

5: Care of Critically Ill Adult Patients With COVID-19

Last Updated: December 16, 2021

Summary Recommendations

Infection Control

- For health care workers who are performing aerosol-generating procedures on patients with COVID-19, the COVID-19 Treatment Guidelines Panel (the Panel) recommends using an N95 respirator (or equivalent or higher-level respirator) rather than surgical masks, in addition to other personal protective equipment (PPE) (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles) **(AIII)**.
- The Panel recommends minimizing the use of aerosol-generating procedures on intensive care unit patients with COVID-19 and carrying out any necessary aerosol-generating procedures in a negative-pressure room, also known as an airborne infection isolation room, when available **(AIII)**.
- For health care workers who are providing usual care for nonventilated patients with COVID-19, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator) or a surgical mask in addition to other PPE (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles) **(AIIa)**.
- For health care workers who are performing non-aerosol-generating procedures on patients with COVID-19 who are on closed-circuit mechanical ventilation, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator) in addition to other PPE (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles) because ventilator circuits may become disrupted unexpectedly **(BIII)**.
- The Panel recommends that endotracheal intubation in patients with COVID-19 be performed by health care providers with extensive airway management experience, if possible **(AIII)**.
- The Panel recommends that intubation be performed using video laryngoscopy, if possible **(CIIa)**.

Hemodynamics

- For adults with COVID-19 and shock, the Panel recommends using dynamic parameters, skin temperature, capillary refilling time, and/or lactate levels over static parameters to assess fluid responsiveness **(BIIa)**.
- For the acute resuscitation of adults with COVID-19 and shock, the Panel recommends using buffered/balanced crystalloids over unbalanced crystalloids **(BIIa)**.
- For the acute resuscitation of adults with COVID-19 and shock, the Panel **recommends against** the initial use of **albumin** for resuscitation **(BI)**.
- For adults with COVID-19 and shock, the Panel recommends **norepinephrine** as the first-line vasopressor **(AI)**.
- For adults with COVID-19 and shock, the Panel recommends titrating vasoactive agents to target a mean arterial pressure (MAP) of 60 to 65 mm Hg over higher MAP targets **(BI)**.
- The Panel **recommends against** using **hydroxyethyl starches** for intravascular volume replacement in patients with sepsis or septic shock **(AI)**.
- When norepinephrine is available, the Panel **recommends against** using **dopamine** for patients with COVID-19 and shock **(AI)**.
- As a second-line vasopressor, the Panel recommends adding either **vasopressin** (up to 0.03 units/min) **(BIIa)** or **epinephrine** **(BIIb)** to norepinephrine to raise MAP to target or adding **vasopressin** (up to 0.03 units/min) **(BIIa)** to decrease norepinephrine dosage.
- The Panel **recommends against** using **low-dose dopamine** for renal protection **(AI)**.
- The Panel recommends using **dobutamine** in patients who show evidence of cardiac dysfunction and persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents **(BIII)**.
- The Panel recommends that all patients who require vasopressors have an arterial catheter placed as soon as practical, if the resources to do so are available **(BIII)**.
- For adults with refractory septic shock who have completed a course of corticosteroids to treat their COVID-19, the Panel recommends using **low-dose corticosteroid therapy** (“shock-reversal”) over no corticosteroid therapy **(BIIa)**.

Oxygenation and Ventilation

- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel recommends high-flow nasal cannula (HFNC) oxygen over noninvasive ventilation (NIV) **(BIIa)**.

- For adults with COVID-19 and acute hypoxemic respiratory failure who do not have an indication for endotracheal intubation and for whom HFNC oxygen is not available, the Panel recommends performing a closely monitored trial of NIV (**BIIa**).
- For adults with persistent hypoxemia who require HFNC oxygen and for whom endotracheal intubation is not indicated, the Panel recommends a trial of awake prone positioning (**BIIa**).
- The Panel **recommends against** using awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation (**AIII**).
- If intubation becomes necessary, the procedure should be performed by an experienced practitioner in a controlled setting due to the enhanced risk of exposing health care practitioners to SARS-CoV-2 during intubation (**AIII**).
- For mechanically ventilated adults with COVID-19 and acute respiratory distress syndrome (ARDS):
 - The Panel recommends using low tidal volume (VT) ventilation (VT 4–8 mL/kg of predicted body weight) over higher VT ventilation (VT >8 mL/kg) (**AI**).
 - The Panel recommends targeting plateau pressures of <30 cm H₂O (**AIIa**).
 - The Panel recommends using a conservative fluid strategy over a liberal fluid strategy (**BIIa**).
 - The Panel **recommends against** the routine use of **inhaled nitric oxide** (**AIIa**).
- For mechanically ventilated adults with COVID-19 and moderate to severe ARDS:
 - The Panel recommends using a higher positive end-expiratory pressure (PEEP) strategy over a lower PEEP strategy (**BIIa**).
 - For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, the Panel recommends prone ventilation for 12 to 16 hours per day over no prone ventilation (**BIIa**).
 - The Panel recommends using, as needed, intermittent boluses of **neuromuscular blocking agents** (NMBAs) or a continuous NMBA infusion to facilitate protective lung ventilation (**BIIa**).
 - In the event of persistent patient-ventilator dyssynchrony, or in cases where a patient requires ongoing deep sedation, prone ventilation, or persistently high plateau pressures, the Panel recommends using a continuous **NMBA** infusion for up to 48 hours, as long as the patient's anxiety and pain can be adequately monitored and controlled (**BIII**).
- For mechanically ventilated adults with COVID-19, severe ARDS, and hypoxemia despite optimized ventilation and other rescue strategies:
 - The Panel recommends using recruitment maneuvers rather than not using recruitment maneuvers (**CIIa**).
 - If recruitment maneuvers are used, the Panel **recommends against** using staircase (incremental PEEP) recruitment maneuvers (**AIIa**).
 - The Panel recommends using an inhaled pulmonary vasodilator as a rescue therapy; if no rapid improvement in oxygenation is observed, the treatment should be tapered off (**CIII**).

Acute Kidney Injury and Renal Replacement Therapy

- For critically ill patients with COVID-19 who have acute kidney injury and who develop indications for renal replacement therapy, the Panel recommends continuous renal replacement therapy (CRRT), if available (**BIII**).
- If CRRT is not available or not possible due to limited resources, the Panel recommends prolonged intermittent renal replacement therapy rather than intermittent hemodialysis (**BIII**).

Pharmacologic Interventions

- In patients with COVID-19 and severe or critical illness, there is insufficient evidence for the Panel to recommend either for or against the use of empiric broad-spectrum antimicrobial therapy in the absence of another indication.
- If antimicrobials are initiated, the Panel recommends reassessing the need for them daily to minimize the adverse effects of unnecessary antimicrobial therapy (**AIII**).

Extracorporeal Membrane Oxygenation

- There is insufficient evidence for the Panel to recommend either for or against the use of extracorporeal membrane oxygenation for patients with COVID-19 and refractory hypoxemia.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

General Considerations

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Severe cases of COVID-19 may be associated with hypoxemic respiratory failure, acute respiratory distress syndrome (ARDS), septic shock, cardiac dysfunction, elevation in multiple inflammatory cytokines, thromboembolic disease, and/or exacerbation of underlying comorbidities. In addition to pulmonary disease, patients with COVID-19 may also experience cardiac, hepatic, renal, and central nervous system disease. Because patients with critical illness are likely to undergo aerosol-generating procedures, they should be placed in airborne infection isolation rooms, when available.

Guidance on diagnostic testing for SARS-CoV-2 can be found in the [Testing for SARS-CoV-2 Infection](#) section.

Most of the recommendations for the management of critically ill patients with COVID-19 are extrapolated from experience with other causes of sepsis.¹ Currently, there is limited information to suggest that the critical care management of patients with COVID-19 should differ substantially from the management of other critically ill patients; however, special precautions to prevent environmental contamination by SARS-CoV-2 are warranted.

As with any patient in the intensive care unit (ICU), successful clinical management of a patient with COVID-19 includes treating both the medical condition that initially resulted in ICU admission and other comorbidities and nosocomial complications.

Comorbid Conditions

Certain attributes and comorbidities (e.g., older age, cardiovascular disease, diabetes, chronic obstructive pulmonary disease, cancer, renal disease, obesity, sickle cell disease, receipt of a solid organ transplant) are associated with an increased risk of severe illness from COVID-19.²

Bacterial Superinfection of COVID-19-Associated Pneumonia

Limited information exists about the frequency and microbiology of pulmonary coinfections and superinfections in patients with COVID-19, such as hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). Some studies from China emphasize the lack of bacterial coinfections in patients with COVID-19, while other studies suggest that these patients experience frequent bacterial complications.³⁻⁸ There is appropriate concern about performing pulmonary diagnostic procedures such as bronchoscopy or other airway sampling procedures that require disruption of a closed airway circuit in patients with COVID-19. Thus, while some clinicians do not routinely start empiric broad-spectrum antimicrobial therapy for patients with severe COVID-19 disease, other experienced clinicians routinely use such therapy. However, empiric broad-spectrum antimicrobial therapy is the standard of care for the treatment of shock. Antibiotic stewardship is critical to avoid reflexive or continued courses of antibiotics.

Inflammatory Response Due to COVID-19

Patients with COVID-19 may express increased levels of pro-inflammatory cytokines and anti-inflammatory cytokines, which has previously been referred to as “cytokine release syndrome” or “cytokine storm,” although these are imprecise terms. However, these terms are misnomers because the magnitude of cytokine elevation in patients with COVID-19 is modest compared to that in patients with many other critical illnesses, such as sepsis and ARDS.^{9,10}

Patients with COVID-19 and severe pulmonary involvement are well described to also manifest extrapulmonary disease and to exhibit laboratory markers of acute inflammation. Patients with these

manifestations of severe pulmonary disease typically progress to critical illness 10 to 12 days after the onset of COVID-19 symptoms.

Multisystem Inflammatory Syndrome in Adults

In addition, there are case reports describing patients who had evidence of acute or recent SARS-CoV-2 infection (documented by a nucleic acid amplification test [NAAT] or antigen or antibody testing) with minimal respiratory symptoms, but with laboratory markers of severe inflammation (e.g., elevated C-reactive protein [CRP], ferritin, D-dimer, cardiac enzymes, liver enzymes, and creatinine) and various other symptoms, including fever and shock; and signs of cardiovascular, gastrointestinal, dermatologic, and neurologic disease. This constellation of signs and symptoms has been designated multisystem inflammatory syndrome in adults (MIS-A).¹¹ To date, most adults in whom MIS-A has been described have survived. This syndrome is similar to a syndrome previously described in children ([multisystem inflammatory syndrome in children \[MIS-C\]](#)).

MIS-A is defined by the following criteria:

1. A severe illness requiring hospitalization in an individual aged ≥ 21 years;
2. Current or past infection with SARS-CoV-2;
3. Severe dysfunction in one or more extrapulmonary organ systems;
4. Laboratory evidence of elevated inflammatory markers (e.g., CRP, ferritin, D-dimer, interleukin [IL]-6);
5. Absence of severe respiratory illness; *and*
6. Absence of an alternative unifying diagnosis.¹¹

Because there is no specific diagnostic test for MIS-A, diagnosis of this inflammatory syndrome is one of exclusion after other causes (e.g., septic shock) have been eliminated. Although there are currently no controlled clinical trial data in patients with MIS-A to guide treatment of the syndrome, case reports have described the use of intravenous immunoglobulin, corticosteroids, or anti-IL-6 therapy.

COVID-19-Induced Cardiac Dysfunction, Including Myocarditis

A growing body of literature describes cardiac injury or dysfunction in approximately 20% of patients who are hospitalized with COVID-19.^{4,6,12-15} COVID-19 may be associated with an array of cardiovascular complications, including acute coronary syndrome, myocarditis, arrhythmias, and thromboembolic disease.¹⁶

Thromboembolic Events and COVID-19

Critically ill patients with COVID-19 have been observed to have a prothrombotic state, which is characterized by the elevation of certain biomarkers, and there is an apparent increase in the incidence of venous thromboembolic disease in this population. In some studies, thromboemboli have been diagnosed in patients who received chemical prophylaxis with heparinoids.¹⁷⁻¹⁹ Autopsy studies provide additional evidence of both thromboembolic disease and microvascular thrombosis in patients with COVID-19.²⁰ Some authors have called for routine surveillance of ICU patients for venous thromboembolism.²¹ See the [Antithrombotic Therapy in Patients with COVID-19](#) section for a more detailed discussion.

Renal and Hepatic Dysfunction Due to COVID-19

Although SARS-CoV-2 is primarily a pulmonary pathogen, renal and hepatic dysfunction are consistently described in patients with severe COVID-19.⁴ In one case series of patients with critical disease, >15% of the patients required continuous renal replacement therapy.⁶ See the [Acute Kidney Injury and Renal](#)

[Replacement Therapy](#) section for a more detailed discussion.

Considerations in Children

Several large epidemiologic studies suggest that rates of ICU admission are substantially lower for children with COVID-19 than for adults with the disease. However, severe disease does occur in children.²²⁻²⁷ The risk factors for severe COVID-19 in children have not yet been established. Data from studies of adults with COVID-19 and extrapolation from data on other pediatric respiratory viruses suggest that children who are severely immunocompromised and those with underlying cardiopulmonary disease may be at higher risk for severe COVID-19.

MIS-C, the postinfectious complication of COVID-19 seen in some children, has been described.^{28,29} Certain symptoms of MIS-C often require ICU-level care, including blood pressure and inotropic support. These symptoms include severe abdominal pain, multisystem inflammation, shock, cardiac dysfunction, and, rarely, coronary artery aneurysm. A minority of children with MIS-C meet the criteria for typical or atypical Kawasaki disease. For details on MIS-C clinical features and the treatments that are being investigated, see the [Special Considerations in Children](#) section.

Interactions Between Drugs Used to Treat COVID-19 and Drugs Used to Treat Comorbidities

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

Sedation Management in Patients With COVID-19

International guidelines provide recommendations on the prevention, detection, and treatment of pain, sedation, and delirium.^{30,31} 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 stay in the ICU for patients without COVID-19.^{32,33}

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

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

The A-F Bundle also provides frontline staff with practical application strategies for each element.³⁴ The A-F Bundle should be incorporated using an interprofessional team model. This approach helps standardize communication among team members, improves survival, and reduces long-term cognitive dysfunction of patients.³⁵ Despite the known benefits of the A-F Bundle, its impact has not been directly assessed in patients with COVID-19; however, the use of the Bundle should be encouraged, when appropriate, to improve ICU patient outcomes. Prolonged mechanical ventilation of COVID-19 patients, coupled with deep sedation and potentially neuromuscular blockade, increases the workload of ICU staff. Additionally, significant drug shortages may force clinicians to use older sedatives with prolonged

durations of action and active metabolites, impeding routine implementation of the [PADIS Guidelines](#). This puts patients at additional risk for ICU and post-ICU complications.

Post-Intensive Care Syndrome

Patients with COVID-19 are reported to experience prolonged delirium and/or encephalopathy. Risk factors that are associated with delirium include the use of mechanical ventilation; the use of restraints; the use of benzodiazepine, opioid, and vasopressor infusions; and the use of antipsychotics.^{36,37} Neurological complications are associated with older age and underlying conditions, such as hypertension and diabetes mellitus.³⁸ Autopsy studies have reported both macrovascular and microvascular thrombosis, with evidence of hypoxic ischemia.³⁹ Adequate management requires careful attention to best sedation practices and vigilance in stroke detection.

Post-intensive care syndrome (PICS) is a spectrum of cognitive, psychiatric, and/or physical disability that affects survivors of critical illness and persists after a patient leaves the ICU.⁴⁰ 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 $\leq 50\%$ of patients who remain in the ICU for ≥ 1 week.⁴¹⁻⁴³ Cognitive dysfunction affects 30% to 80% of patients discharged from the ICU.⁴⁴⁻⁴⁶ About 50% of ICU survivors do not return to work within 1 year after discharge.⁴⁷ 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 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. In one study, a third of family members who had main decision-making roles experienced mental health problems, such as depression, anxiety, and PTSD.⁴⁸

Early reports suggest that some patients with COVID-19 who have been treated in the ICU express manifestations of PICS.⁴⁹ Although specific therapies for COVID-19-induced PICS are not yet available, physicians should maintain a high index of suspicion for cognitive impairment and other related problems in survivors of severe or critical COVID-19 illness.

Other Intensive Care Unit-Related Complications

Patients who are critically ill with COVID-19 are at risk for nosocomial infections and other complications of critical illness care, such as VAP, HAP, catheter-related bloodstream infections, and venous thromboembolism. When treating patients with COVID-19, clinicians also need to minimize the risk of conventional ICU complications to optimize the likelihood of a successful ICU outcome.

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 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 when needed.

Surrogate decision makers should be identified for all critically ill patients with COVID-19 at hospital admission. Infection-control policies for COVID-19 often create communication barriers for surrogate decision makers, and most surrogates will not be physically present when discussing treatment options with clinicians. Many decision-making discussions will occur via telecommunication.

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Infection Control

Last Updated: October 9, 2020

Health care workers should follow the infection control policies and procedures issued by their health care institutions.

Recommendation

- For health care workers who are performing aerosol-generating procedures on patients with COVID-19, the COVID-19 Treatment Guidelines Panel (the Panel) recommends using an N95 respirator (or equivalent or higher-level respirator) rather than surgical masks, in addition to other personal protective equipment (PPE) (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) **(AIII)**.
- Aerosol-generating procedures include endotracheal intubation and extubation, sputum induction, bronchoscopy, mini-bronchoalveolar lavage, open suctioning of airways, manual ventilation, unintentional or intentional ventilator disconnections, noninvasive positive pressure ventilation (NIPPV) (e.g., bilevel positive airway pressure [BiPAP], continuous positive airway pressure [CPAP]), cardiopulmonary resuscitation, and, potentially, nebulizer administration and high-flow oxygen delivery. Caution regarding aerosol generation is appropriate in situations such as tracheostomy and proning, where ventilator disconnections are likely to occur.

Rationale

During the severe acute respiratory syndrome (SARS) epidemic, aerosol-generating procedures increased the risk of infection among health care workers.^{1,2} N95 respirators block 95% to 99% of aerosol particles; however, medical staff must be fit-tested for the type used.³ Surgical masks block large particles, droplets, and sprays, but are less effective in blocking small particles (<5 µm) and aerosols.⁴

Recommendation

- The Panel recommends minimizing the use of aerosol-generating procedures on intensive care unit patients with COVID-19 and carrying out any necessary aerosol-generating procedures in a negative-pressure room, also known as an airborne infection isolation room (AIIR), when available **(AIII)**.
- The Panel recognizes that aerosol-generating procedures are necessary to perform in some patients, and that such procedures can be carried out with a high degree of safety if infection control guidelines are followed.

Rationale

AIIRs lower the risk of cross-contamination among rooms and lower the risk of infection for staff and patients outside the room when aerosol-generating procedures are performed. AIIRs were effective in preventing virus spread during the SARS epidemic.² If an AIIR is not available, a high-efficiency particulate air (HEPA) filter should be used, especially for patients on high-flow nasal cannula or noninvasive ventilation. HEPA filters reduce virus transmission in simulations.⁵

Recommendations

- For health care workers who are providing usual care for nonventilated patients with COVID-19, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator) or a surgical mask, in addition to other PPE (i.e., gloves, gown, and eye protection such as a face shield

or safety goggles) (**AIIa**).

- For health care workers who are performing non-aerosol-generating procedures on patients with COVID-19 who are on closed-circuit mechanical ventilation, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator) in addition to other PPE (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) because ventilator circuits may become disrupted unexpectedly (**BIII**).

Rationale

There is evidence from studies of viral diseases, including SARS, that both surgical masks and N95 respirators reduce the risk of transmission.⁶ Moreover, surgical masks are probably not inferior to N95 respirators for preventing the transmission of respiratory viral infections; a recent systematic review and meta-analysis of randomized controlled trials that compared the protective effects of medical masks and N95 respirators demonstrated that the use of medical masks did not increase the incidence of laboratory-confirmed viral respiratory infections (including coronavirus infections) or clinical respiratory illness.⁷

Recommendations

- The Panel recommends that endotracheal intubation in patients with COVID-19 be performed by health care providers with extensive airway management experience, if possible (**AIII**).
- The Panel recommends that intubation be performed using video laryngoscopy, if possible (**CIIa**).

Rationale

Practices that maximize the chances of first-pass success and minimize aerosolization should be used when intubating patients with suspected or confirmed COVID-19.^{8,9} Thus, the Panel recommends that the health care worker with the most experience and skill in airway management be the first to attempt intubation. The close facial proximity of direct laryngoscopy can expose health care providers to higher concentrations of viral aerosols. It is also important to avoid having unnecessary staff in the room during intubation procedures.

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Hemodynamics

Last Updated: July 8, 2021

Most of the hemodynamic recommendations below are similar to those previously published in the *Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016*. Ultimately, adult patients with COVID-19 who require fluid resuscitation or hemodynamic management of shock should be treated and managed identically to adult patients with septic shock.¹

Recommendation

- For adults with COVID-19 and shock, the COVID-19 Treatment Guidelines Panel (the Panel) recommends using dynamic parameters, skin temperature, capillary refilling time, and/or lactate levels over static parameters to assess fluid responsiveness (**BIIa**).

Rationale

In a systematic review and meta-analysis of 13 randomized clinical trials in intensive care unit (ICU) patients without COVID-19 (n = 1,652),² dynamic assessment to guide fluid therapy reduced mortality (risk ratio 0.59; 95% CI, 0.42–0.83), ICU length of stay (weighted mean difference -1.16 days; 95% CI, -1.97 to -0.36), and duration of mechanical ventilation (weighted mean difference -2.98 hours; 95% CI, -5.08 to -0.89). Dynamic parameters used in these trials included stroke volume variation (SVV), pulse pressure variation (PPV), and stroke volume change with passive leg raise or fluid challenge. Passive leg raising, followed by PPV and SVV, appears to predict fluid responsiveness with the greatest accuracy.³ The static parameters included components of early goal-directed therapy (e.g., central venous pressure, mean arterial pressure [MAP]).

Resuscitation of patients with shock who do not have COVID-19 based on serum lactate levels has been summarized in a systematic review and meta-analysis of seven randomized clinical trials (n = 1,301). Compared with central venous oxygen saturation-guided therapy, early lactate clearance-directed therapy was associated with a reduction in mortality (relative ratio 0.68; 95% CI, 0.56–0.82), shorter ICU stay (mean difference -1.64 days; 95% CI, -3.23 to -0.05), and shorter duration of mechanical ventilation (mean difference -10.22 hours; 95% CI, -15.94 to -4.50).⁴

Recommendation

- For the acute resuscitation of adults with COVID-19 and shock, the Panel recommends using buffered/balanced crystalloids over unbalanced crystalloids (**BIIa**).

Rationale

A pragmatic randomized trial compared the use of balanced and unbalanced crystalloids for intravenous (IV) fluid administration in critically ill adults without COVID-19 (n = 15,802). The rate of the composite outcome of death, new renal-replacement therapy, or persistent renal dysfunction was lower in the balanced crystalloids group than in the unbalanced crystalloids group (OR 0.90; 95% CI, 0.82–0.99; *P* = 0.04).⁵ A secondary analysis compared outcomes in a subset of patients with sepsis (n = 1,641). Compared to treatment with unbalanced crystalloids, treatment with balanced crystalloids resulted in fewer deaths (aOR 0.74; 95% CI, 0.59–0.93; *P* = 0.01) and more vasopressor-free and renal replacement-free days.⁶ A subsequent meta-analysis of 21 non-COVID-19 randomized controlled trials (n = 20,213) that included the pragmatic trial cited above compared balanced crystalloids to 0.9% saline for resuscitation of critically ill adults and children. The trial reported nonsignificant differences between the treatment groups in hospital mortality (OR 0.91; 95% CI, 0.83–1.01) and acute kidney injury (OR

0.92; 95% CI, 0.84–1.00).⁷

Recommendation

- For the acute resuscitation of adults with COVID-19 and shock, the Panel **recommends against** the initial use of **albumin** for resuscitation (**BI**).

Rationale

A meta-analysis of 20 non-COVID-19 randomized controlled trials (n = 13,047) that compared the use of albumin or fresh-frozen plasma to crystalloids in critically ill patients found no difference in all-cause mortality between the treatment groups.⁸ In contrast, a meta-analysis of 17 non-COVID-19 randomized controlled trials (n = 1,977) that compared the use of albumin to crystalloids specifically in patients with sepsis observed a reduction in mortality among the patients who received albumin (OR 0.82; 95% CI, 0.67–1.0; *P* = 0.047).⁹ Given the higher cost of albumin and the lack of a definitive clinical benefit, the Panel **recommends against** the routine use of **albumin** for initial acute resuscitation of patients with COVID-19 and shock (**BI**).

Recommendation

- For adults with COVID-19 and shock, the Panel recommends **norepinephrine** as the first-choice vasopressor (**AI**).

Rationale

Norepinephrine increases MAP due to its vasoconstrictive effects, with little change in heart rate and less increase in stroke volume compared to dopamine. Dopamine increases MAP and cardiac output, primarily due to an increase in stroke volume and heart rate. Norepinephrine is more potent than dopamine and may be more effective at reversing hypotension in patients with septic shock. Dopamine may be particularly useful in patients with compromised systolic function, but it causes more tachycardia and may be more arrhythmogenic than norepinephrine.¹⁰ It may also influence the endocrine response via the hypothalamic pituitary axis and have immunosuppressive effects.¹¹ A systematic review and meta-analysis of 11, non-COVID-19 randomized controlled trials that compared vasopressors used to treat patients with septic shock found that norepinephrine use resulted in lower all-cause mortality (RR 0.89; 95% CI, 0.81–0.98) and a lower risk of arrhythmias (RR 0.48; 95% CI, 0.40–0.58) than dopamine use.¹² Although the beta-1 activity of dopamine would be useful in patients with myocardial dysfunction, the greater risk of arrhythmias limits its use.^{13,14}

Recommendation

- For adults with COVID-19 and shock, the Panel recommends titrating vasoactive agents to target a MAP of 60 to 65 mm Hg, over higher MAP targets (**BI**).

Rationale

A recent individual patient-data meta-analysis of two, non-COVID-19 randomized controlled trials (n = 894) comparing higher versus lower blood pressure targets for vasopressor therapy in adult patients with shock reported no significant difference between the patients in the higher and lower target groups in 28-day mortality (OR 1.15; 95% CI, 0.87–1.52), 90-day mortality (OR 1.08; 95% CI, 0.84–1.44), myocardial injury (OR 1.47; 95% CI, 0.64–3.56), or limb ischemia (OR 0.92; 95% CI, 0.36–2.10).¹⁵ The risk of arrhythmias was increased in patients allocated to the higher target group (OR 2.50; 95% CI, 1.35–4.77). Similarly, the recently published “65 Trial,” a randomized clinical trial in patients without COVID-19 (n = 2,463), reported no significant difference in mortality between patients with

vasopressor therapy guided by a MAP target of 60 to 65 mm Hg and those with treatment guided by a higher, standard of care MAP target (41% vs. 43.8%; RR 0.93; 95% CI, 0.85–1.03).¹⁶ With an indication of improved outcome with lower MAP targets (and no firm indication of harm), the Panel recommends titrating vasoactive agents to a MAP target of 60 to 65 mm Hg (**BI**).

Additional Recommendations for Adults With COVID-19 and Shock Based on General Principles of Critical Care

- The Panel **recommends against** using hydroxyethyl starches for intravascular volume replacement in adult patients with COVID-19 and sepsis or septic shock (**AI**).
- When norepinephrine is available, the Panel **recommends against** using **dopamine** for adult patients with COVID-19 and shock (**AI**).
- As a second line vasopressor, the Panel recommends adding either **vasopressin** (up to 0.03 units/min) (**BIIa**) or **epinephrine** (**BIIb**) to norepinephrine to raise MAP to target or adding vasopressin (up to 0.03 units/min) (**BIIa**) to decrease norepinephrine dosage.
- The Panel **recommends against** using **low-dose dopamine** for renal protection (**AI**).
- The Panel recommends using **dobutamine** in adult patients with COVID-19 who show evidence of cardiac dysfunction and persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents (**BIII**).
- The Panel recommends that all adult patients with COVID-19 who require vasopressors have an arterial catheter placed as soon as practical, if resources are available (**BIII**).
- For adult patients with refractory septic shock who have completed a course of corticosteroids to treat COVID-19, the Panel recommends using low-dose corticosteroid therapy (“shock-reversal”) over no corticosteroid therapy (**BIIa**).
 - A typical corticosteroid regimen in septic shock is hydrocortisone 200 mg IV per day administered either as an infusion or in intermittent doses. The duration of hydrocortisone therapy is usually a clinical decision.
 - Adult patients who are receiving corticosteroids for COVID-19 are receiving sufficient replacement therapy such that they do not require additional hydrocortisone.

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Oxygenation and Ventilation

Last Updated: December 16, 2021

The COVID-19 Treatment Guidelines Panel's (the Panel) recommendations in this section were informed by the recommendations from the Surviving Sepsis Campaign Guidelines for managing [adult sepsis](#), [pediatric sepsis](#), and [COVID-19](#).

Severe illness in people with COVID-19 typically occurs approximately 1 week after the onset of symptoms. The most common symptom is dyspnea, which is often accompanied by hypoxemia. Patients with severe disease typically require supplemental oxygen and should be monitored closely for worsening respiratory status, because some patients may progress to acute respiratory distress syndrome (ARDS).

Goal of Oxygenation

The optimal oxygen saturation (SpO₂) in adults with COVID-19 who are receiving supplemental oxygen is unknown. However, a target SpO₂ of 92% to 96% seems logical, considering that indirect evidence from patients without COVID-19 suggests that an SpO₂ of <92% or >96% may be harmful.

The potential harm of maintaining an SpO₂ of <92% was demonstrated during a trial that randomly assigned patients with ARDS who did not have COVID-19 to either a conservative oxygen strategy (target SpO₂ of 88% to 92%) or a liberal oxygen strategy (target SpO₂ of ≥96%). The trial was stopped early due to futility after enrolling 205 patients, but increased mortality was observed at Day 90 in the conservative oxygen strategy arm (between-group risk difference of 14%; 95% CI, 0.7% to 27%) and a trend toward increased mortality was observed at Day 28 (between-group risk difference of 8%; 95% CI, -5% to 21%).¹

The results of a meta-analysis of 25 randomized trials that involved patients without COVID-19 demonstrate the potential harm of maintaining an SpO₂ of >96%. This study found that a liberal oxygen strategy (median SpO₂ of 96%) was associated with an increased risk of in-hospital mortality when compared to a more conservative SpO₂ strategy (relative risk 1.21; 95% CI, 1.03–1.43).²

Acute Hypoxemic Respiratory Failure

In adults with COVID-19 and acute hypoxemic respiratory failure, conventional oxygen therapy may be insufficient to meet the oxygen needs of the patient. Options for providing enhanced respiratory support include high-flow nasal canula (HFNC) oxygen, noninvasive ventilation (NIV), intubation and mechanical ventilation, or extracorporeal membrane oxygenation. In this section, mechanical ventilation refers to the delivery of positive pressure ventilation through an endotracheal or tracheostomy tube. NIV refers to the delivery of positive pressure ventilation through a noninvasive interface, such as a face mask or nasal mask.

Nonmechanically Ventilated Adults With Acute Hypoxemic Respiratory Failure

High-Flow Nasal Cannula Oxygen and Noninvasive Ventilation

Recommendations

- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel recommends HFNC oxygen over NIV (**BIIa**).
- For adults with COVID-19 and acute hypoxemic respiratory failure who do not have an indication for endotracheal intubation and for whom HFNC oxygen is not available, the Panel recommends performing a closely monitored trial of NIV (**BIIa**).

Rationale

HFNC oxygen is preferred over NIV in patients with acute hypoxemic respiratory failure; this guidance is based on data from an unblinded clinical trial in patients without COVID-19 who had acute hypoxemic respiratory failure. Study participants were randomized to receive HFNC oxygen, conventional oxygen therapy, or NIV. The patients in the HFNC oxygen arm had more ventilator-free days (mean of 24 days) than those in the conventional oxygen therapy arm (mean of 22 days) or NIV arm (mean of 19 days; $P = 0.02$). In addition, 90-day mortality was lower in the HFNC oxygen arm than in either the conventional oxygen therapy arm (HR 2.01; 95% CI, 1.01–3.99) or the NIV arm (HR 2.50; 95% CI, 1.31–4.78).³ In the subgroup of more severely hypoxemic patients (those with a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen [$\text{PaO}_2/\text{FiO}_2$] ≤ 200 mm Hg), the intubation rate was lower for the HFNC oxygen arm than for the conventional oxygen therapy or NIV arms (HR 2.07 and 2.57, respectively).

The trial's findings were corroborated by a meta-analysis of 8 trials with 1,084 participants that was conducted to assess the effectiveness of oxygenation strategies prior to intubation. Compared to NIV, HFNC oxygen reduced the rate of intubation (OR 0.48; 95% CI, 0.31–0.73) and intensive care unit (ICU) mortality (OR 0.36; 95% CI, 0.20–0.63).⁴

NIV is an aerosol-generating procedure, and it may increase the risk of nosocomial transmission of SARS-CoV-2.^{5,6} It remains unclear whether the use of HFNC oxygen results in a lower risk of nosocomial SARS-CoV-2 transmission than NIV.

Awake Prone Positioning in Nonmechanically Ventilated Adults

Recommendations

- For patients with persistent hypoxemia who require HFNC oxygen and for whom endotracheal intubation is not indicated, the Panel recommends a trial of awake prone positioning (**BIIa**).
- The Panel **recommends against** using awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation (**AIII**).

Additional Considerations

- Patients who can adjust their position independently and tolerate lying prone can be considered for awake prone positioning.
- Awake prone positioning is acceptable and feasible for pregnant patients and can be performed in the left lateral decubitus position or the fully prone position.⁷
- Some patients do not tolerate awake prone positioning. Failure rates as high as 63% have been reported in the literature.⁸
- Awake proning **should not be used** as a substitute for intubation and mechanical ventilation in patients with refractory hypoxemia who otherwise meet the indications for these interventions.
- Awake proning may be infeasible or impractical in patients with:
 - Spinal instability
 - Facial or pelvic fractures
 - An open chest or unstable chest wall
- Awake prone positioning should be used with caution in patients with confusion or delirium, hemodynamic instability, an inability to independently change position, recent abdominal surgery, or recent nausea or vomiting.

Rationale

Awake proning, or having a nonintubated patient lie on their stomach, may improve oxygenation and prevent the patient from progressing to requiring intubation and mechanical ventilation. Although prone positioning has been shown to improve oxygenation and outcomes in patients with moderate to severe ARDS who are receiving mechanical ventilation,^{9,10} there is less evidence regarding the benefit of prone positioning in awake patients who require supplemental oxygen without mechanical ventilation. Several case series of patients with COVID-19 who required oxygen or NIV have similarly reported that awake prone positioning improves oxygenation,¹¹⁻¹⁴ and some series have also reported low intubation rates after proning.^{11,13}

The Awake Prone Positioning Meta-Trial Group conducted the largest trial to date on awake prone positioning. This was a prospective, multinational meta-trial of 6 open-label, randomized controlled superiority trials that compared awake prone positioning to standard care in adults who required HFNC oxygen for acute hypoxemic respiratory failure due to COVID-19.

The study enrolled 1,126 patients between April 2, 2020, and January 26, 2021; the intention-to-treat analysis included 1,121 patients. Two hundred twenty-three of 564 patients (40%) who underwent awake prone positioning met the primary composite outcome of intubation or death within 28 days of enrollment; among the 557 patients who received standard care, 257 (46%) met the primary endpoint (relative risk 0.86; 95% CI, 0.75–0.98). Regarding the individual components of the composite endpoint, the incidence of intubation at Day 28 was lower in the awake prone positioning arm than in the standard care arm (HR for intubation 0.75; 95% CI, 0.62–0.91). There was no difference in 28-day mortality between the awake prone positioning arm and the standard care arm (HR for mortality 0.87; 95% CI, 0.68–1.11). During the first 14 days of the study, the median daily duration of awake prone positioning was 5.0 hours (IQR 1.6–8.8 hours). However, the median daily duration varied from 1.6 hours to 8.6 hours across the individual trials. Longer daily durations for awake prone positioning occurred more frequently in patients who experienced treatment success by Day 28. This study evaluated the incidences of certain adverse events, including skin breakdown, vomiting, and central or arterial line dislodgement. These events occurred infrequently during the study, and the incidences for these events were similar between the arms. No cardiac arrests occurred during awake prone positioning.¹⁵

Though the optimal daily duration of awake prone positioning is unclear, only 25 of 151 patients (17%) who had an average of ≥ 8 hours of awake prone positioning per day met the primary endpoint of intubation or death in the Awake Prone Positioning Meta-Trial, compared with 198 of 413 patients (48%) who remained in awake prone positioning for < 8 hours per day. This is consistent with past clinical trials of prone positioning in mechanically ventilated patients with ARDS, during which clinical benefits were observed with longer durations of prone positioning.^{9,10}

Intubation for Mechanical Ventilation

Recommendation

- If intubation becomes necessary, the procedure should be performed by an experienced practitioner in a controlled setting due to the enhanced risk of exposing health care practitioners to SARS-CoV-2 during intubation (**AIII**).

Rationale

It is essential to closely monitor hypoxemic patients with COVID-19 for signs of respiratory decompensation. To ensure the safety of both patients and health care workers, intubation should be performed in a controlled setting by an experienced practitioner.

Mechanically Ventilated Adults

General Considerations

Recommendations

For mechanically ventilated adults with COVID-19 and ARDS:

- The Panel recommends using low tidal volume (VT) ventilation (VT 4–8 mL/kg of predicted body weight) over higher VT ventilation (VT >8 mL/kg) (**AI**).
- The Panel recommends targeting plateau pressures of <30 cm H₂O (**AIIa**).
- The Panel recommends using a conservative fluid strategy over a liberal fluid strategy (**BIIa**).
- The Panel **recommends against** the routine use of **inhaled nitric oxide** (**AIIa**).

Rationale

There is no evidence that ventilator management of patients with hypoxemic respiratory failure due to COVID-19 should differ from ventilator management of patients with hypoxemic respiratory failure due to other causes.

Positive End-Expiratory Pressure and Prone Positioning in Mechanically Ventilated Adults With Moderate to Severe Acute Respiratory Distress Syndrome

Recommendations

For mechanically ventilated adults with COVID-19 and moderate to severe ARDS:

- The Panel recommends using a higher positive end-expiratory pressure (PEEP) strategy over a lower PEEP strategy (**BIIa**).
- For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, the Panel recommends prone ventilation for 12 to 16 hours per day over no prone ventilation (**BIIa**).

Rationale

PEEP is beneficial in patients with ARDS because it prevents alveolar collapse, improves oxygenation, and minimizes atelectotrauma, a source of ventilator-induced lung injury. A meta-analysis of individual patient data from the 3 largest trials that compared lower and higher levels of PEEP in patients without COVID-19 found lower rates of ICU mortality and in-hospital mortality with higher levels of PEEP in those with moderate (PaO₂/FiO₂ 100–200 mm Hg) and severe ARDS (PaO₂/FiO₂ <100 mm Hg).¹⁶

Although there is no clear standard as to what constitutes a high level of PEEP, a conventional threshold is >10 cm H₂O.¹⁷ Recent reports have suggested that, in contrast to patients with non-COVID-19 causes of ARDS, some patients with moderate or severe ARDS due to COVID-19 have normal static lung compliance. In these patients, higher PEEP levels may cause harm by compromising hemodynamics and cardiovascular performance.^{18,19} Other studies reported that patients with moderate to severe ARDS due to COVID-19 had low lung compliance, similar to the lung compliance seen in patients with conventional ARDS.^{20–23} These seemingly contradictory observations suggest that COVID-19 patients with ARDS are a heterogeneous population, and assessment for responsiveness to higher levels of PEEP should be individualized based on oxygenation and lung compliance. Clinicians should monitor patients for known side effects of higher levels of PEEP, such as barotrauma and hypotension.

In the pre-pandemic PROSEVA study of patients with moderate or severe early ARDS (PaO₂/FiO₂ <150 mm Hg) who required mechanical ventilation, the patients who were randomized to undergo prone positioning for ≥16 hours per day had improved survival compared to those who remained in the supine

position throughout their course of mechanical ventilation.⁹ A meta-analysis evaluated the results of the PROSEVA study and 7 other randomized controlled trials that investigated the use of prone positioning in people with ARDS. The subgroup analysis revealed that patients who remained prone for ≥ 12 hours per day had a lower mortality rate than those who remained in the supine position (risk ratio 0.74; 95% CI, 0.56–0.99). Prone positioning improved oxygenation in all of the trials; patients in the prone positioning arms had higher PaO₂/FiO₂ on Day 4 than those in the supine positioning arms (mean difference of 23.5 mm Hg; 95% CI, 12.4–34.5).²⁴

The use of prone positioning may be associated with serious adverse events, including unplanned extubation or central catheter removal; however, the meta-analysis found no differences in the frequencies of these events between the prone positioning and supine positioning arms. The use of prone positioning was associated with an increase in the frequency of pressure sores (risk ratio 1.22; 95% CI, 1.06–1.41) and endotracheal tube obstruction (risk ratio 1.76; 95% CI, 1.24–2.50) in the 3 studies that evaluated these complications.

Neuromuscular Blockade in Mechanically Ventilated Adults With Moderate to Severe Acute Respiratory Distress Syndrome

Recommendations

For mechanically ventilated adults with COVID-19 and moderate to severe ARDS:

- The Panel recommends using, as needed, intermittent boluses of **neuromuscular blocking agents** (NMBA) or a continuous NMBA infusion to facilitate protective lung ventilation (**BIIa**).
- In the event of persistent patient-ventilator dyssynchrony, or in cases where a patient requires ongoing deep sedation, prone ventilation, or persistently high plateau pressures, the Panel recommends using a continuous **NMBA** infusion for up to 48 hours, as long as the patient's anxiety and pain can be adequately monitored and controlled (**BIII**).

Rationale

The recommendation for intermittent boluses of NMBA or a continuous infusion of NMBA to facilitate lung protection may require a health care provider to enter the patient's room frequently for close clinical monitoring. Therefore, in some situations, the risks of SARS-CoV-2 exposure and the need to use personal protective equipment for each entry into a patient's room may outweigh the benefit of NMBA treatment.

Rescue Therapies for Mechanically Ventilated Adults With Acute Respiratory Distress Syndrome

Recommendations

For mechanically ventilated adults with COVID-19, severe ARDS, and hypoxemia despite optimized ventilation and other rescue strategies:

- The Panel recommends using recruitment maneuvers rather than not using recruitment maneuvers (**CIIa**).
- If recruitment maneuvers are used, the Panel **recommends against** using staircase (incremental PEEP) recruitment maneuvers (**AIIa**).
- The Panel recommends using an inhaled pulmonary vasodilator as a rescue therapy; if no rapid improvement in oxygenation is observed, the treatment should be tapered off (**CIII**).

Rationale

A recruitment maneuver refers to a temporary increase in airway pressure during mechanical

ventilation to open collapsed alveoli and improve oxygenation. No studies have assessed the effect of recruitment maneuvers on oxygenation in severe ARDS due to COVID-19. However, a systematic review and meta-analysis of 6 trials of recruitment maneuvers in patients with ARDS who did not have COVID-19 found that recruitment maneuvers reduced mortality, improved oxygenation 24 hours after the maneuver, and decreased the need for rescue therapy.²⁵ Because recruitment maneuvers can cause barotrauma or hypotension, patients should be closely monitored during recruitment maneuvers. If a patient decompensates during recruitment maneuvers, the maneuver should be stopped immediately. The importance of properly performing recruitment maneuvers was illustrated by an analysis of 8 randomized controlled trials in patients without COVID-19 (n = 2,544) that found that recruitment maneuvers did not reduce hospital mortality (risk ratio 0.90; 95% CI, 0.78–1.04). A subgroup analysis found that traditional recruitment maneuvers significantly reduced hospital mortality (risk ratio 0.85; 95% CI, 0.75–0.97), whereas incremental PEEP titration recruitment maneuvers increased mortality (risk ratio 1.06; 95% CI, 0.97–1.17).²⁶

Although there are no published studies of inhaled nitric oxide in patients with COVID-19, a Cochrane review of 13 trials that evaluated inhaled nitric oxide use in patients with ARDS found no mortality benefit.²⁷ Because the review showed a transient benefit for oxygenation, it is reasonable to attempt using inhaled nitric oxide as a rescue therapy in patients with COVID-19 and severe ARDS after other options have failed. However, if the use of nitric oxide does not improve a patient's oxygenation, it should be tapered quickly to avoid rebound pulmonary vasoconstriction, which may occur when nitric oxide is discontinued after prolonged use.

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Acute Kidney Injury and Renal Replacement Therapy

Last Updated: December 17, 2020

Recommendations

- For critically ill adults with COVID-19 who have acute kidney injury (AKI) and who develop indications for renal replacement therapy (RRT), the COVID-19 Treatment Guidelines Panel (the Panel) recommends continuous renal replacement therapy (CRRT), if available **(BIII)**.
- If CRRT is not available or not possible due to limited resources, the Panel recommends prolonged intermittent renal replacement therapy (PIRRT) rather than intermittent hemodialysis (IHD) **(BIII)**.

Rationale

AKI that requires RRT occurs in approximately 22% of patients with COVID-19 who are admitted to the intensive care unit.¹ Evidence pertaining to RRT in patients with COVID-19 is scarce. Until additional evidence is available, the Panel suggests using the same indications for RRT in patients with COVID-19 as those used for other critically ill patients.²

RRT modalities have not been compared in COVID-19 patients; the Panel's recommendations are motivated by the desire to minimize the risk of viral transmission to health care workers. The Panel considers CRRT to be the preferred RRT modality. CRRT is preferable to PIRRT because medication dosing for CRRT is more easily optimized and CRRT does not require nursing staff to enter the patient's room to begin and end dialysis sessions. CRRT and PIRRT are both preferable to IHD because neither requires a dedicated hemodialysis nurse.³ Peritoneal dialysis has also been used during surge situations in patients with COVID-19.

In situations where there may be insufficient CRRT machines or equipment to meet demand, the Panel advocates performing PIRRT instead of CRRT, and then using the machine for another patient after appropriate cleaning.

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Pharmacologic Interventions

Last Updated: July 8, 2021

Therapeutic Management of Adults with COVID-19

See [Therapeutic Management of Hospitalized Adults with COVID-19](#) for the COVID-19 Treatment Guidelines Panel's (the Panel) recommendations on when to use the following drugs alone or in combination: baricitinib, dexamethasone, remdesivir, and tocilizumab.

Immune-Based Therapy

See the [Immunomodulators](#) sections for additional recommendations regarding the use of immunomodulators not listed above.

Adjunctive Therapy

Recommendations regarding adjunctive therapy in the critical care setting, including antithrombotic therapy and vitamin C, can be found in [Antithrombotic Therapy in Patients With COVID-19](#) and in the [Supplements](#) sections.

Empiric Broad-Spectrum Antimicrobial Therapy

Recommendations

- In patients with severe or critical COVID-19, there is insufficient evidence for the Panel to recommend either for or against empiric broad-spectrum antimicrobial therapy in the absence of another indication.
- If antimicrobials are initiated, the Panel recommends that their use should be reassessed daily to minimize the adverse consequences of unnecessary antimicrobial therapy (**AIII**).

Rationale

At this time, there are no reliable estimates of the incidence or prevalence of copathogens with SARS-CoV-2.

Some experts routinely administer broad-spectrum antibiotics as empiric therapy for bacterial pneumonia to all patients with COVID-19 and moderate or severe hypoxemia. Other experts administer antibiotics only for specific situations, such as the presence of a lobar infiltrate on a chest X-ray, leukocytosis, an elevated serum lactate level, microbiologic data, or shock.

Gram stain, culture, or other testing of respiratory specimens is often not available due to concerns about aerosolization of SARS-CoV-2 during diagnostic procedures or when processing specimens.

There are no clinical trials that have evaluated the use of empiric antimicrobial agents in patients with COVID-19 or other severe coronavirus infections.

Extracorporeal Membrane Oxygenation

Last Updated: December 17, 2020

Recommendation

- There is insufficient evidence to recommend either for or against the use of extracorporeal membrane oxygenation (ECMO) in adults with COVID-19 and refractory hypoxemia.

Rationale

ECMO has been used as a short-term rescue therapy in patients with acute respiratory distress syndrome (ARDS) caused by COVID-19 and refractory hypoxemia. However, there is no conclusive evidence that ECMO is responsible for better clinical outcomes regardless of the cause of hypoxemic respiratory failure.¹⁻⁴

The clinical outcomes for patients with ARDS who are treated with ECMO are variable and depend on multiple factors, including the etiology of hypoxemic respiratory failure, the severity of pulmonary and extrapulmonary illness, the presence of comorbidities, and the ECMO experience of the individual center.⁵⁻⁷ A recent case series of 83 COVID-19 patients in Paris reported a 60-day mortality of 31% for patients on ECMO.⁸ This mortality was similar to the mortality observed in a 2018 study of non-COVID-19 patients with ARDS who were treated with ECMO during the ECMO to Rescue Lung Injury in Severe ARDS (EOLIA) trial; that study reported a mortality of 35% at Day 60.³

The Extracorporeal Life Support Organization (ELSO) Registry provides the largest multicenter outcome dataset of patients with confirmed COVID-19 who received ECMO support and whose data were voluntarily submitted. A recent cohort study evaluated ELSO Registry data for 1,035 COVID-19 patients who initiated ECMO between January 16 and May 1, 2020, at 213 hospitals in 36 countries. This study reported an estimated cumulative in-hospital mortality of 37.4% in these patients 90 days after they initiated ECMO (95% CI; 34.4% to 40.4%).⁹ Without a controlled trial that evaluates the use of ECMO in patients with COVID-19 and hypoxemic respiratory failure (e.g., ARDS), the benefits of ECMO cannot be clearly defined for this patient population.

Ideally, clinicians who are interested in using ECMO should try to enter their patients into clinical trials or clinical registries so that more informative data can be obtained. The following resources provide more information on the use of ECMO in patients with COVID-19:

- [The ELSO ECMO in COVID-19 website](#)
- A list of [clinical trials that are evaluating ECMO in patients with COVID-19](#) on [ClinicalTrials.gov](#)

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