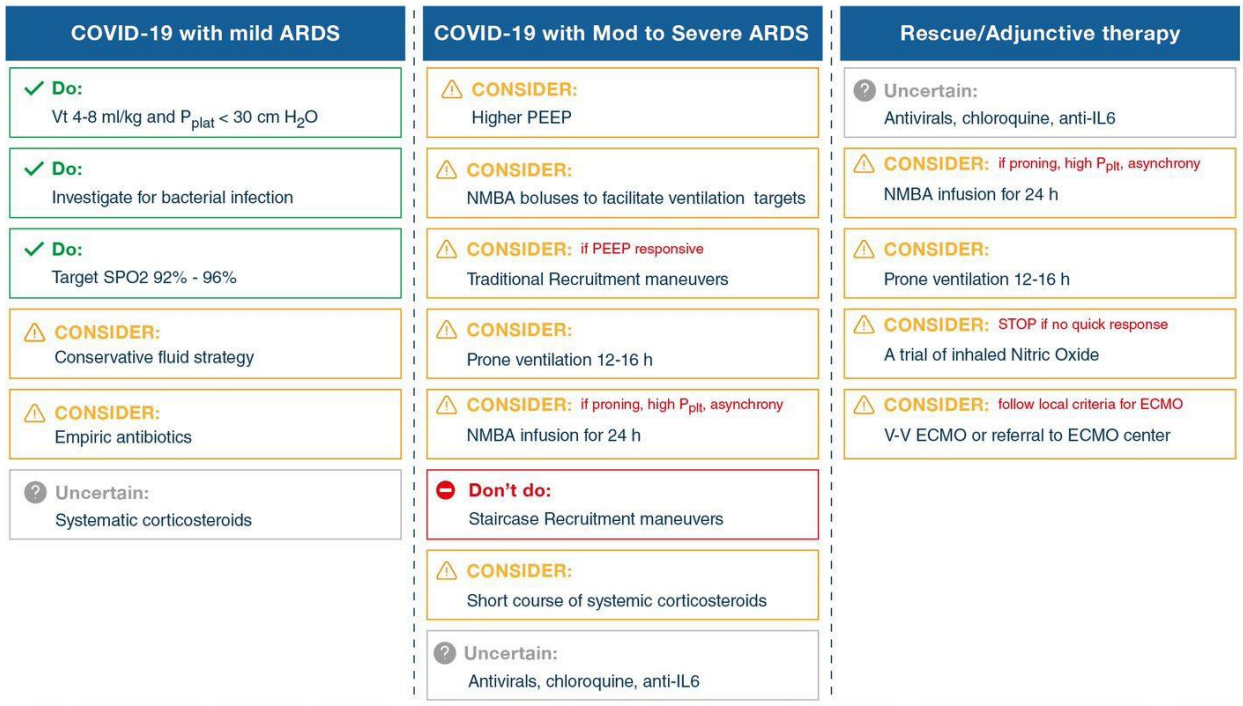

Figure 3.

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

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

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_2O.	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_2O), 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

	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.	
43	In mechanically ventilated patients with COVID-19 and respiratory failure, we **suggest** using empiric antimicrobials/antibacterial agents, over no antimicrobials. **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.	Weak
44	For critically ill adults with COVID-19 who develop fever, we **suggest** using acetaminophen/paracetamol for temperature control, over no treatment.	Weak
45	In critically ill adults with COVID-19, we **suggest against** the routine use of standard intravenous immunoglobulins (IVIG).	Weak
46	In critically ill adults with COVID-19, we **suggest against** the routine use of convalescent plasma.	Weak
47.1	In critically ill adults with COVID-19: we **suggest against** the routine use of lopinavir/ritonavir.	Weak
47.2	**There is insufficient evidence to issue a recommendation** on the use of other antiviral agents in critically ill adults with COVID-19.	No recommendation
48	**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.	No recommendation
49	**There is insufficient evidence to issue a recommendation** on the use of chloroquine or hydroxychloroquine in critically ill adults with COVID-19.	No recommendation
50	**There is insufficient evidence to issue a recommendation** on the use of tocilizumab in critically ill adults with COVID-19.	No recommendation