Version 2.0 04/05/2020

MASSACHUSETTS GENERAL HOSPITAL

This document was prepared (in March/April, 2020) by and for MGH medical professionals (a.k.a. clinicians, care givers) and is being made available publicly for informational purposes only, in the context of a public health emergency related to COVID-19 (a.k.a. the coronavirus) and in connection with the state of emergency declared by the Governor of the Commonwealth of Massachusetts and the President of the United States. It is neither an attempt to substitute for the practice of medicine nor as a substitute for the provision of any medical professional services. Furthermore, the content is not meant to be complete, exhaustive, or a substitute for medical professional advice, diagnosis, or treatment. The information herein should be adapted to each specific patient based on the treating medical professional's independent professional judgment and consideration of the patient's needs, the resources available at the location from where the medical professional services are being provided (e.g., healthcare institution, ambulatory clinic, physician's office, etc.), and any other unique circumstances. This information should not be used to replace, substitute for, or overrule a qualified medical professional's judgment.

This website may contain third party materials and/or links to third party materials and third party websites for your information and convenience. Partners is not responsible for the availability, accuracy, or content of any of those third party materials or websites nor does it endorse them. Prior to accessing this information or these third party websites you may be asked to agree to additional terms and conditions provided by such third parties which govern access to and use of those websites or materials.

Version 2.0 Drafted 4/5/2020

MASSACHUSETTS GENERAL HOSPITAL

Massachusetts General Hospital
Treatment Guidance for Critically Ill Patients with COVID-19

- This document was developed by members of the Division of Pulmonary and Critical Care Medicine at MGH in collaboration with the Department of Anesthesia, Critical Care and Pain Medicine, the division of Cardiology, Respiratory Therapy and Pharmacy to provide guidance to frontline clinicians caring for patients with COVID-19 in the ICU.
- This is a living document that may be updated as more data emerge. These guidelines are maintained by Dr. C. Corey Hardin. Comments and requests for updates should be sent to charles.hardin@mgh.harvard.edu .

Executive Summary:

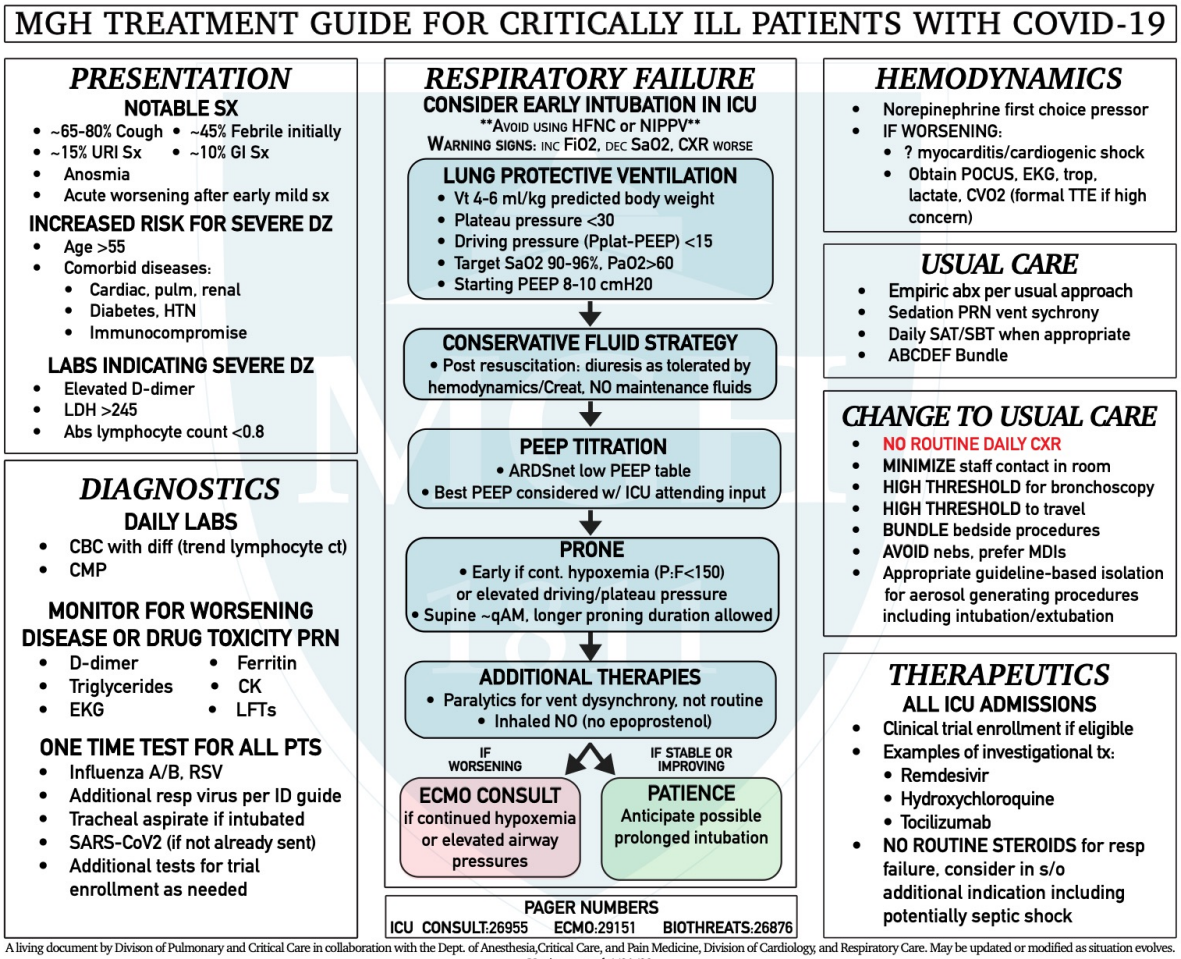

Figure 1: Summary of Critical Care Protocol for COVID-19

MASSACHUSETTS GENERAL HOSPITAL

It is expected that somewhere between 5-15% of hospitalized patients with COVID-19 will develop critical illness). Features of critical illness associated with COVID-19 include hypoxemia, respiratory failure, the Acute Respiratory Distress Syndrome (ARDS), shock (both distributive and, in reported cases, cardiogenic) and multiple organ dysfunction syndrome (MODS). ICU management should focus on lung protective ventilation, avoidance of fluid overload, and support of organ function while minimizing risk of transmission with appropriate isolation[1]. Additionally, attempts should be made to minimize the number of personnel providing care, reduce low-value diagnostics such as routine daily chest x-rays, and avoid aerosol-generating procedures such as bronchoscopy without strong indications. Measures to support organ function include supplemental oxygen, intubation and lung protective mechanical ventilation. Prone positioning has proven beneficial in patients with ARDS and there is some experience with providing this therapy to non-intubated patients. Provided adequate resources are available, intubation is currently preferable to high-flow nasal canula or non-invasive positive pressure ventilation. There have been reports of rapid deterioration after the onset of hypoxemia. Therefore, an increasing oxygen requirement in any COVID-19 patient should prompt consideration of ICU transfer and intubation. The decision to intubate should be made early in order to facilitate deliberate planning, minimization of aerosol generation and in order to avoid the propagation of lung injury associated with large, spontaneously generated transpulmonary pressures.

The most common severe manifestation of COVID-19 in the ICU is ARDS. Management of ARDS in the setting of COVID-19 does not differ significantly from management of ARDS due to other causes. Ventilation should be provided in the volume control mode with low tidal volumes. PEEP should be titrated according to usual unit protocol. Early consideration should be given to prone ventilation if P_aO_2/F_iO_2 (P:F hereafter) is less than ~150 to 200 after 12 hours of mechanical ventilation and PEEP titration, depending on illness trajectory (may wish to prone earlier if rapid deterioration). Inhaled pulmonary vasodilators may be used in the case of refractory hypoxemia. If patients fail to respond to these measures either due to persistent hypoxemia or unacceptably high airway pressures, and if there are no contraindications, it is appropriate to consider extra-corporal membrane oxygenation (ECMO).

There are variable reports of a late viral myocarditis that is associated with cardiogenic shock. Sudden deterioration in an ICU patient with COVID-19 should prompt work-up for cardiac dysfunction. Such a workup should include EKG, high-sensitivity troponin, central venous oxygen saturation (if available), lactate, and point of care ultrasound (POCUS).

No specific treatments for COVID-19 have been conclusively demonstrated to provide benefit. It is appropriate to consider antiviral medication (e.g. remdesivir, chloroquine, etc.) in the context of clinical trials or compassionate/off-label use programs. However, it is important to monitor for possible drug-related toxicities. Antiviral medications should be given in consultation with ID and in compliance with the separate MGH protocol for anti-infective therapy in COVID-19. Steroids are not currently recommended for the treatment of viral pneumonia and ARDS due to COVID-19 in the absence of an additional indication.

Clinical Features

The initial presentation of COVID-19 is non-specific and may include fever, malaise, sore throat, anosmia, and myalgias. No single symptom is present in a majority of cases. Fever is the most common presenting symptom but is present on presentation in less than half of cases. In published case series, the median time to ICU transfer from symptom onset is approximately 7-10 days Mortality is high, with estimates ranging from 20-60% in ICU patients. The most common reason for ICU transfer is hypoxemia and respiratory failure. Patient characteristics associated with need for critical care include older age (>60), male sex, and presence of comorbidities including cardiac disease, diabetes, and chronic respiratory disease. Laboratory values that are significantly associated with need for mechanical ventilation in published series include lymphopenia, elevated troponin, elevated creatinine, elevated LDH and increased D-dimer . Procalcitonin is often normal and total white count can be normal. Most, but not all, patients have abnormalities on chest imaging. These include bilateral patchy opacities, interstitial changes, ground-glass opacities and consolidation.

Triage

ICU patients with COVID-19 who are expected to need aerosol-generating procedures such as bronchoscopy and intubation, which may have to be performed emergently, should be treated with appropriate isolation precautions to reduce the risk of nosocomial transmission. Please refer to the triage grid for COVID-19 patients for preferred locations and precautions. There have been reports of rapid decompensation in patients with hypoxemia (P:F < 300, room air O2 saturation < 93%). ICU transfer should be considered in any patient with escalating oxygen requirement. Warning signs of deterioration include lymphopenia, increasing lactate, increasing CRP and progression in chest radiograph abnormalities.

General ICU Care

It is important to conduct care in such a way as to minimize the risk to staff and eliminate the possibility of nosocomial transmission. To this end, patients should be treated under appropriate isolation precautions as indicated in the separate infection control protocol. Efforts should be made to minimize the number of staff in and out of patient rooms. On rounds, it is not necessary for the entire ICU team to enter the room.

Fluid Resuscitation: Patients with hypoxemic respiratory failure should be managed with a conservative fluid strategy[2]. Such a strategy should **only** be implemented after initial resuscitation when the patient is not intravascularly volume depleted and/or is out of shock. Patients with fever have high insensible loss that may not be reflected in the measured total body balance. Fluid resuscitation of patients in shock should be limited to patients who have indications of volume responsiveness. Fluid responsiveness in patients with shock can be assessed by a variety of methods including passive leg raise, pulse pressure variation, and ultrasound assessment of IVC distensibility[3]. CVP trends or extreme CVP values may provide additional information. Post-resuscitation, a

conservative fluid strategy includes avoiding maintenance fluids and early initiation of diuresis as tolerated by hemodynamics and renal function. Positive fluid balance should be avoided.

Empiric Antimicrobial Therapy: The incidence of bacterial superinfection in COVID-19 is unknown. Initiation of empiric antibiotics should follow usual practice with rapid de-escalation, as outlined in the ATS/IDSA guidelines[4] for severe community acquired pneumonia (or hospital acquired pneumonia if acquired > 48 hours from admission). Isolated elevated procalcitonin levels in the absence of bacterial superinfection in COVID-19 patients have been described and may not be beneficial for decisions on antibacterial therapy. Invasive diagnostic techniques such as bronchoscopy or mini-BAL offer no benefit over blind tracheal suctioning using an in-line catheter and dramatically increase the risk to staff. Diagnostic bronchoscopy should generally be avoided in COVID-19 patients given the low additional diagnostic yield and high risk to health care workers.

Imaging: Routine daily chest x-rays have been demonstrated to have no effect on outcome in the ICU[5] and should be avoided in the care of COVID-19 patients. Radiographic findings consistent with a diagnosis of COVID-19 are discussed above (See Clinical Features). Possible indications for chest radiography subsequent to ICU admission include hemoptysis, suspected atelectasis due to mucous plugging, and rapidly progressive hypoxemia. Various patterns (primarily bilateral ground glass opacity and/or consolidation) on chest CT have been associated with COVID-19 but these are non-specific and are not expected to inform daily management. Transport of patients to the CT scanner presents a risk of viral transmission to staff and other patients, as well as to the critically ill patient undergoing transport. CT imaging of COVID-19 patients will also result in the need to temporarily close the scanner for several hours after the study for cleaning. For these reasons, chest CT should be reserved for situations in which an alternative diagnosis (i.e. pulmonary embolus) is suspected. Follow usual unit protocols for DVT prophylaxis.

Laboratory Investigation: Recommended daily labs include CBC with differential (in order to trend total lymphocyte count), complete metabolic panel, CPK, and LDH. Progressive elevations in CRP have been associated with poor outcome. Concerns have developed around polypharmacy given the intense interest in novel anti-viral therapies. We therefore recommend routine monitoring of LFT's and periodic monitoring of CK as well as daily EKG to monitor for QTc prolongation. Patients with respiratory failure frequently require high levels of sedation. For patients on propofol we recommend monitoring of triglycerides. In the event of clinical deterioration, studies to consider include d-dimer, central venous oxygen saturation, CRP, lactate, and LDH. Bacterial and fungal superinfection have been reported in a minority of cases, so sputum culture and routine blood cultures on ICU admission are reasonable. Please see the separate ID document for initial laboratory workup for COVID-19 disease.

Aerosol generating therapies: Procedures including bronchoscopy, endotracheal intubation, extubation, nebulizer administration, and tracheostomy change are associated with a high risk of aerosolization and subsequent viral transmission. Such procedures should be conducted with all staff wearing and N95 respirator and other appropriate PPE. For a full list of aerosol generating procedures, please see the separate infection control protocols. The decision to intubate should be made early in

the course of clinical deterioration. Avoid routine bronchoscopy and perform only if less invasive tests have not yielded sufficient diagnostic information. Respiratory samples for diagnosis of bacterial superinfection may be obtained by close-loop endotracheal aspirate. Inhaled medications should be given by metered dose inhaler instead of nebulizer whenever possible to decrease the risk of viral transmission. Ventilators should be set up with adaptors in the dry arm of the circuit to facilitate subsequent use of inhalers without opening the circuit.

Non-invasive respiratory support

In published series from China and other countries, significant numbers of patients were treated with high-flow nasal cannula (HFNC) and non-invasive positive pressure ventilation (NPPV). Concerns have been expressed about the potential for HFNC and NIPPV to generate infectious aerosols and recent data indicates viral particles can persist for some time after aerosol generating procedures[6]. **Where mechanical ventilation is available, it is the preferred means of respiratory support in patients with COVID-19 associated respiratory failure**. In patients with other etiologies of respiratory failure, HFNC and NIPPV should be offered in accordance with usual indications. In particular, we should to continue to offer NIPPV in patients with hypercarbic respiratory failure and known COPD. Should there be a need to employ NIPPV or HFNC in a patient with known or suspected COVID-19 these therapies should only be provided in the context of Strict Isolation after appropriate consultation with the MICU attending and Respiratory Care leadership.

Decision to Intubate

As above, the decision to intubate should be taken deliberately, in consultation with the intubation team, and should be performed according to the most recent infection control guidelines. Indications for intubation include increased work of breathing(WOB) (accessory muscle use, tachypnea) and persistent or rapidly worsening hypoxemia. As noted above, some patients will deteriorate quickly. In the presence of bilateral infiltrates and hypoxemia, mechanical ventilation with low tidal volumes may be less injurious than continued vigorous spontaneous breathing with or without non-invasive support[7], but this benefit has to be weighed against the need for sedation often associated with mechanical ventilation. In the particular case of COVID-19, mechanical ventilation results in the patient breathing in a closed, filtered circuit that may reduce the risk of viral transmission. Additionally, non-emergent intubation allows staff adequate time to don PPE and prepare for the procedure. Therefore, as resources allow, early intubation is preferred. The precise timing of intubation must be left to the judgement of the individual clinician. The guiding principle is to strike an appropriate balance between limiting trans-pulmonary pressures (including spontaneously generated transpulmonary pressures) and the risks of the heavy sedation that is often associated with mechanical ventilation of patients in hypoxemic respiratory failure. In patients with moderately escalating FiO2 who have not yet developed a severe increase in WOB, consider a trial of prone positioning prior to intubation. This is best implemented according to the separate MGH protocol for prone position in non-intubated patients.

Management of Respiratory Failure

MASSACHUSETTS GENERAL HOSPITAL

The majority of patients with COVID-19 associated hypoxemic respiratory failure develop ARDS. Management of ARDS in the setting of COVID-19 does not meaningfully differ from standard ARDS management[1]. Patients should be initially placed on volume-assist control ventilation with tidal volume of less than or equal to 6cc/kg ideal body weight (IBW, calculated from height), a set rate up to 35 breaths per minute, and moderate (8-10 cmH_2O) positive end-expiratory pressure (PEEP). We recommend an **initial** moderate PEEP instead of **initial** recourse to PEEP titration procedures or PEEP/FiO2 tables. Plateau airway pressure (P_{plat}, pressure measured during an end-inspiratory pause) should be maintained below 30 cmH_2O and driving pressure (P_{plat} – PEEP) should be maintained < 15 cmH_2O. Hypercarbia is acceptable (*permissive hypercarbia*). If there is no evidence of increased intracranial pressure the goal should be to maintain arterial pH > 7.25.

Adjustment of ventilator settings

Patients with ARDS may fail to respond to initial ventilator settings, either through persistent high airway pressures (P_{plat} > 30 cmH_20 and/or driving pressure >15 cmH_2O) or persistent hypoxemia Severity of hypoxemia can be assessed by means of the P:F ratio. Although ideally oxygen saturation should be maintained above 90% it is generally felt to be more important to minimize airway pressures. Goal indices of oxygen are (SpO2 > 90, P:F > 150 mmHg). The following steps may be taken to optimize ventilatory settings:

Tidal Volume: If P_{plat} is above 30 cm H_20 and/or driving pressure >15 cmH_2O, consider reducing the V_t below 6cc/kg to as low as 4cc/kg IBW. The lower limit on the ability to decrease tidal volume is determined by the associated decrease in minute ventilation and thus hypercarbia. Respiratory rate can be increased as needed to compensate as long this does not result in significant auto-PEEP. Auto-PEEP is indicated by an expiratory flow curve on the ventilator screen that does not return to zero prior the initiation of the next inspiration.

PEEP Optimization: In the presence of persistent hypoxemia on initial vent settings (S_pO_2 < 90%, P:F < 150 mmHg) requiring high F_iO_2 (~0.6 or more), attempts should be made to formally optimize the choice of PEEP. There is no method of PEEP optimization that is clearly superior to any other[8] and PEEP optimization should proceed according to usual ICU protocol. Usual ICU protocol may involve recruitment maneuvers and decremental PEEP trial with PEEP selected by best tidal compliance. However, recruitment maneuvers may be associated with harm and generally should be performed cautiously. In particular, multiple recruitment maneuvers within a short amount of time should be avoided.

Lower PEEP/higher FiO2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Figure 2: ARDSnet Low - PEEP High FiO2 Table.

If individualized PEEP titration is not available, PEEP may reasonably be set using the ARDSnet low-PEEP table reproduced above.

Prone Ventilation: Prone ventilation for ARDS is strongly recommended in current clinical practice[9] guidelines and should be implemented early in COVID-19 patients. Current indications for prone ventilation are a persistent hypoxemia defined as P:F < 150 for 12 hours (some clinicians favor < 200 and sooner initiation of prone positioning) after optimal PEEP titration as noted above. Prone ventilation results in a host of improvements to lung mechanics and should be instituted via the MGH prone positioning guideline posted on Apollo. Prone ventilation can be carried out in the patient's current bed and requires minimal additional equipment. Absolute contraindications to prone ventilation include an inability to turn neck (e.g. fixed or unstable c-spine) and sternal instability. Vascular access lines, chest tubes, and CVVH lines are not contraindications to prone ventilation. Extreme hemodynamic instability is a relative contraindication although consideration should also be given to the possibility that hemodynamics may improve with resolution of hypoxemia. The proning procedure itself should be carried out with staff adhering to current infection control guidance on PPE as outlined in the separate infection control protocols. A bolus of paralytic agent should be given prior to proning (similar consideration apply to the return to supine position). There is no need for ongoing neuromuscular blockade after the proning procedure itself, except as necessitated by vent asynchrony. The patient should be maintained in the prone position until at least the morning after proning. Thereafter, that patient may be assessed for suitability to return to supine position once each morning (qAM). PEEP requirements frequently decrease in the prone position and consideration should be given to decreasing PEEP after proning and increasing PEEP prior to return to the supine position in order to prevent de-recruitment. In particular, ½ of the difference in PEEP between the supine and prone position may be added back prior to return to the supine position (for example, if PEEP is 8 in the prone position , but was 12 in the supine position, then consider increasing PEEP to 10 prior to return to supine condition). If P:F remains greater than 150 (some clinicians prefer 200) and driving pressure is less than 15 at the end of the 2 hour period of supine ventilation on PEEP of 10 cmH_2O or less, prone ventilation may be discontinued.

Ventilator Asynchrony: Patients with ARDS may have a high respiratory drive, so attempts to minimize tidal volume and airway pressure can result in ventilator asynchrony. This can manifest in multiple ways including double triggering (see figure):

MASSACHUSETTS GENERAL HOSPITAL

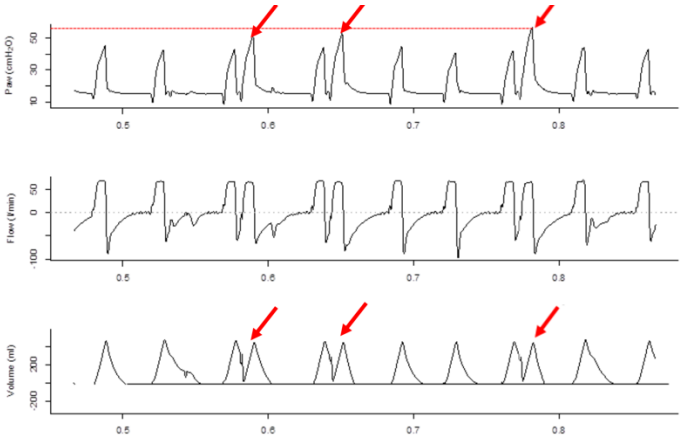

Figure 3: From JAMA. 2017;318(14):1335-1345

Ventilator asynchrony such as double triggering results in high tidal volumes and airway pressures that can be injurious. Increasing inspiratory flow may decrease dyspnea, but if asynchrony is persistent despite reasonable efforts at titrating up sedation, then consider bolus neuromuscular blockade (see Fig. 4). If persistent vent asynchrony despite repeated bolus dose NMB (> 3 boluses in 2 hrs) then the initiation of continuous neuromuscular blockade can be considered. Continuous neuromuscular blockade should be only undertaken in response to persistent asynchrony or persistent high airway pressures (by eliminating tone of chest wall muscles, neuromuscular blockade can decrease chest wall compliance and thus decreases pressures at any given volume). We do not recommend routine neuromuscular blockade[10]. If double triggering increases with deep sedation, consider the diagnosis of "reverse triggering" or entrainment. This reflex breathing pattern may abate with reducing sedation.

Pulmonary Vasodilators: In cases of persistent hypoxemia despite optimization of ventilator settings and initiation of prone ventilation, patients may be started on inhaled pulmonary vasodilators[11]. This should consist of a trial of inhaled nitric oxide (iNO) at 40ppm, with increases in dose up to 80ppm as needed. A successful trial of iNO is indicated by a 20% increase P_aO_2. If the patient responds to iNO, its use should be maintained. If there is no improvement in oxygenation with iNO, its use should be discontinued per respiratory care weaning protocol. If iNO is used at high doses for prolonged periods of time, it can lead to elevated methemoglobin levels so monitoring is recommended in this situation. We do not recommend use of inhaled prostacyclin analogues for COVID-19 patients given the increased risk of aerosol generation.

ECMO: Patients with persistent hypoxemia or unacceptable airway pressures despite the optimization of ventilator settings, prone positioning, neuromuscular blockade, and inhaled pulmonary vasodilators are deemed to have refractory ARDS and the team should consider if the patient is appropriate for extra-corporal membrane oxygenation (ECMO)[12,13]. The determination of ECMO candidacy is done in consultation with the ECMO team (reached via the Heart ICU intensivist, see pager numbers in Figure 1) and according to the ECMO guidelines posted on Apollo. Early involvement of the ECMO team is recommended since venous access sheaths can be placed in anticipation of the need for ECMO. Candidates for ECMO should be transferred to Blake 7 and this can be facilitated by contacting the MICU triage attending via the critical care consults pager (pager 26955).

Monitoring Labs

Due to the intense interest in novel therapeutics for SARS-CoV-2, many COVID-19 patients in ICU end up on a large number of medications, both as part of clinical trials and on the basis of compassionate use, potentially with overlapping toxicities. For this reason, close attention should be paid to possible issues with polypharmacy. Labs which should be checked daily include LFTs, CPK, and EKG for QTc prolongation.

Sedation Management

The cornerstone of management of ARDS is low-tidal volume ventilation (LTVV). ARDS causes hypoxemic respiratory failure and increased respiratory drive. LTVV in the setting of increased respiratory drive will therefore often result in a need for increased levels of sedation to maintain ventilator synchrony. Some patients will ultimately require neuromuscular blockade to achieve synchrony. The following recommendations (Fig, 4) should be utilized to guide sedation & mitigate potential shortages. For full details, please see separate sedation management document from pharmacy.

MASSACHUSETTS GENERAL HOSPITAL

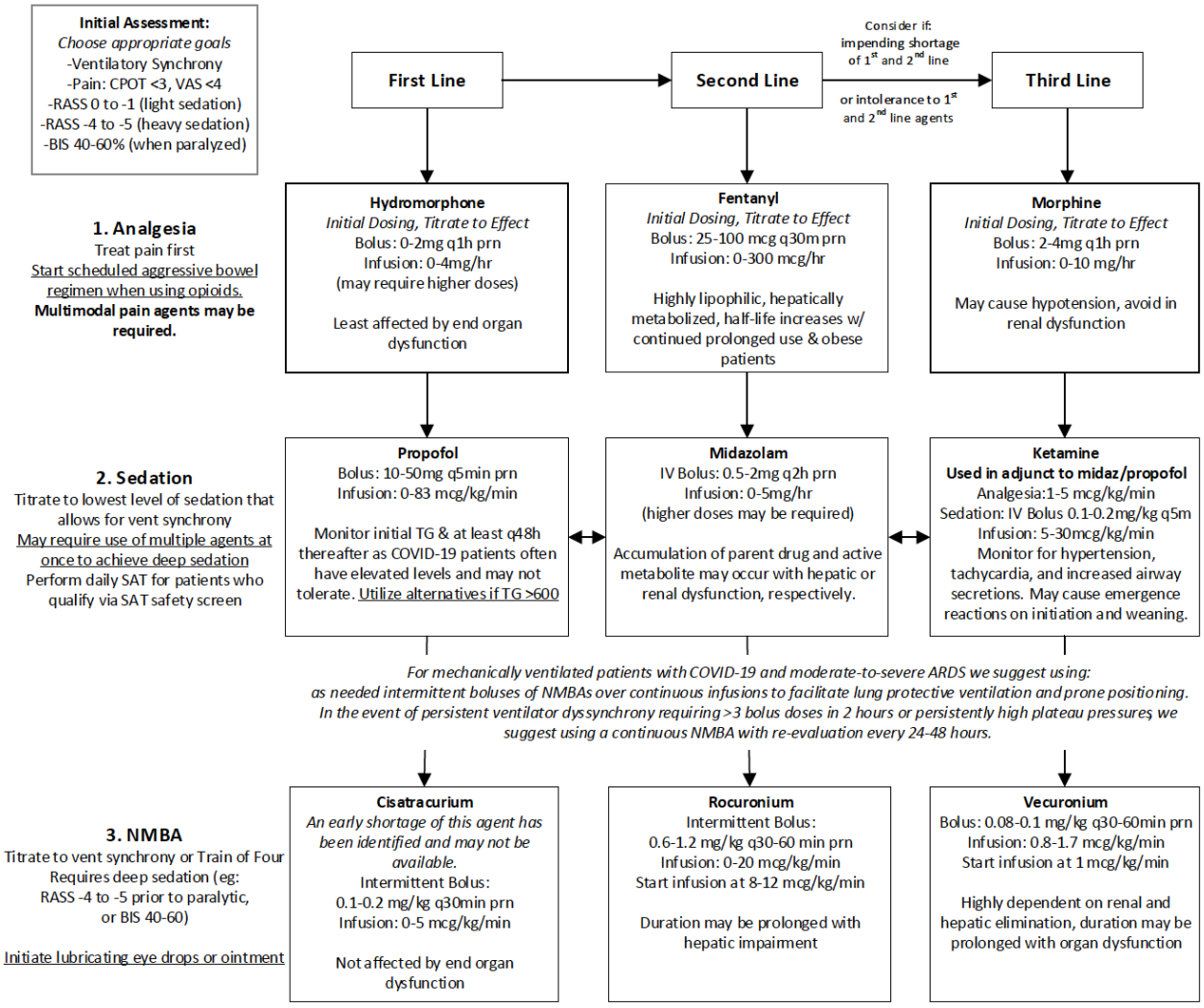

Figure 4: Sedation protocol for mechanical ventialted COVID-19 patients

Liberalization of ventilation strategy and extubation

In the MGH experience to date, it has been apparent that patients with ARDS in the setting of COVID-19 respond well to PEEP. This is also true of ARDS in general, in which the primary mechanism of hypoxemia is shunt that can be reduced via appropriate recruitment. In addition, should an extubation fail, it will result in an additional aerosol generating procedure which put the intubation team at risk. As a consequence, we recommend a cautious approach to vent weaning and spontaneous breathing trials. We recommend that the switch fromvolume control to pressure support not occur until the patient has a P:F safely above 200 with a PEEP of 8 or less. We recommend a P:F threshold of 230. In the absence of obesity, PEEP should be weaned to 5 cmH_2O before a spontaneous breathing trial (SBT) is appropriate. A spontaneous breathing trial should consist of a period of 2 hours on 0/0. Once the SBT is passed, extubation is appropriate.

There is no benefit to early tracheostomy in general medical ICU patients, and by extension in COVID-19 patients. Discussions around tracheostomy should be informed by the separate tracheostomy guideline maintain by the Department of Surgery. There will be no tracheostomies performed on COVID-19 patients prior to 14 days, in order to minimize the risk of performing an unnecessary aerosol generating procedure.

Hemodynamic Management

Initial reports from China and Italy indicate a predominance of isolated respiratory failure associated with COVID-19. In other words, patients with COVID-19 associated respiratory failure have a lower than expected incidence of associated organ failures such as shock and renal failure. Notwithstanding the above, shock and renal failure do occur. It is reasonable to treat these patients with usual protocols for distributive shock (norepinephrine/vasopressin as initial pressors, titrated to MAP > 65 mmHg, tailored fluid resuscitation, and monitoring of C_VO_2 and lactate[14]. There have been variable reports from China and Seattle of patients with cardiogenic shock secondary to myocarditis occurring late in their clinical course. One series from China reported myocarditis in 7% of patients. Therefore, a high index of suspicion must be maintained for the development of cardiogenic shock and viral myocarditis. In addition to exam findings (hypotension, cold extremities, delayed capillary refill) patients in whom cardiogenic shock is suspected should have EKG, lactate and central venous oxygen saturation checked. Based on availability, consider point of care ultrasound (POCUS) and cardiology consult. Formal echocardiogram may be obtained as well though myocarditis in association with COVID-19 is most likely to be managed medically. Weigh the risk of additional staff exposure against any expected therapeutic changes Such patients may require the addition of inotropes (epinephrine or dobutamine) to achieve hemodynamic stability. Confirmed or suspected presence of myocarditis should be discussed with the ECMO team if patients are being considered for extra-corporal support as it may have implications for choice of ECMO therapy (veno-arterial *versus* veno-venous).

Monitoring of coagulation and anticoagulation strategies

In many cases, ICU patients with COVID-29 have elevated d-dimer and non-specific derangements in the coagulation cascade. There are anecdotal, though not peer-reviewed, reports of hypercoagulability. Patients should be managed according to the separate hematology protocol posted on Apollo. All patients presenting to the ICU should have the following labs checked (if not before): d-dimer, PT, PTT, fibrinogen and CBC with differential. The preceding labs should be monitored every two days. In patients who develop worsening coagulopathy and/or DIC consider hematology consult. An increase in d-dimer is not currently an indication for intitaition of therapeutic anticoagulation All patients with COIVD-19 should receive standard prophylactic anti-coagulation with LMWH in the absence of severe bleeding or plt count < 25,000. Patients who develop renal failure and are started on anticoagulation while on CVVH should have factor Xa monitored. Please see the separate guidelines from Hematology for details on management of anticoagulation and abnormal parameters of coagulation in COVID-19 patients.

MASSACHUSETTS GENERAL HOSPITAL

Specific Therapies and Immunomodulation

There are no specific anti-viral therapies that have been proven to be effective in the settings of COVID-19. Investigational agents should be provided in consultation with Infectious Disease and in accordance with the separate MGH protocol for anti-infective treatment of COVID-19. Both bacterial and fungal superinfection has been reported. Immunomodulatory therapies such anti-IL-6ra should be provided in the context of ongoing clinical trials, access to which may be facilitated by infectious disease. In the absence of a secondary indication (exacerbation of COPD, transplant recipients, adrenal insufficiency) corticosteroids should be avoided in the setting of COVID-19.

1. Alhazzani W. Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19).

2. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wiedemann HP, Wheeler AP, et al. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006;354(24):2564–75.

3. Finfer SR, Vincent J-L, De Backer D. Circulatory Shock. N Engl J Med 2013;369(18):1726–34.

4. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63(5):e61–e111.

5. Oba Y, Zaza T. Abandoning Daily Routine Chest Radiography in the Intensive Care Unit: Meta-Analysis. Radiology 2010;255(2):386–95.

6. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med 2020;:NEJMc2004973.

7. Brochard L, Slutsky A, Pesenti A. Mechanical Ventilation to Minimize Progression of Lung Injury in Acute Respiratory Failure. Am J Respir Crit Care Med 2017;195(4):438–42.

8. Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators, Cavalcanti AB, Suzumura ÉA, et al. Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. JAMA 2017;318(14):1335–45.

9. Guérin C, Reignier J, Richard J-C, et al. Prone Positioning in Severe Acute Respiratory Distress Syndrome. N Engl J Med 2013;368(23):2159–68.

MASSACHUSETTS GENERAL HOSPITAL

10. The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network. Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome. N Engl J Med 2019;380(21):1997–2008.

11. Gebistorf F, Karam O, Wetterslev J, Afshari A. Inhaled nitric oxide for acute respiratory distress syndrome (ARDS) in children and adults. Cochrane Database of Systematic Reviews 2016;66(6):365.

12. Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. The Lancet 2009;374(9698):1351–63.

13. Combes A, Hajage D, Capellier G, et al. Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome. N Engl J Med 2018;378(21):1965–75.

14. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Critical Care Medicine 2017;45(3):486–552.