Northwell CoVID-19 (SARS CoV) Guideline

Quick Reference

Patients who develop progressive hypoxia (with or without dyspnea) can develop ARDS rapidly. This is a quick reference for general management of Critically ill CoVID-19 patients.

INTUBATION			
Pre-Oxygenation	NRB and Nasal Cannula: NO NIV or HFNC		
RSI with video laryngoscopy- if possible	Reduces cough/gag, less exposure to operator		
Hypoxia and hypotension occur quickly	Norepinephrine read to be infused; High PEEP post intubation; Avoid phenylephrine pushes		
Place NGT/OGT, CVC- if needed	Bundles care and allows 1 xray; use US if possible		
Ventilator Management			
Mode	**Assist-Volume Control**	**APRV**	
	Tidal Volume: 4-6ml/Kg Rate: 14 + (pt specific) PEEP: 10+ FiO2: 1.0 (initially) PaO2 goal: 70+ PaCO2: allow hypercapnia if needed SpO2 goal: 90%	P-high: 30-35cmH20 P-low: 0-5 T-high: 5 seconds T-low: 0.5 seconds PaO2 goal: 70+ PaCO2: allow hypercapnia if needed SpO2 goal: 90%	
High-PEEP ARDSnet	**FiO2**	**PEEP**	
	0.3	5→8→10→12→14	
	0.4	14→16	
	0.5	16→18→20	
	0.8	20→22	
	0.8	22→24….	
	1.0	24+	
ARDS Management			
PEEP	High PEEP Algorithm (above)		
Analgesia/Sedation	Improves ventilator synchrony	Fentanyl	Dexmedetomidine Propofol Midazolam
Paralysis	Improves ventilator synchrony	Cisatracurium	
Prone Positioning	Posterior aeration/oxygenation	*Link to NH prone papers* https://www.nejm.org/doi/full/10.1056/NEJMoa1214103	
ECMO	Escalation of treatment to Acute Lung Injury Center *http://b.link/ECMO* or 718.413.1745 (LIJ MICU attending) or 1833-NYCECMO		
Labs	**Required (admit)**	**Daily**	**Q3 days**
	CBC w/diff	CBC w/diff	
	CMP, Mg, Phos	CMP, Mg, Phos	

	PT/PTT/INR/D-dimer		PT/PTT/INR/D-dimer
If these labs are available recommendations are to order them for both prognostication and evidence gathering. Treatments, other than general medical care, are not currently changed by these labs (i.e. elevated d-dimer; no suggestion to start anticoagulation)	Fibrinogen/Haptoglobin/LDH		Fibrinogen/Haptoglobin/LDH
	ESR/CRP	CRP	ESR
	Procalcitonin		
	Ferritin		Ferritin
	Lactate		
	Troponin/CK		Troponin/CK
	T cell subset		T cell subset
	G6PD		
Quest diagnostics, Core Lab Test Catalog	Natural Killer Cells	Core lab test catalog available in SCM on top banner; order form is downtime document	
Cytokine Panel, Core Lab Test Catalog	Interleukin 6 and 8		
Treatment options			
Steroids-Methylprednisolone	May increase viral shedding early in disease	Patient may require it for other conditions	Later stages of disease (CoVID-19 with ARDS) may require them
Remdesivir	Theoretical model in MERS	Gilead Pharmaceuticals compassionate use	
Lopinavir/ritonavir + ribavirin	Theoretical model in SARS & MERS lab/animal/ human studies.	No clear clinical benefit in treatment. Likely post exposure prophylaxis for SARS/MERS	More widely available than Remdesivir.
Chloroquine Hydroxychlorquine	Theoretical model in SARS- lab/animal data	Theory suggested more efficacious in CoVID-19 than SARS.	
Tocilizumab	No evidence. Theory to reduce “cytokine storm” (IL-6)	Anecdotal suggestion of clinical improvements.	
Anakinra	No evidence. Theory to reduce “cytokine storm” (IL-1).		
Ascorbic Acid	Clinical studies suggest improved mortality, though secondary analysis of most recent studies note sub-groups (ARDS) many not have morality improvement.		
Thiamine	Literature similar to ascorbic acid- based on studies on thiamine + ascorbic acid + hydrocortisone which demonstrated improved outcomes (i.e. mortality) in septic (shock) patients. Limited evidence by itself.		

Statement of Purpose

As CoVID-19 (SARS CoV-2) is beginning to move more rapidly and our Critical Care areas are starting to house more patients, Critical Care within Northwell should seize the opportunity to work together across a unified front.

This document is designed to be a dynamic workspace for our Critical Care teams to pool information, share experiences, and disseminate best practices. While new information arises daily about CoVID-19, the aim here is to amalgamate the information, provide guidance of best practices, and references for theoretical options based on similar diseases and the pathophysiologic response to them.

This is *not* designed to be the end-all be-all for treatment, management, or information. Please use it as a guide where specific patient needs may vary. If you find errors, updates, or additions please email chertz@northwell.edu.

We will update the document weekly or more often as newer information arises. Dr. Hugh Cassiere and Dr. Mangala Narasimhan were crucial partners in collating much of this information.

Patient Course to Critical Illness

After an incubation period (2-7 days) non-specific symptoms develop, though fevers and cough appear to be most common. Most symptoms are mild. Hospitalized patients commonly have dyspnea, sputum production and shortness of breath.

Areas of Concern

Hypoxemia

More literature is demonstrating "Silent Hypoxemia," meaning you'll see it, though the patient may not notice it (i.e. no dyspnea). *Rapid progression* to respiratory failure is a concern. Patients go from a few liters' nasal cannula to non-rebreather to intubation within hours. DO NOT USE Non-Invasive ventilation or High flow Oxygen- these aerosolize the droplets and risk further spread of CoVID-19

Acute Respiratory Distress Syndrome

Profound hypoxemia with P:F ratios < 150 being common. Many require FiO2 >0.8 and seem to respond well to higher PEEP ventilator strategies. Venous-Venous (VV) Extracorporeal Membrane Oxygenation (ECMO) *may be* beneficial after maximizing standard ARDS therapy *including* prone positioning

Lung Ultrasound Findings

Lung ultrasound provides a quick way to evaluate patients while not having to potentially expose other Team Members (radiology) or transport patients through a hospital (CT). Initially CT was used to describe bilateral ground glass opacities, after which the patient was screened for CoVID-19, this is a limited resource for many of us. LUS solves this.

Progression of B-lines from scattered to coalescent is a concerning finding. Furthermore, any consolidations or subpleural collections should further raise concern. Pre-planning for intubation should being if you start to see this progression.

Significant Laboratory Findings

General

Lymphopenia is common. Other non-descript or subtle abnormalities are also common: thrombocytopenia, Aminotransferase elevations, etc.

C-Reactive Protein

Inflammatory marker with *potential* relationship to disease severity, mortality, and progression. Values in the 100's (mg/L) are concerning for increased mortality. Trending this may help prognosticate disease.

Erythrocyte Sedimentation Rate

Inflammatory marker with *potential* relationship to disease severity, mortality, and progression. Trending this may help prognosticate disease.

Ferritin

Inflammatory marker with *potential* relationship to disease severity, mortality, and progression. Trending this may help prognosticate disease.

Procalcitonin

Commonly low (normal) increases raise concern for secondary bacterial infection should be considered.

D-Dimer

Will be elevated, still unsure what to do with this, at the moment anticoagulation is *not* recommended.

Lactate Dehydrogenase

Will be elevated, again marker of disease severity

Troponin

Usually not elevated, *despite* described cardiac decompensation. Increase should raise concern for cardiac demise, *especially* if new shock state developes

Natural Kill Cells, Interleukins (6, 8), T-Cell Subsets

Will be abnormal; may correlate with "cytokine storm" and direct viral impact on immune function. May contribute to concerns of Hemophagocytic lymphohistiocytosis (HLH) conversion.

Glucose-6-phophate dehydrogenase (G6PD) testing

Evaluates for patient deficiency as several experimental medications can lead toward massive hemolysis

Coagulation Profiles

Commonly normal, if increases in PT/aPTT, drop in Fibrinogen and Haptoglobin, concerns for disseminated intravascular coagulopathy. Mortality exceedingly high in this subgroup

Disease Pathophysiology

Two disease phases are suggested: *Replicative*- Innate immune reaction, mild symptoms. *Adaptive Immunity*- appears, in severe cases, to be overactive (reactive) and leads to the "cytokine storm" theory

ARDS

As noted above- is likely due to both an immune reaction *and* direct insult via CoVID-19.

Cytokine Storm

The current working theory is the overactivity of our immune/inflammatory pathways trigger massive cytokine release/reaction. This appears to be isolated to the respiratory system initially, though more cases are reporting sudden cardiovascular collapse *after* recovery from ARDS, thus concerns for cardiac involvement as well. This is also the theory on which several of the experimental treatments are based off of. Markers of inflammation- CRP, ESR, Ferritin may be used to trend this. Also appears to contribute to the HLH conversion in some patients

Theoretical Pharmacologic Interventions

General

Currently *all* pharmacologic interventions are based on theory, none have been used in RCTs or approved for use in CoVID-19. The working theories are based on SARS and MERS in the past; of which none demonstrated significant clinical efficacy over "standard" ARDS therapy. *Random testing of medications on human subjects without consent or IRB enrollment is NOT ethical NOR a standard practice in medicine or Northwell.*

None of these medications have been demonstrated to improve out comes nor do we know when they are most useful (early or late stages). Immunomodulators (i.e. IL-6 or IL-1 inhibitors) may be beneficial earlier in the treatment course as may Remdesivir. These medications SHOULD NOT be used without weighing the risk/benefit profiles as they can manifest profound side-effects. Dosing, mechanism of action, and pharmacokinetics (i.e. what if patient is on CRRT) are too complex to be discussed here.

Steroids

Various evidence for use. Concerns in "early" stages for increased viral replication, though this is based off of work on SARS CoV-1. Recently, information noting improvement with methylprednisolone, though not clinically significant. May be required for shock state or other etiology as well.

Remdesivir

Evidence extrapolated from MERS lab and animal studies

Lopinavir/ritonavir + ribavirin

Evidence extrapolated from SARS and MERS lab, animal, and human studies. No clear clinical benefit in treatment, more likely (SARS, MERS) in post exposure prophylaxis. More widely available than Remdesivir.

Chloroquine/Hydroxychlorquine

Evidence extrapolated from SARS lab and animal studies. In lab theory suggested more efficacious in CoVID-19 than SARS.

Tocilizumab

No evidence. Theory to reduce "cytokine storm" (IL-6) with anecdotal suggestion of clinical improvements.

Anakinra
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Ascorbic Acid
Clinical studies suggest improved mortality, though secondary analysis of most recent studies note sub-groups (ARDS) many not have morality improvement.

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Oxygen, Intubation, and Ventilator Management

Oxygen
Patients may rapidly progress to ARDS with rapidly increasing oxygen needs. This is despite dyspnea initially (silent hypoxia). Patients who start requiring supplemental oxygen should be re-evaluated frequently. Ideally LUS would also be performed as a baseline measure. If a patient starts to require more supplemental oxygen (i.e. 2 liters → 5 liters nasal cannula) continuous pulse oximetry may be considered. Patients who require venturi masks or non-rebreathers *must* be evaluated by a Critical Care provider (ideally before this point) and should be intubated sooner rather than later. Most patients who progress to this point will be intubated.

Intubation
Standard set-up and check-lists for intubation should remain.

Pre-oxygenation via NRB and nasal cannula are recommended. DO NOT use NIV or High Flow Oxygen- increase aerosolization of CoVID-19. *Limited BVM*, use with PEEP valve and, if possible, filter (potentially reduces aerosolized CoVID-19).

Awake intubation is not suggested due to increase potential for coughing. Most experienced airway technician should intubate. Induction medications per patient needs. RSI suggested to reduce risk of coughing, gagging.

Hypotension AND hypoxia occur rapidly post intubation. Have norepinephrine infusions ready at bedside. Would avoid phenylephrine “pushes” for risk of cardiovascular collapse/sudden death. May require high PEEP (>15cmH2O) immediately post intubation.

Post-intubation Bundled Care
Place Naso-gastric or oro-gastic tube. If central venous access is required, place this as well. Allows for single xray (if required). Can use ultrasound to ensure CVC is in correct position.

Ventilator Management
Conventional ventilator modes (i.e. assist control, volume control) are suggested for ease of trouble shooting and wider knowledge base. Advanced modes can be considered, such as Airway Pressure Release Ventilation (APRV), which should be implemented earlier in course of disease.

Most patients require FiO2 > 0.80 and respond well to higher PEEP management for ARDS.

Common ARDS management with High PEEP (15+) is not uncommon. Goals for lower tidal volumes (6ml/Kg or less) is suggested in order to keep plateau pressures < 30cmH2O. Table *modified* from ARDSnet; modified for simplicity. Could consider lung recruitment maneuvers as well.

FiO2	PEEP
0.3	5→8→10→12→14
0.4	14→16
0.5	16→18→20
0.8	20→22
0.9	22→24….
1.0	24+

Prone Position

Demonstrated in ARDS to improve oxygenation and potentially clinically outcomes.

VV-ECMO

Early evaluation by the Acute Lung Injury center is recommended for patients who do not improve with maximal ARDS therapy including paralysis and prone position.

Escalation of treatment to Acute Lung Injury Center *http://b.link/ECMO* or 718.413.1745 (LIJ MICU attending) or 1833-NYCECMO.

General Considerations in Treatment/Therapy

Most patients develop single organ failure, though acute kidney injury can occur. Diuretics in the setting of ARDS can be considered as most of the CoVID-19 patients are not in shock state. IV fluids are not recommended unless in shock state.

Early goals of treatment and patient preferences are required. Patients remain intubated for upwards of 10-14 days (even longer). All complications of ARDS management should be presumed to occur, including prolonged physical, emotional, and cognitive recovery.

Ethics

General

References

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