Introduction to Critical Care Management of Adults With COVID-19

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COVID-19 can progress to critical illness, including hypoxemic respiratory failure, acute respiratory distress syndrome (ARDS), septic shock, thromboembolic disease, renal and hepatic dysfunction, cardiac dysfunction, central nervous system disease, and exacerbation of underlying comorbidities in both adults and children.

In these Guidelines, many of the early recommendations for managing critically ill adults with COVID-19 were extrapolated from experience with other causes of sepsis and respiratory failure. However, the amount of research on the management of these patients has grown, and the COVID-19 Treatment Guidelines Panel’s (the Panel) current recommendations have been informed by that research.

Treating patients with COVID-19 in the intensive care unit (ICU) often requires managing underlying illnesses or COVID-19–related morbidities. Clinicians also need to focus on preventing ICU-related complications, as they would for any patient admitted to the ICU.

Selected Clinical Manifestations of COVID-19 Critical Illness

**Severe Pulmonary Disease**

Most patients who are critically ill with COVID-19 have severe pulmonary disease. Almost all of these patients meet the diagnostic criteria for ARDS. Patients with COVID-19 and severe pulmonary involvement often manifest extrapulmonary disease and exhibit laboratory markers of acute inflammation. Patients typically progress to critical illness 10 to 12 days after the onset of COVID-19 symptoms.

**Inflammatory Response**

Many critically ill patients with COVID-19 meet the criteria for virus-induced sepsis because they have life-threatening organ dysfunction related to a dysregulated host response to SARS-CoV-2 infection. Patients with COVID-19 may express increased levels of pro-inflammatory cytokines and anti-inflammatory cytokines, a condition that has been called “cytokine release syndrome” or a “cytokine storm,” but these terms are imprecise and misnomers. The magnitude of cytokine elevation in many critically ill patients with COVID-19 is modest compared to the levels in patients with sepsis and ARDS not related to COVID-19.

**Thromboembolic Events**

Prothrombotic states and higher rates of venous thromboembolic disease have been observed in adults who are critically ill with COVID-19. In some studies, thromboemboli were diagnosed in patients who received prophylactic doses of heparin. Autopsy studies provide additional evidence of thromboembolic disease and microvascular thrombosis in patients with COVID-19. See Antithrombotic Therapy in Patients With COVID-19 for a more detailed discussion.

**Renal and Hepatic Dysfunction**

Although SARS-CoV-2 is primarily a pulmonary pathogen, renal and hepatic dysfunction are consistently described in adults with severe COVID-19. In a cohort of critically ill adults in Brazil, the development of acute kidney injury that required renal replacement therapy was associated with a poor
prognosis. In addition, liver and renal dysfunction may be related to medication side effects or result from shock and poor oxygen delivery.

**Cardiac Dysfunction, Including Myocarditis**
The published literature describes cardiac injury or dysfunction in some (up to 24% in the early years of the pandemic) hospitalized adults with COVID-19. COVID-19 may be associated with an array of cardiovascular complications, including acute coronary syndrome, myocarditis, stress (takotsubo) cardiomyopathy, arrhythmias, and thromboembolic disease.

**Central and Peripheral Nervous System Dysfunction**
Neurologic manifestations in critically ill patients with acute COVID-19 include thromboembolic or hemorrhagic stroke, cerebral sinus venous thrombosis, seizure, myopathy, and meningoencephalitis. Neurologic manifestations are more common in patients with severe disease. Neuropathologic autopsy studies have reported both macrovascular and microvascular thrombosis with evidence of hypoxic ischemia. Guillain-Barré syndrome has been associated with recent SARS-CoV-2 infection. Critically ill patients with COVID-19 may present with delirium or develop delirium during hospitalization. Risk factors associated with delirium include the use of mechanical ventilation, restraints, benzodiazepines, opioids, vasopressors, and antipsychotics. Adequate management of critically ill patients with COVID-19 includes the use of best practices for sedation and monitoring for stroke.

**Multisystem Inflammatory Syndrome in Adults**
Case reports have described patients who had minimal respiratory symptoms during a recent or current SARS-CoV-2 infection but who were hospitalized with symptoms such as fever or signs of shock. Laboratory evidence indicated that these patients had severe inflammation. The patients also had signs of cardiovascular, gastrointestinal, dermatologic, and neurologic disease. This constellation of signs and symptoms has been designated multisystem inflammatory syndrome in adults (MIS-A). The Centers for Disease Control and Prevention has developed a case definition for MIS-A. This syndrome is similar to multisystem inflammatory syndrome in children (MIS-C), which has been well described.

A diagnosis of MIS-A may be made after other causes for the condition (e.g., bacterial sepsis) have been excluded. Although there are currently no controlled clinical trial data from patients with MIS-A to guide treatment of the syndrome, case reports have described the use of intravenous immunoglobulin, corticosteroids, or interleukin-1 inhibitor therapy. Some observational evidence supports the Panel’s recommendations for the therapeutic management of MIS-C, and those recommendations can be applied to MIS-A in most circumstances. See Therapeutic Management of Hospitalized Children With MIS-C, Plus a Discussion on MIS-A for more information.

**Other Complications Related to Intensive Care Units**
When treating patients with COVID-19, clinicians need to minimize the risk of conventional ICU complications. Patients who are critically ill with COVID-19 are at risk for nosocomial infections, such as ventilator-associated pneumonia, hospital-acquired pneumonia, and catheter-related bloodstream infections, and for other complications of critical illness care.

**Additional Considerations**

**Drug-Drug Interactions**
All patients in the ICU should be routinely monitored for drug-drug interactions. The potential for drug-drug interactions between investigational medications or any medications used off-label to treat...
COVID-19 and concurrent drugs should be considered.

**Sedation Management**

International guidelines provide recommendations on the prevention, detection, and treatment of pain, sedation, and delirium in ICU patients. Sedation management strategies, such as maintaining a light level of sedation (when appropriate) and minimizing sedative exposure, have shortened the duration of mechanical ventilation and the length of ICU stay among patients without COVID-19.

The Society of Critical Care Medicine (SCCM) ICU Liberation Campaign promotes the ICU Liberation Bundle (A–F) to improve post-ICU patient outcomes. The A–F Liberation Bundle includes the following elements:

A. Assess, prevent, and manage pain
B. Both spontaneous awakening trials and breathing trials
C. Choice of analgesia and sedation
D. Delirium: assess, prevent, and manage
E. Early mobility and exercise
F. Family engagement and empowerment

The A–F Liberation Bundle provides frontline staff with practical application strategies for each element, and an interprofessional team model should be used to incorporate the elements. This approach helps standardize communication among team members, improves survival, and reduces long-term cognitive dysfunction of patients. The elements of the A–F Liberation Bundle represent the steps required to implement the SCCM Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU.

Despite the known benefits of the A–F Liberation Bundle, its impact has not been directly assessed in patients with COVID-19. However, implementing the elements of the bundle should be encouraged to improve patient outcomes in the ICU.

Some factors may impede routine implementation of the A–F Liberation Bundle and increase the risk of ICU and post-ICU complications. For example, staff workload increases when patients with COVID-19 require prolonged mechanical ventilation, deep sedation, or neuromuscular blockade. In addition, drug shortages, which were common early in the pandemic, may affect the choice of analgesia or sedation. During a drug shortage, older sedatives that have prolonged durations of action and active metabolites are more likely to be prescribed.

**Post-Intensive Care Syndrome**

Post-intensive care syndrome (PICS) is a spectrum of physical, cognitive, and/or psychiatric disability that affects survivors of critical illness and persists after a patient leaves the ICU. Patients with PICS may present with varying levels of impairment, including profound muscle weakness (ICU-acquired weakness); problems with thinking and judgment (cognitive dysfunction); and mental health problems, such as problems sleeping, post-traumatic stress disorder (PTSD), depression, and anxiety. ICU-acquired weakness affects 33% of all patients who receive mechanical ventilation, 50% of patients with sepsis, and ≤50% of patients who remain in the ICU for ≥1 week. Cognitive dysfunction affects 30% to 80% of patients discharged from the ICU. About 50% of ICU survivors do not return to work within 1 year after discharge.

Although no single risk factor has been associated with PICS, there are opportunities to minimize
the risk of PICS through medication management (using the A–F Liberation Bundle), physical rehabilitation, follow-up clinics, family support, and improved education about the syndrome. PICS also affects family members who participate in the care of their loved ones. One study reported that a third of family members who had major decision-making roles experienced mental health problems, such as depression, anxiety, and post-traumatic stress disorder.\textsuperscript{40}

Some patients with COVID-19 who have been treated in the ICU express manifestations of PICS.\textsuperscript{41} Although specific therapies for PICS induced by COVID-19 are not yet available, health care providers should be aware that cognitive impairment or related problems may develop in patients who have had severe or critical COVID-19.

**Advance Care Planning and Goals of Care**

The advance care plans and the goals of care for all critically ill patients must be assessed at hospital admission and regularly thereafter. This is an essential element of care for all patients. Information on palliative care for patients with COVID-19 can be found at the [National Coalition for Hospice and Palliative Care](https://www.nationalcoalitionhospicepalliativecare.org) website.

To guide shared decision making in cases of serious illness, advance care planning should include identifying existing advance directives that outline a patient’s preferences and values. Values and care preferences should be discussed, documented, and revisited regularly for patients with or without prior directives. Specialty palliative care teams can facilitate communication between clinicians and surrogate decision makers, support frontline clinicians, and provide direct patient care services.

At hospital admission, surrogate decision makers should be identified for all critically ill patients with COVID-19. Early in the pandemic, infection-control policies for COVID-19 often created communication barriers for surrogate decision makers. At that time, most discussions between clinicians and surrogate decision makers about treatment options occurred through telecommunication. However, many of those policies have been rescinded, and health care providers and surrogate decision makers should communicate in person when possible.

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**References**


