Michigan Medicine COVID-19 Adult Critical Care Consensus Recommendations

Guiding Principle: To provide summary recommendations for the management of critically ill patients suspected of having COVID-19 that is translatable and scalable across all adult critical care units at Michigan Medicine.

Disclaimer: Traditional high-level evidence (i.e. RCTs) is not yet available and most recommendations are the result of expert consensus or informed by the reported experience of other institutions affected by the pandemic. Information is changing rapidly and therefore this document will remain dynamic and updated frequently as new data to inform best practice becomes available.

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I. **Pathophysiology**

**Respiratory**

The primary pathology for critically ill patients with COVID-19 is rapidly progressive acute respiratory failure. Patients may quickly progress to acute respiratory distress syndrome (ARDS). Diffuse alveolar damage is noted and pneumocytes with viral cytopathic effect are seen implying a direct, virus induced, injury as compared to a secondary, hyper-inflammatory response. (Xu et al 2/17)

**Inflammatory**

Some patients respond to COVID19 with a severe over expression of inflammatory mediators. This has been described as a “cytokine storm syndrome” (CSS) which is noted to occur in other inflammatory states such as sepsis, hemophagocytic lymphohistiocytosis (HLH), and CAR-T therapy. It is unknown which patients are at risk of developing cytokine storm, and ferritin, CRP and IL-6 are early biomarkers that may predict higher risk of CSS development. These patients have a much higher incidence of developing multi-organ dysfunction, rapid decline and death. Currently there is no specific treatment targeting COVID-19 induced cytokine storm, however Michigan Medicine is developing a biomarker risk stratification strategy and investigational treatment trials are underway.

**Cardiac**

COVID-19 may present with elevated troponin which represents a myocarditis reaction rather than type-1 cardiac ischemia. Elevated troponin is strongly associated with mortality, however it’s unclear to the degree of this representing the degree of cardiac contribution vs. a marker of overall severity of illness, since elevated troponin levels have been associated with mortality in a variety of critical illness and injury. Up to 7% of patients die of fulminant myocarditis and 33% of patients may die with myocarditis contributing in some way. (Ruan 3/3/20). Arrhythmias have been reported and Wang et al. reported arrhythmias resulted in 12% of ICU transfers. (Wang 2/7)
II. Diagnosis and Monitoring

Laboratory diagnostics

The only confirmative diagnosis is to test directly for the Novel Corona Virus (severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2). This causes the disease known more commonly as COVID-19. Please review frequently updated testing guidelines for the most up to date process.

Biomarkers associated with inflammation are elevated. (Ruan 3/3/20). Ferritin and C-reactive protein have both been associated with COVID-19 and also track the severity of disease. Young and colleagues noted low CRP levels in patients not requiring oxygen (11 mg/L) compared to patients who became hypoxemic (66 mg/L) (Young 3/3). Ruan also found that survivors had a medial CRP level of 40 mg/L compared to non-survivors who had a median CRP level of 125 mg/L (Ruan 3/3/20).

Routine ICU comprehensive lab studies evaluating multi-organ injury are suggested upon presentation and repeated daily with the addition of CRP, LDH, ferritin, d-dimer and procalcitonin. A biomarker risk stratification strategy is currently being developed and will be included in this document once available.

Reported abnormalities include:

- Lymphopenia in about 80% of patients (Guan 2/28, Yang 2/21)
- Mild thrombocytopenia however usually > 100,000. More profound thrombocytopenia is associated with increased mortality (Ruan 3/3).
- Elevated D-dimer. Most coagulation studies are normal, however microthrombosis and associated ischemic events are very common (including stroke). D-dimer levels should be monitored frequently (Gattinoni - unpublished). Disseminated intravascular coagulation may progress over time and is associated with a poor prognosis (Tang et al 2020).
- Elevated transaminases are common. Liver biopsy specimens of the patient with COVID-19 shows moderate microvesicular steatosis and mild lobular and portal activity, reflected in transaminitis. Clinical meaning unknown at this time, intrinsic measures of hepatic function such as coagulation studies have been relatively normal.
- Procalcitonin does not appear to be elevated in isolated COVID-19 infection. Procalcitonin levels were shown to be < 0.5 in 95% of patients (Guan 2/28). If elevated, there is likely another bacterial source or co-infection. Suggest referring to https://www.med.umich.edu/asp/pdf/adult_guidelines/COVID-19-treatment.pdf for incorporation of procalcitonin levels into antibiotic stewardship after the initial presentation.

Radiology

General description of lung findings in both chest x-ray and CT scans is patchy ground glass opacities located usually peripheral and basal. Over time these may coalesce into a
consolidation. (Shi 2/24). Pleural effusions are uncommon and have been reported in 5% of cases. Other uncommon findings are cavitation, lymphadenopathy, or masses.

CT is more sensitive than chest x-ray in identifying early less severe or asymptomatic COVID-19 patients with peripheral lung involvement. One series reported a sensitivity of 86% of CT vs 59% chest x-ray early in mildly or asymptomatic COVID-19 patients. (Guan)

Ultrasound findings are relatively non-specific but include

- Thickening of pleural line, a spectrum of findings ranging from patches of B lines to peripheral consolidations.
- Sensitivity and specificity are not well defined
- Daily Lung Recovery – unclear that we should be using this to monitor progression of daily lung changes/recovery compared to chest x-ray.

The Italian Group for the Evaluation of Interventions in Critical Care (GiViTI) suggests that lung ultrasound may be useful in the early identification of patients likely to respond to high PEEP vs prone ventilation. A pattern of widespread B-lines may identify recruitable patients likely to respond to high PEEP, while a predominantly A-pattern anteriorly with posterior consolidations may identify patients likely to respond to prone ventilation. However, this approach has NOT been systematically evaluated nor validated.

Current recommendations are to use a portable chest x-ray initially to establish a baseline and rule out other causes of dyspnea such as pneumothorax or effusion. Chest CT should be utilized if there are other general concerns for current presentation. However, chest CT should not be routinely used where COVID-19 is the only diagnosis being considered due to the time to clean and risk of personnel exposure without much added benefit in management.

### III. Treatment and Management

There are no specific treatment strategies targeted for COVID-19 patients. However, there are some aspects of standard critical care principles that are more useful in critically ill COVID+ patients. Treatment strategies are based upon World Health Organization and the Society of Critical Care Medicine (SCCM) recommendations based upon a modified Surviving Sepsis Campaign Guideline (see Appendix 1). These have not yet been accepted by the Critical Care Medicine journal. They follow a “best evidence” approach with PICO guided questions and detailed literature review by an international, multidisciplinary panel of critical care experts. This guideline will be updated as more information becomes available.

**Hemodynamic Support**

Reported hemodynamic collapse and shock varies in reports from 1% to 35% in COVID-19 patients. This depends greatly on the patient population, comorbidities, age, severity of
illness and the definition of “shock” being used. Up to 40% of patients had “shock” as a major reason of death and this may be related to the reported fulminant myocarditis (Ruan).

In regard to fluid resuscitation, it is recommended dynamic parameters be used to assess fluid responsiveness (i.e. passive leg lift, lactate, capillary refill, skin temperature) to guide volume resuscitation as opposed to static parameters. During the acute resuscitation phase, it is suggested a conservative vs liberal fluid strategy may be beneficial, where balanced crystalloids (Ringers Lactate) is the resuscitation fluid of choice.

If goal mean arterial pressure (MAP) cannot be achieved with a limited fluid strategy, vasoactive agents should be added. The vasopressor of choice as a first line agent is norepinephrine to achieve MAP 60-65 mmHg. If there is evidence of cardiac dysfunction, then dobutamine or milrinone may be added. As fulminant myocarditis is generally regarded as a bi-ventricular disease, critical care management principles of cardiogenic shock apply. Consequently, there is little evidence to suggest single ventricle mechanical support like IABP or Impella would be of benefit, however, there may be a role for ECMO in selected patients.

**Ventilatory Support**

The prevalence of hypoxic respiratory failure with COVID-19 is up to 20%. It appears that up to 14% will develop severe enough pulmonary disease to require invasive mechanical ventilation. (Wu Z 2020). There is limited data describing risk factors of developing acute respiratory failure requiring mechanical ventilation and mortality was over 50% in those patients. A reasonable SpO2 target range is between 92% and 96%. Supplemental oxygen should be started once SpO2 is 90%. If persistent hypoxia despite supplemental oxygen, consider a trial of HFNC. If HFNC is preferred over NIPPV however if HFNC is not available and no need for intubation, a brief trial of NIPPV can be attempted as long as patient is rapidly assessed for signs of worsening respiratory failure. In areas where ventilator supply is limited, the use of HFNC may be a safe and effective strategy and does not seem to increase risk of disease transmission. In SARS, healthcare workers exposed to HFNC were not at increased risk of developing the disease. (Raboud J, 2010 PLoS One 5:e10717). However, as airway intervention requires significantly more time in this population due to need for complete PPE and airborne precautions, any worsening of respiratory failure despite use of HFNC or NIPPV, early consideration of need for mechanical ventilation is encouraged.

There are currently no studies addressing the optimal strategy for managing COVID-19 patients requiring mechanical ventilation. Several experts concur that mechanically ventilated patients with COVID-19 should be managed similarly to other patients with acute respiratory failure in the ICU and follow ARDS management when applicable. The main ventilator strategy is to minimize ventilator induced lung injury by using low tidal volume (Vt) ventilation with Vt of 4-8 mL/kg of predicted body weight and keeping plateau pressure below 30 mmH2O. Also, by utilizing a higher positive end expiratory pressure (PEEP)
strategy, mortality was improved in ARDS patients. (Briel M, 2010, JAMA). Recruitment maneuvers should be attempted when applicable. Neuromuscular blockade (N MBA) should be used if moderate to severe ARDS and worsening hypoxemia despite optimizing ventilation strategy and in cases of ventilator dys-synchrony (see Pharmacological agents section). Proning should be considered in moderate to severe ARDS when the above interventions have been attempted without significant improvement. Proning takes a significant amount of training and resource coordination and should only be attempted by personnel competent in its use. If severe ARDS with worsening hypoxia persists, a trial of inhaled pulmonary vasodilator can be attempted but should be rapidly tapered if patient does not respond.

Pharmacological agents


Per Pharmacy’s recently developed antiviral treatment recommendations (Michigan Medicine Guidance for Diagnosis and Treatment of COVID-19 in Adults and Children) there is no current evidence from randomized controlled trials to recommend any specific anti-COVID-19 treatment for patients with suspected or confirmed COVID-19 infection. In consultation with Infectious Disease, treatment should be considered in symptomatic patients requiring hospitalization or those with conditions associated with severe disease*. Per the guidelines referenced above, the several agents are considered investigational/for compassionate use, and decision to use these should be made only with close attention to the patient’s clinical status, comorbidities, and interacting medications. These may be considered at Michigan Medicine in consultation with Infectious Disease.

*Risk Factors Associated with Severe COVID-19:

1. Age > 65 Years
2. Chronic cardiovascular, pulmonary, hepatic, renal, hematologic, or neurologic conditions
3. Immunocompromised
4. Pregnancy
5. Residents of nursing homes or long-term care facilities

Other Therapeutics

1. Antibiotics – patients presenting with sepsis symptoms should follow surviving sepsis guidelines, including early broad-spectrum antibiotics including atypical pneumonia coverage, until a more specific, targeted diagnosis can be made. See procalcitonin section in Diagnosis and Testing on how it may be utilized to guide antibiotic utilization.
2. **Steroids** – There currently is no evidence supporting routine use of corticosteroids even with hypoxic respiratory failure and on mechanical ventilation. However, if on mechanical ventilation and developing signs/symptoms of ARDS, a trial of corticosteroids is recommended. Additionally, steroids should be continued if necessary, for other chronic disease states (asthma, COPD), or for vasopressor refractory shock (recommend hydrocortisone 200mg daily either as infusion or in divided bolus doses).

3. **Paralytics** – The routine use of paralytics are not recommended and should be reserved for consideration in patients moderate to severe ARDS or with ventilator dyssynchrony and or high plateau pressures > 30 cm H20. In these cases, we suggest using as needed intermittent boluses of neuromuscular blocking agents (NMBA) over continuous NMBA infusion, to facilitate lung protective ventilation strategies.

   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.

   In initial airway management higher doses of paralytics are recommended to optimize intubating conditions and decrease change of coughing/gagging (Rocuronium 1.2-1.6 mg/kg; Succinylcholine 1.5-2.0 mg/kg). See Appendix 2 for comprehensive airway management guidance.

**IV. Suggested system-based management approach:**

*See recent SCCM Surviving Sepsis – COVID-19 (Appendix 1) for additional recommendations*

The overall management of COVID-19 is the management of a severe viral pneumonia leading to respiratory failure, ARDS, and multiorgan dysfunction (Murthy et al, WHO Guideline).

1. **Neurologic:** no specific neurologic targets. Sedation should target a Richmond Agitation-Sedation Scale of 0 to -1, while keeping patients safe and able to tolerate lung protective ventilation and proning.
   a. **Recommend** that myocardial depressants such as propofol be used with caution; based on recent data (Wang et al.), acute cardiac injury and dysrhythmias have been noted. May also see paradoxical myocardial depression with ketamine in patients who are in a catecholamine depleted state.
   b. **Recommend** analgosedation with the use of short acting potent opiate agents such as Fentanyl in the event of arrhythmias and/or hemodynamic instability. Recommend the use of benzodiazepines should patients fail opiate adjuncts.
2. **CV**: acute cardiac injury has been noted in 7.2% with a 16.7% arrhythmia rate (Wang et al).
   a. **Recommend screening for myocardial injury** with ECG, troponin testing. Recommend obtaining transthoracic echocardiography to evaluate LV function, especially in patients with persistent hemodynamic instability, arrhythmias, or with cardiac risk factors.
   b. **MAP Target**: 60-65 mmHg
   c. **Fluid Management**: recommend comprehensive evaluation of patient’s volume status based on physical exam, critical care ultrasound, ventricular function and presence of pulmonary edema. **Recommend** conservative fluid management in patients without evidence of shock, in order to prevent exacerbation of ARDS.
   d. **Vasopressors**: usual management per septic shock guidelines. **Recommend** Norepinephrine as first line pressor, vasopressin as second line pressor.
   e. **Inotropes**: recommend that inotropes be used with caution, as patients that manifest cardiac injury may be prone to arrhythmias. The use of inotropes should be considered after evaluation of LV function with bedside echocardiography, and after weighing the patient’s perfusion status vs risk for arrhythmia. Dobutamine should be first line inotrope but if significant arrhythmias may consider use of milrinone.

3. **Respiratory**: Critically ill patients with COVID-19 are at risk of progressing to ARDS. Typical ARDS management for viral pneumonias (Lung protective ventilation, avoiding excess volume resuscitation) are key.
   a. **Recommend** supplemental oxygen on initial presentation if hypoxic to a goal SpO2 of 92-96%. Escalate to heated high flow nasal cannulae (with flow rates of up to 50 LPM) if worsening hypoxia despite 6L/min. Rapid progression of hypoxemic respiratory failure may become apparent in these patients. Patients have been reported to quickly fail supplemental oxygen therapy; in cases like these, the patients will likely continue their progression of respiratory failure and early endotracheal intubation should be considered.
   b. **Non-Invasive Ventilation – is not suggested** in COVID-19 patients, due to its risk of aerosolizing secretions under high pressure as well as its lack of proven efficacy as a primary treatment strategy in ARDS. However, if HFNC is not available and patient does not require intubation, a brief trial can be attempted but should be closely followed by serial re-evaluation. If evidence of progressive respiratory failure despite NIPPV, progress to endotracheal intubation should be considered.
   c. **Recommend** - MDI with spacer as an alternative to nebulized bronchodilator therapy. Small volume nebulizers can be filtered for use, and Tavis masks (filtered face masks) are being made available on a limited basis.
   d. **Recommend against** “breaking” the ventilator circuit at all costs. Any predicted circuit disconnections should occur with the vent on stand-by and the tube clamped prior to disconnection.
   e. **Endotracheal Intubation**: recommend that an experienced provider with the greatest likelihood of first pass success intubate using airborne precautions. A negative pressure room designated for Aerosol Generating Procedures (AGP)
should be used whenever possible. Refer to ED or Anesthesia Airway Management Guidelines for more information (Appendix 3).

f. **Ventilator Management** – **recommend** lung protective Strategy (4-8 cc/kg ideal body weight, Plateau pressures < 30 cm H2O) of ARDS management as cornerstone of treatment (WHO Guideline).
   i. **Consider** maintaining driving pressure ≤ 12-15 cm H2O
   ii. **Hypercapnea** – permitted if meeting pH goal of 7.30-7.45
   iii. **PEEP** – **recommend** that the ARDSNet PEEP table be used as a guide for PEEP titration. There is limited evidence to suggest that the low PEEP vs higher PEEP arm is more beneficial. Anecdotal reports from Singapore and other centers suggest COVID-19 patients benefit from higher PEEP. This suggests that COVID-19’s parenchymal problem may be atelectasis and alveolar edema, and as a result, these patients may require higher PEEPs and higher mean airway pressures for optimal lung recruitment. No RCT evidence is available.
   iv. **Neuromuscular Blockers** – **suggested** in patients with severe ARDS and strong respiratory drive that are at risk for volutrauma/barotrauma or with ventilator dyssynchrony. Should be started as intermittent dosing and escalated to infusion if needed.

g. **Proning** – **recommended** in patients with severe ARDS (PaO2:Fio2 <100-150). Prone ventilation for >12 hours is recommended (WHO Guidelines). Proning must be balanced with the use of human resources and expertise to be performed correctly.

h. **Fluid Management** – **recommend** conservative fluid management in patients with ARDS without evidence of tissue hypoperfusion, in order to prevent exacerbation of ARDS. This has been shown to shorten the duration of mechanical ventilation.

i. **Bronchoscopy** – **is not recommended** and is relatively contraindicated in patients with suspected and confirmed COVID-19 infections (Wahidi et al. American Association for Bronchology and Interventional Pulmonology Statement). Consider bronchoscopy in patients with post-viral pneumonia, mucus plugging, or unclear diagnosis.

j. **ECMO** – **rarely recommended**, due to the need for significant provider and institutional resources, exposure risk, and limited outcome data showing the success of ECMO in this population. Early reports suggest very high mortality of patients that are placed on ECMO. Discuss with ECMO on call and OCA. See Appendix 3 for further guidance.

4. **Renal**: there is no evidence that COVID-19 predisposes patients to higher rates of renal failure requiring CRRT compared to other viruses.
   a. **Recommend** routine management per KDIGO guidelines.

5. **GI**:
   a. **Recommend** routine enteral nutrition within 7d.
6. Hematological:
   a. Labs – recommend obtaining CBC with Diff, CRP, LDH, Ferritin, CPK, PT/PTT/INR.

7. ID:
   a. Labs – Recommend Blood cultures, respiratory viral panel, CRP, urine strep antigen, legionella antigen, gram stain and culture, procalcitonin.
   b. Co-Infection – recommended that an RPAN be obtained on these patients, as there are some early unpublished data that suggest COVID-19 patients may be co-infected with other viruses. Bacterial co-infection is possible and procalcitonin elevation may be used as an adjunct to other testing for confirmation.
   c. Treatment – recommend broad spectrum antibiotics for empiric community acquired and atypical pneumonia coverage (e.g. Unasyn/Azithromycin or Ceftriaxone/Azithromycin, Doxycycline if QTC > 500). Broaden antibiotics to include MRSA or anti-pseudomonal coverage in states of septic shock, or with risk factors for multi-drug resistant organisms.
   d. Steroids – suggested only in cases of moderate to severe ARDS, vasopressor-refractory shock (hydrocortisone 200mg IV daily either as intermittent bolus dosing or infusion), adrenal insufficiency, or other chronic condition requiring their use (i.e. COPD exacerbation or asthma exacerbation).
   e. Anti-viral Agents - there is no current evidence from randomized controlled trials to recommend any specific anti-COVID-19 treatment for patients with suspected or confirmed COVID-19 infection. All anti-virals should be considered in consultation with Infectious Disease. The latest guidance can be found at: https://www.med.umich.edu/asp/pdf/adult_guidelines/COVID-19-treatment.pdf

8. Endocrinology: No specific issues reported. Patients with diabetes mellitus are at higher risk for infection.
   a. Recommend euglycemia (Glu 120-180) with the use of insulin sliding scales or insulin drips as needed.
   b. Do not recommend the routine use of corticosteroids.

9. Prophylaxis:

10. Special Considerations:
    a. CPR: Recommend placement of supraglottic airway with viral filter and ETCO2 in line. Use supraglottic airway device if able to ventilate. If not, chest compressions should be paused during intubation to limit aerosolization of the virus.
       i. Recommend the use of the LUCAS mechanical CPR device (where available) for compressions in order minimize the use of PPE during codes.
    b. Resuscitation Logistics – for the sake of PPE conservation and for first-pass success, recommend a single provider intubate, and place an orogastric tube,
central line, +/- arterial line after intubation when necessary. Use of a video assisted laryngoscope (Glidescope or C-Mac) is recommended to help provide more distance between the patient and intubator. A viral filter should be used on BVM and iGel and a passive pre-oxygenation approach utilized when possible (avoid bagging). See Appendix 2

c. ECMO – current experience is very limited. Call OCA and EMCO attending on call for approval. See Appendix 3

V. References


Wahidi et al. American Association for Bronchology and Interventional Pulmonology (AABIP) Statement on the Use of Bronchoscopy and Respiratory Specimen Collection in Patients with Suspected or Confirmed COVID-19 Infection (unpublished, provided by Pepe de Cardenas)


APPENDIX 1: SURVIVING SEPSIS CAMPAIGN TOP 50 RECOMMENDATIONS


I. Infection Control
   Recommendation:

   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 recommendation, low quality evidence).

   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 recommendation, low quality evidence).

   5. For healthcare workers performing endotracheal intubation on patients with COVID-19, we suggest using video-guided laryngoscopy, over direct laryngoscopy, if available (weak recommendation, low quality evidence).

   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).

II. Laboratory Diagnosis and Specimens
   Recommendations:

   7. For intubated and mechanically ventilated adults with suspicion of COVID-19:

   7.1. For diagnostic testing, we suggest obtaining lower respiratory tract samples in preference to upper respiratory tract (nasopharyngeal or oropharyngeal) samples (weak recommendation, low quality evidence).
7.2. With regard to lower respiratory samples, we suggest obtaining endotracheal aspirates in preference to bronchial wash or bronchoalveolar lavage samples (weak recommendation, low quality evidence).

### III. Supportive Care

#### a. Hemodynamic Support

**Fluid therapy**

**Recommendation:**

8. In adults with COVID-19 and shock we suggest using dynamic parameters (skin temperature, capillary refill time, and/or serum lactate) over static parameters in order to assess fluid responsiveness (weak recommendation, low quality evidence).

9. For the acute resuscitation of adults with COVID-19 and shock we suggest using a conservative over a liberal fluid strategy (weak recommendation, very low-quality evidence).

10. For the acute resuscitation of adults with COVID-19 and shock we recommend using crystalloids over colloids (strong recommendation, moderate quality evidence).

11. For the acute resuscitation of adults with COVID-19 and shock we suggest using buffered/balanced crystalloids over unbalanced crystalloids (weak recommendation, moderate quality evidence).

12. For the acute resuscitation of adults with COVID-19 and shock we recommend against using hydroxyethyl starches (strong recommendation, moderate quality evidence).

13. For the acute resuscitation of adults with COVID-19 and shock we suggest against using gelatins (weak recommendation, low quality evidence).

14. For the acute resuscitation of adults with COVID-19 and shock we suggest against using dextrans (weak recommendation, low quality evidence).

15. For the acute resuscitation of adults with COVID-19 and shock we suggest against the routine use of albumin for initial resuscitation (weak recommendation, moderate quality evidence).

**Vasoactive agents**

**Recommendation:**

16. For adults with COVID-19 and shock we suggest using norepinephrine as the first line vasoactive agent, over other agents (weak recommendation, low quality evidence).
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 recommendation, low quality evidence)

18. For adults with COVID 19 and shock we recommend against using dopamine if norepinephrine is available (strong recommendation, high quality evidence)

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 recommendation, moderate quality evidence)

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 recommendation, low quality evidence)

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 recommendation, very low-quality evidence)

22. For adults with COVID 19 and refractory shock we suggest using low dose corticosteroid therapy (“shock reversal”), over no corticosteroid therapy (weak recommendation, low quality evidence)

Remark:
A typical corticosteroid regimen in septic shock is intravenous hydrocortisone 200 mg per day administered either as an infusion or intermittent doses

b. Ventilatory Support

Recommendations

23. In adults with COVID 19, we suggest starting supplemental oxygen if the peripheral oxygen saturation (SPO 2 is 92% (weak recommendation, low quality evidence) and recommend starting supplemental oxygen if SPO 2 is 90% (strong recommendation, moderate quality evidence).

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 recommendation, moderate quality evidence).

25. For adults with COVID 19 and acute hypoxemic respiratory failure despite conventional oxygen therapy we suggest using HFNC over conventional oxygen therapy (weak recommendation, low quality evidence)

26. In adults with COVID 19 and acute hypoxemic respiratory failure we suggest using HFNC over NIPPV (weak recommendation, low quality evidence).
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 recommendation, very low-quality evidence).

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.

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 recommendation, moderate quality evidence).

31. For mechanically ventilated adults with COVID-19 and ARDS we recommend targeting plateau pressures (Pplat) of <30 cm H2O (strong recommendation, moderate quality evidence).

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 (weak recommendation, low quality evidence).

Remark:
If using a higher PEEP strategy (i.e., PEEP> 10 cm H2O), clinicians should monitor patients for barotrauma.

33. For mechanically ventilated adults with COVID-19 and ARDS, we suggest using a conservative fluid strategy over a liberal fluid strategy (weak recommendation, low quality evidence).

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 recommendation, low quality evidence).

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

35.1. We suggest using as needed intermittent boluses of neuromuscular blocking agents (NMBA) over continuous NMBA infusion, to facilitate protective lung ventilation (weak recommendation, low quality evidence).
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 recommendation, low quality evidence).

36. In mechanically ventilated adults with COVID-19 ARDS, we recommend against the routine use of inhaled nitric oxide (strong recommendation, low quality evidence).

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 recommendation, very low-quality evidence).

38. For mechanically ventilated adults with COVID-19 and hypoxemia despite optimizing ventilation, we suggest using recruitment maneuvers, over not using recruitment maneuvers (weak recommendation, low quality evidence).

39. If recruitment maneuvers are used, we recommend against using staircase incremental PEEP recruitment maneuvers (strong recommendation, moderate quality evidence).

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 (weak recommendation, low quality evidence).

IV. COVID-19 Therapy

Recommendations

41. In mechanically ventilated adults with COVID-19 and respiratory failure (without ARDS), we suggest against the routine use of systemic corticosteroids (weak recommendation, low quality evidence).

42. In mechanically ventilated adults with COVID-19 and ARDS, we suggest using systemic corticosteroids, over not using corticosteroids (weak recommendation, low quality evidence).

43. In mechanically ventilated patients with COVID-19 and respiratory failure, we suggest using empiric antimicrobials/antibacterial agents, over no antimicrobials (Weak recommendation, low quality evidence).

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.

44. For critically ill adults with COVID-19 who develop fever, we suggest using acetaminophen/paracetamol for temperature control, over no treatment (Weak recommendation, low quality evidence).

45. In critically ill adults with COVID-19, we suggest against the routine use of standard intravenous immunoglobulins (IVIG) (Weak recommendation, very low-quality evidence).

46. In critically ill adults with COVID-19, we suggest against the routine use of convalescent plasma (Weak recommendation, very low-quality evidence).

47. In critically ill adults with COVID-19:
   47.1. we suggest against the routine use of lopinavir/ritonavir (weak recommendation, low quality evidence).
   47.2. There is insufficient evidence to issue a recommendation on the use of other antiviral agents in critically ill adults with COVID-19.

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.

49. There is insufficient evidence to issue a recommendation on the use of chloroquine or hydroxychloroquine in critically ill adults with COVID-19.

50. There is insufficient evidence to issue a recommendation on the use of tocilizumab in critically ill adults with COVID-19.
APPENDIX 2 – COVID-19 AIRWAY MANAGEMENT ALGORITHM

MICHIGAN MEDICINE ADULT EMERGENCY SERVICE COVID-19 AIRWAY MANAGEMENT ALGORITHM

**PREPARATION**

**Location & Timing**
- Negative Pressure Room if possible
- Consider early intubation given time needed for preparation
- If potential difficult airway let Anesthesia know early given time for response and PPE prep time. Add scalpel and 6-0 ETT to COVID table

**Assemble Team**
- In-Room: 2 Experienced airway operators, 2 Resus/EC3 nurses, 1 RT
- Out-of-Room: 1 Runner/PPE Monitor (in full PPE), EC3 Team Lead to read off this algorithm
- Minimize number of healthcare providers needed to complete procedure safely while maximizing protection

**PPE**
- Hand Hygiene for at least 20 seconds
- In-Room personnel, Runner, and PPE Monitor must DON ON: Inner gloves → impermeable gown w/ thumbs through thumb holes → Outer gloves → N95 or PAPR → goggles → OR cap
- PPE Monitor: Supervise all donning and doffing of PPE to ensure no cross contamination
- All team members wear role stickers on outside of PPE (on COVID table)

**PRE-CHECK and PRE-BRIEF**

**Equipment Check**
- COVID glidescope is charged and working
- COVID table is adequately stocked and located directly outside of room
- Two-way communication device is active

**Pre-oxygenation Plan**
- Determine the optimal pre-oxygenation strategy. Options include:
  - 6L NC O2 with surgical mask on patient OR
  - BVM + PEEP valve with 2-hand tight mask seal, viral filter, and 6L/min O2 connected to ETCO2 adaptor and 15L/min inlet O2. Use PEEP as needed. DO NOT BAG. OR
  - HFNC up to 50L/min using the Drager with surgical mask on patient

**Intubation Plan**
- Plan A: RSI with VL. Provider with best chance for first past success should intubate
- Plan B: Rescue Oxygenation - iGel with viral filter between iGel and BVM. Bag with minimum flow rate and pressure needed for re-oxygenation. If fails, use BVM w/o iGel but must use two-person technique, adequate mask seal, in-line viral filter, and OPA/NPA as needed
- Plan C: Front of Neck Access - scalpel, bougie, 6-0 ETT

**Medication Plan**
- In-Room: RSI with Ketamine (0.5 - 1 mg/kg) or Etomidate (0.3 mg/kg) and high dose Rocuronium (1.2-1.6 mg/kg) or Sux (1.5-2.0 mg/kg) to suppress gag/cough and optimize intubating conditions
- In-Room: Sedation - Pre-prime Propofol, Fentanyl, and Midazolam gtt. Bring pump into the room
- Out-of-Room: Hemodynamic optimization - Phenytoin syringe, Norepi gtt, Bicarbonate
**PROCEDURE**

**Organize**
- Personnel, COVID table, drugs, glidescope into the room
- Door closed
- Set up viral filter and ETCO2 in line on BVM and ventilator circuit (see photos)
- Set up closed suctioning system (Yankauer) with tight seal on canister
- BP cuff set for q3 min and opposite arm from pulse ox

**Optimize**
- Correct hypotension, hypoxemia, and acidosis
- Pre-oxygenate using the pre-determined strategy
- Use Wedge as needed to optimize airway anatomy with ear-to-ternal notch position
- If patient is agitated, consider small dose of ketamine (10-30mg) IV

**Induction & Intubate**
- **PERFORM TIME OUT**
  - Administer RSI meds then wait 1 min. Do not bag during apneic period unless life threatening hypoxemia
  - Turn off HFNC if applicable then take off surgical mask. Intubate
  - Inflate cuff FIRST, then ventilate with BVM

**POST CHECKS**

**Tube Safe?**
- Confirm ETCO2 waveform and secure ETT
  - Transfer to vent: Clamp ETT --> remove BVM --> connect ETT to vent --> unclamp ETT
  - Planned disconnections: Always put ventilator in Standby Mode and clamp ETT prior to disconnecting

**Brain/Heart Safe?**
- Start analgesedation
- Send ABG/VBG, correct acidosis
- HOB 30 degrees

**Lungs Safe?**
- TV < 6-8 mL/kg IBW
- Pplat < 30
- Adequate exp time/autoPEEP
- Insert OG tube

**In Room**
- Place glidescope blade and any soiled equip in red bag. Seal and leave in room
- Remove outer "dirty" gloves. Wipe down glidescope, COVID table, and unused equipment with Oxivir. Put unused equipment into the "dirty" bin
- Push glidescope and COVID table out of room (w/foot) --> take off inner gloves --> hand hygiene --> exit room

**Out-of-Room:**
- Hand hygiene --> new gloves --> remove cap --> hand hygiene --> remove goggle --> hand hygiene --> remove N95 --> hand hygiene --> wash face w/ soap/water --> hand hygiene
- Glidescope and COVID table wiped down again by PPE monitor

**DEBRIEF**
BVM Setup – For Pre-oxygenation

BVM Setup – For Post-intubation
Airway Table (In Room - Stocked)
Airway Response Guidelines for Outside of OR airways

Please review the material and use appropriate isolation precautions. Plan ahead as it takes time to apply all the barrier precautions.

**BEFORE**

1. **Prior to intubation:** Don the appropriate respiratory protection, gloves x 2, eye protection, and gown x 2. Pay close attention to avoid self-contamination (buddy system). Before and after all procedures, practice appropriate hand hygiene.

2. **Get GlideScope GO & Airway Bag from staging area.** (Also take Code GlideScope and Code bag to stay outside pt room.)

**DURING**

3. **Clothing:** Wear 2 gowns, 2 pairs of gloves, a fit tested N-95 respirator or a PAPR (for those not fit-tested for or unable to use an N-95 mask) + eye protection. (PAPR: powered air-purifying respirator)

4. **Staffing:** Anesthesia Faculty and CA-3 (UH) or CRNA/Fellow (C&W)

5. **Monitoring:** Perform pre-procedure time out. Check standards, access, Instruments, drugs, ventilator and suction

6. **Considerations:** Avoid CPAP, BIPAP, High-Flow Nasal O2 suctioning and AFOI unless clinically necessary.

7. **Plan for rapid sequence induction (RSI):** RSI may need to be modified, if patient is unable to tolerate 30 s of apnea, or has a contraindication to succinylcholine. If manual ventilation is anticipated, small tidal volumes should be applied or LMA considered.

8. **Oxygenation:** 5 minutes of pre-oxygenation with oxygen 100% and RSI to avoid potential aerosolization of virus from airways.

9. **Check filter:** Ensure hydrophobic HME filter placed between facemask and breathing circuit or between facemask and Ambu bag or circuit.

10. **Intubate:** Intubate with GlideScope GO and confirm correct position of tracheal tube. Try to avoid ETT suction.

11. **Ventilate:** Institute mechanical ventilation and stabilize patient. Ensure HME filter in place.

**AFTER**

12. **Clean equipment:** All airway equipment is discarded except GlideScope GO. GO is disinfected and passed outside the room.

13. **Remove protective equipment:** Doff all PPE in room except N-95 or PAPR and eye protection.

14. **Before and after all procedures:** Practice appropriate hand hygiene.
APPENDIX 3: ECMO PLANNING

ECMO Consultation in-hospital:

- ECMO consults will be performed in any location, including the ED and the RICU
- ECMO consult for severe hypoxemia is to Adult Respiratory Cannulation on ECMO paging site
- ECMO consult for cardiovascular collapse is to Adult Cardiac Cannulation on ECMO paging site
- ECMO Charge Specialist (pager 9766) can also be called to facilitate ECMO consults
- All ECMO consults will be discussed with Jonathan Haft (ECMO Director) for review and to ensure awareness of ECMO capacity
- If there is no destination ICU bed available to provide ECMO care, the ECMO attending will discuss with OCA in the moment to make a final decision about whether ECMO will be offered or not

Selection criteria for appropriate ECMO candidates:

- Persistent severe hypoxemia despite maximal MV and rescue approaches (high PEEP, prone position, inhaled nitric oxide) and no absolute contraindications present (irreversible pulmonary disease, severe multiple organ failure, severe comorbidities, contraindication to anticoagulation, anoxic brain injury)
- Cardiovascular collapse, cardiogenic shock with no absolute contraindications present (see above)

ECMO Cannulation in-hospital:

- ECMO cannulation will be performed in any location, including the ED and the RICU
- If the decision is made by the ECMO team to cannulate, and the patient is critically ill and unstable, the cannulation (either VV- or VA-ECMO) will be done on-site with the essential ECMO team who brings the ECMO circuit and cart to the bedside for ECMO cannulation
- In rare cases, if the ECMO team decides that the cannulation should be performed in the SICU and the patient is stable for transfer, the patient could be transferred to the SICU for ECMO cannulation
- Cannulation may be performed in the OR when fluoroscopy is indicated for bicaval ECMO cannulation
- For improved PPE during ECMO cannulation due to increased blood exposure risk, white disposable coverall bunny suits will be used by nonsurgical personnel with all other recommended PPE (N-95 or PAPR, eye goggles, gloves, etc). Surgeons will wear impervious surgical gowns.
- After cannulation outside of the destination ICU, if a SICU bed is not immediately available, the essential ECMO team (ECMO specialists and ECMO Cannulation team –
SICU/CVC-ICU Attending and Fellow(s)) will stay with the patient until transfer is complete.

Patient care after ECMO Cannulation:

- VV-ECMO patients cannulated for severe hypoxemia will be managed on 5D
- VA-ECMO patients cannulated for cardiogenic shock associated with COVID-19 (suspected/confirmed) will be managed on 5D with assistance of CVC-ICU nursing and CVC-ICU Adult Cardiac Surgery ECMO Attending staff
- SICU Attending, Fellow staff will need to be increased to provide care for these patients
- There are only 2 negative pressure rooms on 5D (Bed 2/40), so ECMO capacity is limited.
- When reverse isolation capacity with negative pressure rooms in the SICU is exceeded, we will take direction from OCA regarding possible use of aerosolization minimization non-negative pressure rooms.

Transfer requests for ECMO Evaluation for Critical Illness associated with COVID-19 (confirmed or suspected):

- OSH “ECMO” Transfer Requests come through the Transfer Center to the SICU Fellow/Attending
- All transfer requests for critically ill patients who are COVID-19 PUI will be discussed with OCA
- Decisions will be made jointly between the ECMO attending (re whether appropriate ECMO candidate and ICU staffing issues) and OCA (re ICU bed capacity issues, primary priority to our current inpatients) to accept and to what location (if ECMO extremely high possibility may transfer directly to 5D)
- Transfer requests for patients already on ECMO at OSH will be discussed with Dr. Haft and OCA

Remote cannulation for ECMO will be considered on a case-by-case basis in discussion with Dr. Haft/OCA
Michigan Critical Care Collaborative Network

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Notes/Summary