JAMA Clinical Guidelines Synopsis

Management of Critically Ill Adults With COVID-19

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GUIDELINE TITLE Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults With COVID-19

DEVELOPER Surviving Sepsis Campaign (SSC)

RELEASE DATE March 23, 2020

TARGET POPULATION Critically ill adults with COVID-19

SELECTED MAJOR RECOMMENDATIONS

Infection Control and Testing

1. For health care workers performing aerosol-generating procedures (eg, endotracheal intubation, nebulized treatments, open suctioning) use of fitted respirator masks is recommended (N95 respirators, FFP2), instead of surgical masks, in addition to other personal protective equipment (PPE) (best practice statement).
2. For usual care of nonventilated patients, or for performing non–aerosol-generating procedures on patients receiving mechanical ventilation, use of medical masks is recommended, instead of respirator masks, in addition to other PPE (weak recommendation, low-quality evidence [LQE]).
3. Diagnostic lower respiratory tract samples (endotracheal aspirates) are preferred over bronchial washings, bronchoalveolar lavage, and upper respiratory tract (nasopharyngeal or oropharyngeal) samples (weak recommendation, LQE).

Hemodynamic Support

1. For acute resuscitation of adults with shock, the following are suggested: measuring dynamic parameters to assess fluid responsiveness (weak recommendation, LQE), using a conservative fluid administration strategy (weak recommendation, very LQE), and using crystalloids over colloids (strong recommendation; moderate QE). Balanced crystalloids are preferred over unbalanced crystalloids (weak recommendation, moderate QE).
2. For adults with shock, the following are suggested: using norepinephrine as the first-line vasoactive (weak recommendation, LQE), use of either vasopressin or epinephrine as the first line if norepinephrine is not available (weak recommendation, LQE). Dopamine is not recommended if norepinephrine is not available (strong recommendation, high QE). Adding vasopressin as a second-line agent is suggested if the target (60-65 mm Hg) mean arterial pressure cannot be achieved by norepinephrine alone (weak recommendation, moderate QE).

Ventilatory Support

1. Starting supplemental oxygen is recommended if the Spo_2 is less than 90% (strong recommendation, moderate QE). Spo_2 should be maintained no higher than 96% (strong recommendation, moderate QE).
2. For acute hypoxemic respiratory failure despite conventional oxygen therapy, use of high-flow nasal cannula (HFNC) is suggested relative to conventional oxygen therapy and noninvasive positive pressure ventilation (NIPPV) (weak recommendation, LQE). If HFNC is not available, a trial of NIPPV is suggested (weak recommendation, very LQE). Close monitoring for worsening of respiratory status and early intubation if worsening occurs is recommended (best practice statement).
3. For adults receiving mechanical ventilation who have acute respiratory distress syndrome (ARDS), use of low tidal volume ventilation (4-8 mL/kg of predicted body weight) is recommended and preferred over higher tidal volumes (>8 mL/kg) (strong recommendation, moderate QE). Targeting plateau pressures of <30 cm H_2O (strong recommendation, moderate QE) is recommended. Using a higher positive end-expiratory pressure (PEEP) strategy over lower PEEP strategy is suggested (weak recommendation, LQE).
4. For adults receiving mechanical ventilation who have moderate to severe ARDS, prone ventilation for 12 to 16 hours is suggested over no prone ventilation (weak recommendation, LQE). Using as-needed neuromuscular blocking agents (NMBAs) instead of continuous NMBA infusion to facilitate protective lung ventilation is suggested (weak recommendation, LQE).
5. For adults receiving mechanical ventilation who have severe ARDS and hypoxemia despite optimizing ventilation, a trial of inhaled pulmonary vasodilator is suggested. If no rapid improvement in oxygenation is observed, the treatment should be tapered (weak recommendation, very LQE). The use of lung recruitment maneuvers (intended to open otherwise closed lung segments, such as 40 cm H_2O inspiratory hold for 40 seconds) is suggested, over not using recruitment maneuvers (weak recommendation, LQE), but using staircase (incremental PEEP) recruitment maneuvers is not recommended (strong recommendation, moderate QE). Use of veno-venous circulation for extracorporeal membrane oxygenation (ECMO) or referral to an ECMO center is suggested, if available, for selected patients (weak recommendation, LQE).

Therapy

1. In adults receiving mechanical ventilation who do not have ARDS, routine use of systematic corticosteroids is suggested against (weak recommendation, LQE). In those with ARDS, use of corticosteroids is suggested (weak recommendation, LQE).
2. In COVID-19 patients receiving mechanical ventilation who have respiratory failure, use of empiric antimicrobial/antibacterial agents is suggested (no evidence rating); assess for deescalation.
3. In critically ill adults with fever, use of pharmacologic agents for temperature control is suggested over nonpharmacologic agents or no treatment. Routine use of standard IV immunoglobulins is not suggested. Convalescent plasma is not suggested. There is insufficient evidence to issue a recommendation on use of any of the following: antiviral agents, recombinant interferons, chloroquine/hydroxychloroquine, or tocilizumab.

Summary of the Clinical Problem

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of COVID-19, a pandemic that has affected more than 400 000 individuals and caused nearly 20 000 deaths as of late March 2020. Approximately 5% to 10% of patients require intensive care unit (ICU) admission and mechanical ventilation.[1]

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Characteristics of the Guideline Source

The Surviving Sepsis Campaign (SSC) has previously published a series of guidelines for sepsis and septic shock. Based on this experience, experts were recruited to write guidelines on the

Table. Guideline Rating

Standard	Rating
Establishing transparency	Good
Management of COI in the guideline development group	Good
Guideline development group composition	Good
Clinical practice guideline–systematic review intersection	Good
Establishing evidence foundations and rating strength for each of the guideline recommendations	Good
Articulation of recommendations	Good
External review	Fair
Updating	Good
Implementation issues	Fair

management of COVID-19 in critically ill adults. These guidelines were authored by 36 experts from 12 countries (**Table**).[2] Recommendations were developed based on limited direct evidence with COVID-19 cases and indirect evidence derived from previous pandemics such as Middle East respiratory syndrome (MERS), severe acute respiratory syndrome (SARS), and other coronavirus infections. Overall, the panel issued 54 statements: 4 best practice statements, 9 strong recommendations, and 35 weak recommendations. (No recommendations were made for the remaining 6 topics.)

Evidence Base

The GRADE method was used, with the actionable guideline questions placed in population, intervention, comparator, outcomes (PICO) format. The first discusses PPE to protect health care workers and prevent nosocomial spread of virus. A recent clinical trial of 2862 health care personnel at 137 outpatient sites compared the use of N95 respirators vs medical masks and found no significant difference in the incidence of laboratory-confirmed influenza (8.2% vs 7.2% health care personnel seasons; difference, 1.0% [95% CI, −0.5% to 2.5%]; P = .18) (adjusted odds ratio, 1.18 [95% CI, 0.95-1.45]).[3] The CDC recently discussed strategies for optimizing the supply of face masks.

Critically ill patients with COVID-19 often develop septic (distributive) shock. Fluid resuscitation guided by dynamic assessment of fluid responsiveness is recommended based on a reduction in mortality (risk ratio, 0.59 [95% CI, 0.42-0.83]; P = .002) in a meta-analysis of 1652 patients in 13 trials.[4] These dynamic measures facilitate a more judicious, rather than liberal, fluid strategy both during and after initial resuscitation.[5]

Benefits and Harms

The panel issued a suggestion against the routine use of systematic corticosteroids for respiratory failure without ARDS in COVID-19, but issued a suggestion for use in patients with ARDS. One retrospective, non–peer-reviewed report of 46 patients[6] suggested treatment with methylprednisolone, 1 to 2 mg/kg/d for 5 to 7 days, was associated with a reduction in duration of fever and the need for supplemental oxygen. The panel also drew on indirect evidence of corticosteroid use in community-acquired pneumonia, ARDS, and other viral infections, using a Cochrane review[7] on the use of steroids in viral pneumonia, updated to include 15 cohort studies on influenza and 10 on coronaviruses. This analysis found an association between corticosteroid use and increased mortality (odds ratio, 2.76 [95% CI, 2.06-3.69]), although the association among patients with coronaviruses was unclear (odds ratio, 0.83 [95% CI, 0.32-2.17]).

The guideline recommendations for management of respiratory failure highlight the competing goals unique to the COVID-19 pandemic. A recommendation for the use of HFNC oxygen therapy is based on findings from a clinical trial that showed a benefit relative to standard oxygen and NIPPV in progression to intubation.[8] The panel also recommended a trial of NIPPV if HFNC is unavailable or ineffective. Following these recommendations may prevent intubation and the need for ventilator support, a scarce resource when there are large numbers of COVID-19 cases. However, HFNC and NIPPV may also aerosolize respiratory droplets, which will increase the need for negative-pressure rooms and N95 or FFP2 masks, which are also a scarce resource.

Discussion

The COVID-19 pandemic has brought unprecedented challenges regarding the ability to generate timely evidence, even as the disease overwhelms health care systems and stresses the clinical workforce. This SSC guideline[2] will be frequently updated online as global evidence accrues, but it reflects the central tenants of best practices for ARDS: low tidal volume strategy, PEEP titration, avoidance of hyperoxia, and a conservative fluid strategy.

Areas in Need of Future Study or Ongoing Research

Many of these recommendations are extrapolated from studies and experience in critically ill patients without COVID-19. However, this pandemic has necessitated flexibility and ingenuity to address its unique challenges, and it will require continued rapid and judicious synthesis of heterogeneous and rapidly evolving data and clinical experience shared by clinicians.

For instance, concern for aerosolization with HFNC and NIPPV and a critical shortage of mechanical ventilators have led to consideration of helmet NIPPV as an alternative in centers with this resource. Additionally, a small single-center clinical trial (n = 83 patients) has suggested decreased intubation and mortality with use of helmet NIPPV compared with face mask.[9] Unfortunately, these investigations used a ventilator to deliver helmet NIPPV. If the intent is to spare patients from invasive mechanical ventilation while limiting exposure to health care workers, helmet NIPPV using a ventilator may be an option. Alternatively, if mechanical ventilators are in short supply, it is possible to deliver helmet NIPPV using a flow generator (≥60 L/min) to deliver oxygen and an expiratory pressure valve to maintain PEEP. The guideline panel noted the option of helmet NIPPV but was not able to make a recommendation, noting uncertainty about its safety and efficacy in COVID-19. Such issues underscore the importance of considering the range of local resources and context in implementing care plans for patients with COVID-19.

COVID-19 Critical Care Guideline: Additional Resources

This guideline was developed collaboratively between the European Society of Intensive Care Medicine (ESICM) and the Society of Critical Care Medicine (SCCM).

Guideline publications

ESICM publication: Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Intensive Care Med*. Published online March 28, 2020. doi:10.1007/s00134-020-06022-5

SCCM publication: Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Crit Care Med*. Published online March 27, 2020. doi:10.1097/CCM.0000000000004363

Additional COVID-19 critical care resources

ESICM: https://www.esicm.org/resources/coronavirus-public-health-emergency/

SCCM: https://www.sccm.org/Disaster

Related resources

JAMA Network Coronavirus Resource Center

Finally, there is a pressing need to address resource allocation, innovative staffing, and alternative delivery models in providing ethical care for critically ill patients when there are insufficient ICU beds during a pandemic.[10]

ARTICLE INFORMATION

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Correction: This article was corrected on April 3, 2020, to include all of the related resources and relevant publications.

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