Inpatient Care of COVID 19

Baseline procedures:

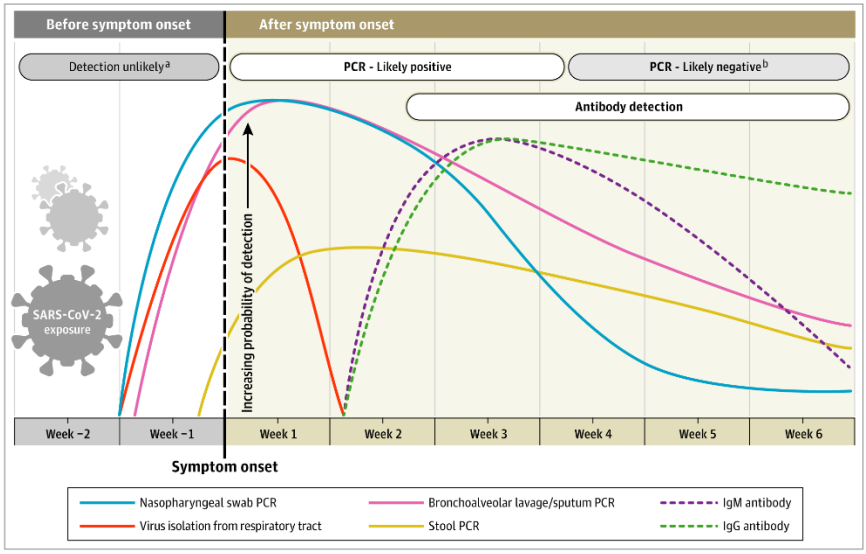
1. A complete medical history, including social history, occupational and family history.
2. Review of prior and concomitant medications.
3. Physical examination.
4. Vital signs, height, weight , SOFA score and qSOFA scores.
5. EKG (Electrocardiogram)
6. Radiologic imaging (Ultra Sound, Chest radiographs) CT scans are not indicated routinely and should be reserved for evaluation of pulmonary complications suggested by persistent pulmonary distress not responsive to standard treatment
7. Pregnancy test (For women of childbearing potential)
8. Hematology; **CBC** ,ABO blood group typing, PT, PTT.
9. Chemistry: Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine (EGFR), glucose, LDH, phosphorus, potassium, total protein, AST, ALT, sodium, Troponin, CPK, **Serum Ferritin, CRP, D dimer**.
10. Review for possible drug-drug interactions and appropriate adjustment
11. Evaluation for supplemental oxygen and early proning where appropriate
12. Unless contraindicated addition of Statins (HMG Co A reductase inhibitors) and Famotidine should be considered.
13. Review for adverse events.

It is strongly recommended that all subjects receive careful evaluation with appropriate diagnostic tests for COVID 19. Please see :

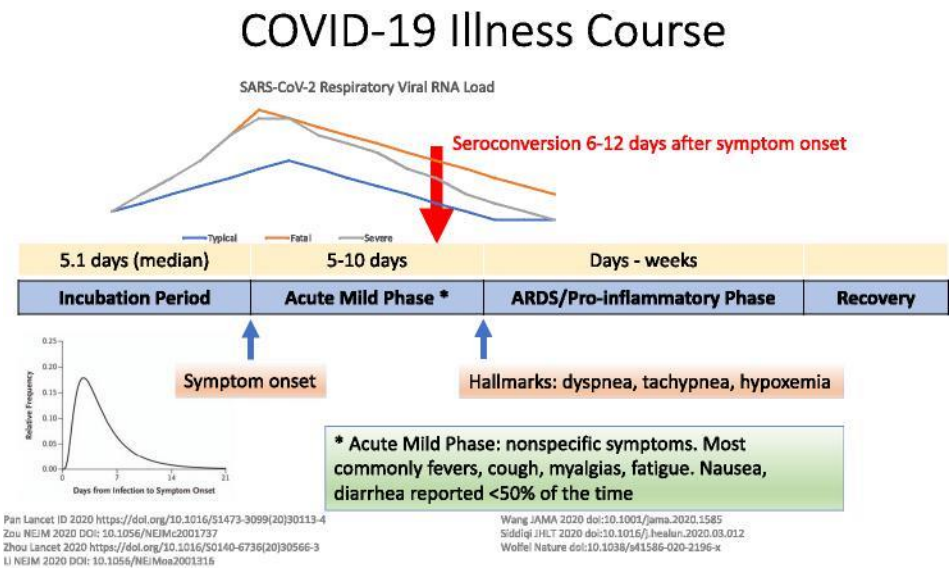
Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. JAMA. Published online May 6, 2020. doi:10.1001/jama.2020.8259.

Estimated Variation Over Time in Diagnostic Tests for Detection of SARS-CoV-2 Infection Relative to Symptom Onset. Estimated time intervals and rates of viral detection are based on data from several published reports. Because of variability in values among studies, estimated time intervals should be considered approximations and the probability of detection of SARS-CoV-2 infection is presented qualitatively. SARS-CoV-2 indicates severe acute respiratory syndrome coronavirus 2; PCR, polymerase chain reaction.

a) Detection only occurs if patients are followed up proactively from the time of exposure.
b) More likely to register a negative than a positive result by PCR of a nasopharyngeal swab.



All subjects need to be characterized as to the stage of illness:



COVID-19 clinical course of illness. The first phase of COVID-19 infection involves an incubation period of variable duration, with a median of 5.1 days. The second is an acute mild phase that most commonly includes flu-like symptoms like cough, fevers, and myalgias, but can also include gastrointestinal symptoms. Some patients progress to an ARDS hyperinflammatory phase that is often marked by dyspnea, tachypnea, and hypoxemia. The respiratory viral load rises before the onset of symptoms and peaks around the onset of symptoms. It declines over the first week. Severe cases have higher viral loads compared with mild cases. Prolonged viral shedding in severe and mild cases is reported.

Clinical care of the individual with COVID 19 infection requires evaluation for risk stratification and levels of CRP; LDH; Ferritin; D dimer, Lymphopenia and alteration of the lymphocyte to neutrophil ratio may assist in identifying individuals at high risk for developing serious illness. See:

Liang W, Liang H, Ou L, et al. Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19. JAMA Intern Med. Published online May 12, 2020. doi:10.1001/jamainternmed.2020.2033

Gong J, Ou J, Qiu X, et al. A Tool to Early Predict Severe Corona Virus Disease 2019 (COVID-19) : A Multicenter Study using the Risk Nomogram in Wuhan and Guangdong, China. Clin Infect Dis. doi:10.1093/cid/ciaa443

Care of the seriously ill individual requires expeditious evaluation of hypoxemia; risk of thrombotic events; coagulopathy; derangements of neurologic, cardiac, hepatic and renal function.

Evaluation and Management of Severe Covid-19. Please see:

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 (e.g., 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

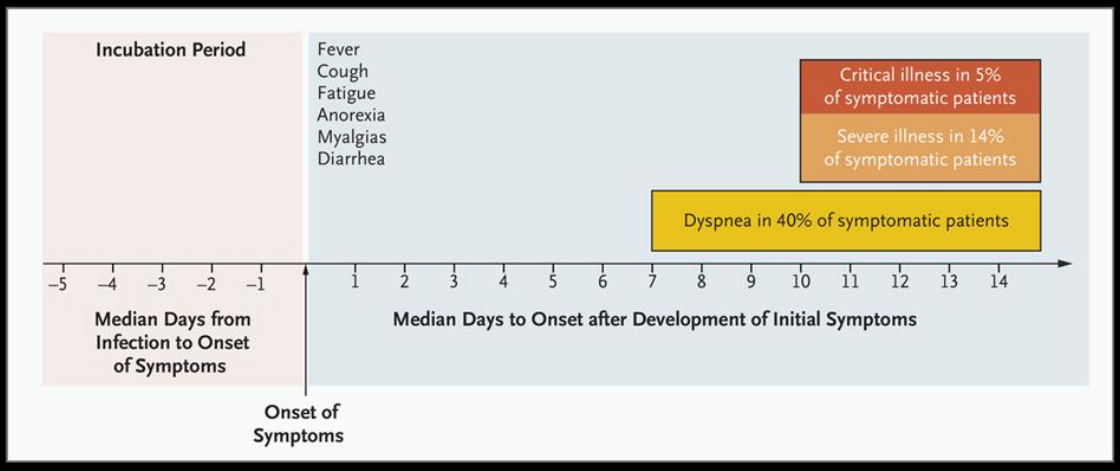
membrane oxygenation (ECMO) or referral to an ECMO center is suggested, if available, for selected patients (weak recommendation, LQE).

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 de-escalation.
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.

Poston JT, Patel BK, Davis AM. Management of Critically Ill Adults With COVID-19. JAMA. 2020;323(18):1839-1841. doi:10.1001/jama.2020.4914

Timeline of Symptoms of Severe Coronavirus Disease 2019 (Covid-19).



DA Berlin et al. N Engl J Med 2020. DOI: 10.1056/NEJMcp2009575

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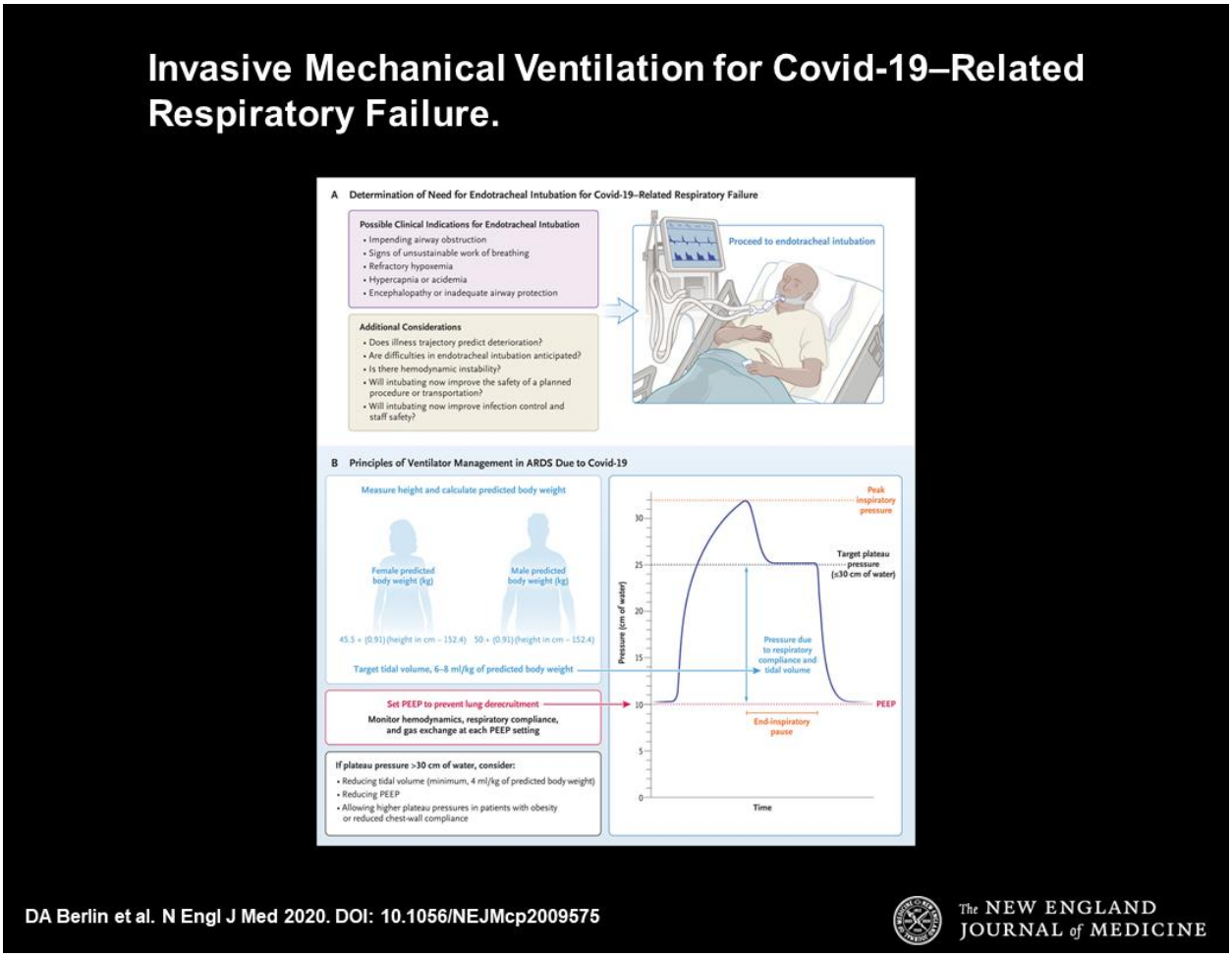
A key management issue is the timing of invasive mechanical ventilation for critically ill COVID 19 individuals and the supportive/ancillary care needed.



Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. New England Journal of Medicine. 2020;0(0):null. doi:10.1056/NEJMcp2009575

Other considerations for supportive care such as use of Dexamethasone, Tocilizumab; HMG CoA reductase inhibitors and/or use of N Acetylcysteine should be considered in each individual as appropriate. In individuals who are not responding to treatment and have evidence of ongoing hypoxia with active inflammation the use of Baricitinib/Tofacitinib can be considered along with prophylaxis for VZV and Pneumocystis. (Co-Trimoxazole or Dapsone; Valacyclovir)

1. *Berndt MC, Andrews RK. Thrombotic thrombocytopenic purpura: reducing the risk? Journal of Clinical Investigation. 2011;121(2):522-524. doi:10.1172/JCI46091*

2. *Knobl P. Inherited and acquired thrombotic thrombocytopenic purpura (TTP) in adults. [Review]. Seminars in Thrombosis & Hemostasis. 2014;40(4):493-502. doi:10.1055/s-0034-1376883*

3. *Martinez de Lizarrondo S, Gakuba C, Herbig BA, et al. Potent Thrombolytic Effect of N-Acetylcysteine on Arterial Thrombi. Circulation. 2017;136(7):646-660. doi:10.1161/CIRCULATIONAHA.117.027290*

4. *Levi M, Scully M, Singer M. The role of ADAMTS-13 in the coagulopathy of sepsis. Journal of Thrombosis and Haemostasis. 2018;16(4):646-651. doi:10.1111/jth.13953*

5. *Fenton JW, Jeske WP, Catalfamo JL, Brezniak DV, Moon DG, Shen GX. Statin Drugs and Dietary Isoprenoids Downregulate Protein Prenylation in Signal Transduction and Are Antithrombotic and Prothrombolytic Agents. Biochemistry (Moscow). 2002;67(1):85-91. doi:10.1023/A:1013956215394*

6. *Weitz-Schmidt G. Statins as anti-inflammatory agents. Trends in Pharmacological Sciences. 2002;23(10):482-487. doi:10.1016/S0165-6147(02)02077-1*

7. *Greenwood J, Steinman L, Zamvil SS. Statin therapy and autoimmune disease: from protein prenylation to immunomodulation. Nature Reviews Immunology. 2006;6(5):358-370. doi:10.1038/nri1839*

At discharge and post discharge the long term impact including ongoing symptoms and disability must be evaluated and a plan for appropriate rehabilitation is strongly recommended.

See:

Covid-19 and Post Intensive Care Syndrome: A Call for Action. doi:10.2340/16501977-2677

Hough CL, Curtis Jr. Long-term sequelae of critical illness: memories and health-related quality of life. Critical Care. 2005;9(2):145. doi:10.1186/cc3483

Use SF-36 to evaluate the impact of COVID 19 on Quality of Life (QOL) and possible disability in individuals after discharge from the hospital.

https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form.html

Other Resources:

https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

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