FRONTLINE COVID INFO/GUIDE

A compilation and synthesis of COVID info created by and for frontline MDs. We aren’t ID experts and this is not a comprehensive guide -- just a document put together to facilitate quick access to good info. Please email at bolleskm@gmail.com to notify of any omissions/errors.

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Last update 03/21/20

CLINICAL GUIDES/GENERAL INFO

COVID One Pager by Nick Mark, MD
EmCrit COVID Review
CDC COVID Site
EB Medicine COVID19 Guide
UpToDate COVID19 (no paywall)
Stanford Grand Rounds on COVID

MAPS & TRACKING

WHO Pandemic Situation Reports
Johns Hopkins Pandemic Map

GUIDELINES & PROTOCOLS

CDC Guidelines
WHO Guidelines
SCCM COVID19 Guidelines
UW COVID Protocols
UCSF COVID Protocols
Mount Sinai Health System Protocols
MGH Treatment protocols
Brigham & Women’s Critical Care Protocols

CONSOLIDATED COVID STUDY REPOSITORIES

NIH LitCOVID
WHO COVID Research
Wiley COVID articles (no paywall)
NEJM COVID articles (no paywall)
JAMA COVID articles
IDSA COVID19 Resource Center

EPIDEMIOLOGY

Patient Characteristics:
• Median hospitalized age varies by country and case report, mostly between 40s-70s (Wang et al, Arentz et al)
• Initial male predominance but less clear as more data appears (Wang et al, Arentz et al)
• Most patients with comorbidities, esp HTN, DM, CVD, chronic respiratory disease
Incubation period: median 5-7 days, 98% within 12 days (Lauer et al, Tian et al)
R₀: around 2-2.5 in general population (WHO), up to 11 aboard cruise ships (Mizumoto & Chowell) but can be lowered through distancing & public health controls
Viral shedding: can be present 1-3 days prior to onset of symptoms, median duration 20 days with durations up to 37 days in recovered patients (Zhou et al)

TRANSMISSION, ISOLATION, & PPE
Transmission via droplet, contact (fomites up to 7hrs on some surfaces); unclear if airborne transmission but may be possible (van Doremalen et al)
Asymptomatic transmission may be possible based on case reports (Bai et al)
Current CDC, WHO, SCCM recommendations: contact and droplet for COVID+ and rule out; airborne if aerosolizing procedure
• In influenza studies, surgical facemasks appear equivalent to N95 in respiratory infection prevention -- though N95 significantly better in vitro, pragmatic benefit unclear (Smith et al, Radonovich et al)
All aerosolizing procedures (intubation, NIPPV, HFNC, suctioning, nebs, bronchoscopy, endoscopy, TEE) should be performed in negative pressure rooms (SCCM)
• HFNC increases droplet spread and should be considered aerosolizing (Ne-Hooi et al)
• Laparoscopy should be considered a potentially aerosolizing procedure, avoid ALL elective procedures and use viral filters if considering (SAGES)
• Avoid aerosolizing procedures when possible
MaskMatch, working to match HCWs needing masks with people looking to donate
Creative solutions as supplies run low:
• 3D printing templates (not tested or validated, but likely better than nothing)
  o Masks, face shields
  o Dual filter masks
  o Face shields
  o Face mask holders/frames (maybe with vacuum bags for filters given HEPA filter inside?)
• N95s > surgical masks > homemade masks > nothing against droplet transmission (van der Sande et al)

CLINICAL FEATURES
Symptoms:
• Adults: fever (99% over 99F in one study, but up to 40% afebrile on admission in another), fatigue (70%), dry cough (59%), anorexia (40%), myalgias (35%), dyspnea (31%), sputum production (27%) (Wang et al, Leung et al, Arentz et al, Guan et al)
  o Symptoms are highly variable and should generally have high index of suspicion for isolation and testing (Lynch)
- Look out for “silent hypoxemia” — profound hypoxemia without respiratory distress (Xie et al)
- GI symptoms (abd pain, diarrhea, N/V) were rare in some case series but common (49%) in others; often preceded respiratory symptoms (Wang et al, Lei et al)
- ARDS present in all intubated patients (Arentz et al)
- Cardiomyopathy in ⅓ of patients (Arentz et al, Ruan et al)
- Presence of shock highly variable (1%-35%) (SCCM)

- Children: more variable -- most common cough (48%), pharyngeal erythema (46%), fever (42%) (Lu et al)
- Pregnancy: very little known, but very small (15) case series without clear difference in outcomes of mild disease or clear adverse impact on fetus/childbirth (Liu et al)

Spectrum of disease: 81% mild, 14% severe, 5% critical (Wu & McGoogan)

Co-infection with other respiratory virus including flu has been described; does not appear common in adults (Ding et al) but may be common in children (Xia et al)

Course:
- Average 7 days from symptom onset to hospitalization (Tian et al)
- Most admitted to ICU within 24hrs of admission (Arentz et al, Wang et al)

LAB FINDINGS
- Sensitivity of nasopharyngeal RT-PCR debatable and may be low (63-67%) for single PCR, increased with repetition (Fang et al, Wang et al)
  - Increased sensitivity with BAL (93%), sputum (72%) (Wang et al) but unclear if bronchoscopy advisable given aerosolization risk (Bouadma et al)
  - Chest CT may be more sensitive (98%) but less specific (Fang et al), but may not be a good use of resources esp. with disinfection times required
- Normal WBC with lymphopenia common (Wang et al, Arentz et al)
- Elevated inflammatory markers (D-dimer, CRP, IL-6, ferritin, LDH) though notably low ESR (Zhou et al)
  - Elevated D-dimer, PT, LDH, IL6, trop, CRP, myoglobin more common in severe disease (Wang et al, Arentz et al, Zhou et al, Ruan et al)
- Procal usually negative or indeterminate, may be elevated in superinfection
  - Small case series in children showed most (80%) with procal >0.05, though unclear if due to COVID or coinfection (Xia et al)
- Seeing some elevation in LFTs but typically not substantial hepatitis
- Prevalence of AKI unclear but may be more common than initially thought and AKI is an independent risk factor for mortality (Naicker et al)
  - Proteinuria in 44-67%, massive albuminuria in ⅓, elevated Cr in 15-20% (Li et al, Cheng et al)

IMAGING
Pulm CCM Guide to Lung Imaging in COVID19
Italian Radiology COVID19 Image Database
- CXRs with hazy, bilateral reticular opacities or GGOs; sensitivity appears variable, but increased after 72hrs (Arentz et al)
- CT: highly sensitive, progression over disease course (Shi et al)
  - Early on (including before symptom onset) may see unilateral, multilobar, peripheral GGOs
    - CT abnormalities prior to laboratory confirmation in 70% (Li & Xia)
  - Progression to bilateral (90%), diffuse (50%) GGOs in most patients (Shi et al)
  - Consolidation with halo sign may be seen in pediatric patients (Xia et al)
  - Lesions predominantly bilateral, lower lobe > upper lobe (Zhao et al)
  - Progression to multifocal consolidation, air bronchograms, traction bronchiectasis, crazy paving appears to be correlated with more severe disease (Zhao et al)
- Lung US findings usually pleural thickening and B lines, seems more sensitive than CXR and less than CT but need to capture a lot of lung area (Peng et al)
  - Butterfly Lung US training videos (no paywall)

OUTCOMES/PREDICTIVE METRICS

Case fatality rates vary widely by country and likely inaccurate at this point given limited capture, overall CFR in largest study thus far (China) was 2.3% (Wu & McGoogan)

Increasing age appears to be a significant predictor of severity & mortality with CFR of 15% in patients over 80 years (Wu & McGoogan, Zhou et al, Ruan et al)
- HCWs appear to get sicker than age would otherwise predict with 14.8% severe or critical cases, higher rates of infection in overwhelmed areas (Wu & McGoogan)
- Kids appear to do relatively well -- 87% discharged home, 12% stable on medical floor, 0.6% mortality (1 patient) (Lu et al)
- Very early data with no clear difference in outcomes in pregnancy (Liu et al)
- Comorbidities significantly increase mortality: CVD (CFR 10.5%, OR 21), diabetes (CFR 7.3%), COPD (CFR 6.3%), HTN (CFR 6.0%), cancer (CFR 5.3%) (Wu & McGoogan, Zhou et al)
- Cause of death: 53% resp failure, 33% resp failure + heart failure, 5% heart failure (Ruan et al)

SOFA score correlated with in-hospital mortality (OR 5.65) (Zhou et al)

Laboratory indicators of severity/mortality
- Lower mortality with early warning system based on age, lymphocyte count, O2 req, CT scan (thresholds unclear) to triage to BID or continuous monitoring, then early ICU transfer for RR>30, SpO2<93%, or HR>120bpm (Sun et al)
- D-dimer > 1 (OR 18.42) (Zhou et al), elevated trop, CRP, and myoglobin correlated with poor outcomes (Ruan et al)
- D-dimer (threshold 0.28) and IL-6 (threshold 24.3) may be a good combo of markers for severe disease (96% sensitivity, 93% specificity in small cohort) (Gao et al) -- please note, paper does not include case definition of mild vs severe disease

PULMONARY.CRITICAL CARE
SCCM COVID19 Guidelines

Highlights: mostly adheres to traditional critical care for shock and ARDS

- Conservative over liberal fluid resuscitation with typical preference for buffered crystalloids > NS > colloids
- If pressors required, recommend norepi first line, vaso second line to target MAP 60-65
  - If cardiac dysfunction despite fluids and norepi, recommend dobutamine
  - Low-dose corticosteroids for refractory shock
- COVID19 specific: recommend HFNC over NIPPV for patients needing more support than conventional NC O2 (high risk for aerosol production/transmission, may depend on local hospital protocols)
  - If HFNC unavailable and no immediate indication for intubation, can consider short NIPPV trial (high risk for aerosol production/transmission, may depend on local hospital protocols)

From SCCM guidelines

- COVID19 specific: recommend early intubation if worsening on HFNC or NIPPV with expert performing, minimal staff in room, negative pressure, and contact + droplet + airborne precautions
- Follow typical ARDS algorithms with LPV (ARDSNet), PEEP (ARDSNet), paralytics (PETAL), proning (PROSEVA)
  - Consider trial of inhaled pulmonary vasodilator as rescue therapy, recommend against inhaled NO
  - Recommend tradition but not staircase recruitment maneuvers
- As a last resort, consider VV ECMO if available, but resource intensive and essentially no data (reportedly used in China but no outcomes data yet)
Other COVID19-specific notes:
- Tend to have better response to high PEEP and better compliance than similarly ill ARDS patients (observations from Italian ICU MDs, no published data)
- May be possible to share/split vents in crisis, though prior studies/explorations primarily in mass trauma not pandemic (Neyman)
- Avoid bronch unless suspected alternate etiology or superinfection given super high infxn risk and no other benefit (Bouadma et al)

Brigham & Women’s Critical Care Protocols
Crit Care MDs COVID respiratory failure algorithm

Critical care for non-intensivists:
- SCCM online training in critical care for non-CCM physicians
- Dr. Jessica Bunin's videos on critical care for non-intensivists: vent management, shock, vasoactive medications, acid base

CARDIOLOGY
ACC/China Meeting Summary
COVID-19: Cardiac and Arrhythmic Complications by Christopher Kovach, MD MSc
CardioNerds on COVID & Cardiology by Pranoti Hiremath, MD
- In one case series, 17% of patients with arrhythmia (44% of ICU patients) and 7% with cardiac injury (22% of ICU patients) (Wang et al)
- Reports of MI, acute onset heart failure, myocarditis, and cardiac arrest (ACC Bulletin); some patients presenting with purely CHF or myocarditis Sx (Zheng et al)
- Overall seeing a high mortality with CV involvement though pathway (stress CM vs direct viral injury vs cytokine storm) currently unclear (Zheng et al)
ACE2 is a functional receptor for SARS-CoV-2 (Zheng et al) which has led to consideration of association between ACE/ARB use and COVID outcomes
  ○ Patients with HTN, heart disease appear overrepresented in COVID diagnoses and mortality but difficult to interpret without age adjustment or cohort studies (Sparks et al)
  ○ No clear evidence of causation or worse outcomes with ACE/ARB (Sparks et al), may have some lung protection from ARB in prior SARS studies
  ○ Professional societies currently recommend continuing ACE/ARB for patients already taking (Sparks et al, ACC)

NEUROLOGY

○ Limited data suggest that hospitalized patients with SARS-CoV-2 with severe infections (≥2 organ systems involved) are at significantly elevated risk of stroke/cerebrovascular events (Li et al) and this is a negative prognostic factor
○ Extremely elevated levels of CRP and D-dimer (>6) are likely indicative of severe generalized inflammatory conditions leading to prothrombotic state responsible for these outcomes (Li et al)
○ SARS-CoV-1 and MERS-CoV have previously demonstrated ability to infiltrate CNS, most likely via olfactory bulb neurons and trans-synaptic spread; prior studies have demonstrated viral antigens in the respiratory centers of the medulla raising questions of a potential contributory effect on pulmonary/respiratory compromise (Li et al)

POTENTIAL COVID-TARGETED TREATMENTS

Investigational:

○ Remedesivir: effective in vitro with chloroquine (Wang et al), clinical trials in progress
○ Chloroquine/Hydroxychloroquine: effective in vitro (Wang et al, Lui et al); may have clinical efficacy (esp. with azithromycin) but unclear validity of studies so far (Gao et al (abstract only), Gautret et al (unable to find working DOI))
  ○ Also in trials for infection prevention/PPx (U Minnesota)
○ Favilavir: approved in China per news reports, not available in US, unable to find studies
○ Tocilizumab: may help cytokine storm, case series of 21 patients in China with clinical improvement and no known adverse events (Xu et al)
○ Convalescent sera: theoretically beneficial (Casadevall & Pirofski), reportedly some cases in China but unable to find data, can’t find trials yet; may also be logistically difficult; SCCM currently recommends against use of convalescent plasma or IVIG
○ ACE2: undergoing small observational trial in China, no results yet
○ Lopinavir-Ritonavir: initial observations & RCT without clear efficacy in COVID19 (Young et al, Cao et al)
  ○ Caveat: Known increased activity in SARS-CoV-1 when used in conjunction with ribavirin (Chu et al) but not used in current COVID studies (EmCrit)
○ Neuraminidase inhibitors (oseltamivir): no in vitro benefit in SARS-CoV-2 (Tan et al)

Controversial:
• Corticosteroids: may have reduced mortality in COVID-related ARDS (HR 0.38) in single, small, uncontrolled trial (Wu et al) but not recommended due to prior SARS data indicating increased viral shedding (Lee et al); WHO & CDC guidelines currently recommend against use but SCCM guidelines recommend use in patients with ARDS (not in patients without ARDS)
  • May consider in patients with other indications (COPD, vasopressor-resistant shock)
  • Not all steroids created equal - dexamethasone may be preferable agent due to relative lack of mineralocorticoid activity, decreasing potential for worsening pulmonary edema while still tamping down inflammatory response
• NSAIDs for symptomatic treatment: WHO initially recommended against, then rescinded; it appears this may have been based off theoretical concern of increasing ACE2 expression and viral entry, unclear if any clinical data of different outcomes

TALKING WITH PATIENTS/FAMILIES
Guide for discussions with patients and families about COVID by Anthony Back, MD
  • Reportedly planning guide for families soon
Vital Talk app with family discussion guides, including for COVID19

SELF CARE
(note: not company endorsements, just seemed like good resources -- take care of yourselves)
Headspace meditation app (free for HCW with NPI)
Down Dog yoga app (free until 04/01)
Les Mills workouts on demand (currently free)
Kansas City Zoo 24hr Penguin Cam