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Coronavirus Disease 2019 (COVID-19)

Interim Clinical Guidance for Managem Patients with Confirmed Coronavirus D (COVID-19)

Summary of Recent Changes

Revisions were made on April 3, 2020, to reflect the following:

- New information about asymptomatic and pre-symptomatic infections
- Non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, as blockers and risk of infection or infection severity
- Information about COVID-19 and potential for SARS-CoV-2 reinfection
- Possibility of infection with both SARS-CoV-2 and other respiratory viruses
- Additional laboratory and imaging findings in COVID-19
- Updated guidelines from the World Health Organization and the Surviving Sepsis Ca
- Inclusion of new resource: Information for Clinicians on Therapeutic Options for CO'
- Inclusion of National Institutes of Health: Coronavirus Disease 2019 (COVID-19) Trea

This interim guidance is for clinicians caring for patients with confirmed infection with sev coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). Cl guidance as more information becomes available.

The National Institutes of Health recently published guidelines on prophylaxis use, testing patients. For more information, please visit: National Institutes of Health: Coronavirus Dis Treatment Guidelines . The recommendations in the guidelines were based on scientifi and will be updated as more data becomes available.

Clinical Presentation

Incubation period

The incubation period for COVID-19 is thought to extend to 14 days, with a median time of symptoms onset.¹⁻³ One study reported that 97.5% of persons with COVID-19 who develo 11.5 days of SARS-CoV-2 infection.³

Presentation

The signs and symptoms of COVID-19 present at illness onset vary, but over the course of COVID-19 will experience the following^{1,4-9}:

- Fever (83–99%)
- Cough (59-82%)
- Fatigue (44–70%)
- Anorexia (40–84%)
- Shortness of breath (31–40%)
- Sputum production (28–33%)
- Myalgias (11–35%)

Atypical presentations have been described, and older adults and persons with medical corpresentation of fever and respiratory symptoms. In one study of 1,099 hospitalized pa 44% at hospital admission but later developed in 89% during hospitalization. Headache, throat, hemoptysis, vomiting, and diarrhea have been reported but are less common (<10 COVID-19 have experienced gastrointestinal symptoms such as diarrhea and nausea prio respiratory tract signs and symptoms. Anosmia or ageusia preceding the onset of respirancedotally reported, but more information is needed to understand its role in identifying

Several studies have reported that the signs and symptoms of COVID-19 in children are si milder compared to adults.¹³⁻¹⁷ For more information on the clinical presentation and cou Information for Pediatric Healthcare Providers.

Asymptomatic and Pre-Symptomatic Infection

Several studies have documented SARS-CoV-2 infection in patients who never develop syr patients not yet symptomatic (pre-symptomatic). ^{14,16,18-28} Since asymptomatic persons are prevalence of asymptomatic infection and detection of pre-symptomatic infection is not v found that as many as 13% of RT-PCR-confirmed cases of SARS-CoV-2 infection in childrer study of skilled nursing facility residents infected with SARS-CoV-2 from a healthcare work asymptomatic or pre-symptomatic at the time of contact tracing evaluation and testing. ²⁶ abnormalities on chest imaging before the onset of symptoms. ^{20,21} Some data suggest that tended to be detected in younger individuals and was less likely to be associated with vira

Asymptomatic and Pre-Symptomatic Transmission

Epidemiologic studies have documented SARS-CoV-2 transmission during the pre-sympto and asymptomatic transmission has been suggested in other reports.^{22,23,32} Virologic stud CoV-2 with RT-PCR low cycle thresholds, indicating larger quantities of viral RNA, and cultured with asymptomatic and pre-symptomatic SARS-CoV-2 infection.^{19,24,26,33} The exact degree shedding that confers risk of transmission is not yet clear. Risk of transmission is thought are symptomatic since viral shedding is greatest at the time of symptom onset and declin days to weeks.³³⁻³⁶ However, the proportion of SARS-CoV-2 transmission in the population symptomatic infection compared to symptomatic infection is unclear.³⁷

Clinical Course

Illness Severity

The largest cohort of >44,000 persons with COVID-19 from China showed that illness seve critical³⁸:

- Mild to moderate (mild symptoms up to mild pneumonia): 81%
- Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
- Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%

In this study, all deaths occurred among patients with critical illness and the overall case f fatality rate among patients with critical disease was 49%.³⁸ Among children in China, illne having asymptomatic, mild or moderate disease, 5% having severe disease, and <1% havi COVID-19 cases with known disposition, the proportion of persons who were hospitalized persons with COVID-19 admitted to the intensive care unit (ICU) was 6%.³⁹

Clinical Progression

Among patients who developed severe disease, the medium time to dyspnea ranged fron to acute respiratory distress syndrome (ARDS) ranged from 8 to 12 days, and the median from 10 to 12 days. ^{5,6,10,11} Clinicians should be aware of the potential for some patients to after illness onset. Among all hospitalized patients, a range of 26% to 32% of patients wer Among all patients, a range of 3% to 17% developed ARDS compared to a range of 20% to and 67% to 85% for patients admitted to the ICU. ^{1,4-6,8,11} Mortality among patients admitted 72% depending on the study. ^{5,8,10,11} The median length of hospitalization among survivors

Risk Factors for Severe Illness

Age is a strong risk factor for severe illness, complications, and death. Among r cases of COVID-19 in China, the case fatality rate was highest among older persons: \geq 80 y 60–69 years: 3.6%, 50–59 years: 1.3%, 40–49 years: 0.4%, <40 years: 0.2%. Early U.S. ep the case fatality was highest in persons aged \geq 85 years (range 10%–27%), followed by 3%-1%–3% for ages 55–64 years, and <1% for ages 0–54 years.

Patients in China with no reported underlying medical conditions had an overall case fata higher for patients with comorbidities: 10.5% for those with cardiovascular disease, 7.3% 6% each for chronic respiratory disease, hypertension, and cancer.⁴² Heart disease, hyper chronic lung disease, and chronic kidney disease have all been associated with increased outcomes.^{1,6,10,11,38,42,43} Accounting for differences in age and prevalence of underlying cor COVID-19 in the United States was similar to China.^{39,40,44}

Medications

It has been hypothesized that angiotensin-converting enzyme (ACE) inhibitors or angioter may increase the risk of SARS-CoV-2 infection and COVID-19 severity.⁴⁵ ACE inhibitors and of angiotensin-converting enzyme 2 (ACE2). SARS-CoV-2 uses the ACE2 receptor to enter indata to suggest a link between ACE inhibitors or ARBs with worse COVID-19 outcomes. The (AHA), the Heart Failure Society of America (HFSA), and the American College of Cardiology recommending continuation of these drugs for patients already receiving them for heart ischemic heart disease.⁴⁶

It has also been hypothesized that non-steroidal anti-inflammatory drugs (NSAIDs) may we there are no data suggesting an association between COVID-19 clinical outcomes and NSA

be found at Healthcare Professionals: Frequently Asked Questions and Answers.

Reinfection

There are no data concerning the possibility of re-infection with SARS-CoV-2 after recovery shedding declines with resolution of symptoms, and may continue for days to weeks. RNA during convalescence does not necessarily indicate the presence of viable infectious correlated with the detection of IgM and IgG antibodies which signal the development of i

Diagnostic Testing

Diagnosis of COVID-19 requires detection of SARS-CoV-2 RNA by reverse transcription pol PCR). Detection of SARS-CoV-2 viral RNA is better in nasopharynx samples compared to the respiratory samples may have better yield than upper respiratory samples. SARS-CoV in stool and blood. Detection of SARS-CoV-2 RNA in blood may be a marker of sever may persist over longer periods among older persons and those who had severe illness refered in the same periods. The same periods among hospitalized patients 12–20 days). The same periods are considered in the same periods are considered patients.

Infection with both SARS-CoV-2 and with other respiratory viruses has been reported, and respiratory pathogen does not rule out COVID-19.⁵³

For more information about testing and specimen collection, handling and storage, visit E for Coronavirus Disease 2019 (COVID-19) and Frequently Asked Questions on COVID-19 T

Laboratory and Radiographic Findings

Laboratory Findings

Lymphopenia is the most common lab finding in COVID-19 and is found in as many as 83° Lymphopenia, neutrophilia, elevated serum alanine aminotransferase and aspartate amir lactate dehydrogenase, high CRP, and high ferritin levels may be associated with greater D-dimer and lymphopenia have been associated with mortality.^{8,11} Procalcitonin is typical may increase among those admitted to the ICU.⁴⁻⁶ Patients with critical illness had high plamakers, suggesting potential immune dysregulation.^{5,55}

Radiographic Findings

Chest radiographs of patients with COVID-19 typically demonstrate bilateral air-space con have unremarkable chest radiographs early in the disease. 1,5,56 Chest CT images from pati demonstrate bilateral, peripheral ground glass opacities. 4,8,38,56-65 Because this chest CT images and overlaps with other infections, the diagnostic value of chest CT imaging for COVID-19 upon interpretations from individual radiologists. 57,66 One study found that 56% of patient of diagnosis had a normal CT58. Conversely, other studies have also identified chest CT ab the detection of SARS-CoV-2 RNA. 56,67 Given the variability in chest imaging findings, chest recommended for the diagnosis of COVID-19. The American College of Radiology also does screening or as a first-line test for diagnosis of COVID-19. (See American College of Radiology)

Clinical Management and Treatment

Mild to Moderate Disease

Patients with a mild clinical presentation (absence of viral pneumonia and hypoxia) may n hospitalization, and many patients will be able to manage their illness at home. The decisi inpatient or outpatient setting should be made on a case-by-case basis. This decision will presentation, requirement for supportive care, potential risk factors for severe disease, at self-isolate at home. Patients with risk factors for severe illness (see People Who Are at Hi should be monitored closely given the possible risk of progression to severe illness in the onset.^{5,6,10,11}

For information regarding infection prevention and control recommendations, please see and Control Recommendations for Patients with Confirmed Coronavirus Disease 2019 (CC Investigation for COVID-19 in Healthcare Settings.

Severe Disease

Some patients with COVID-19 will have severe disease requiring hospitalization for manage for COVID-19 is currently FDA approved. Corticosteroids have been widely used in hospital illness in China^{6,8,10,11}; however, the benefit of corticosteroid use cannot be determined by observational data. By contrast, patients with MERS-CoV or influenza who were given cort have prolonged viral replication, receive mechanical ventilation, and have higher mortality should be avoided unless indicated for other reasons, such as management of chronic ob exacerbation or septic shock. More information can be found at Healthcare Professionals and Answers.

Inpatient management revolves around the supportive management of the most commo COVID-19: pneumonia, hypoxemic respiratory failure/ARDS, sepsis and septic shock, card acute kidney injury, and complications from prolonged hospitalization including secondar thromboembolism, gastrointestinal bleeding, and critical illness polyneuropathy/myopath

The Infectious Diseases Society of America has released guidelines on the treatment and COVID-19. For more information, please visit: Infectious Diseases Society of America Guid Management of Patients with COVID-19 Infection.

The World Health Organization and the Surviving Sepsis Campaign have both released co inpatient management of patients with COVID-19, including those who are critically ill. For Guidance on Clinical management of severe acute respiratory infection when novel coron suspected (WHO) and Surviving Sepsis Campaign: Guidelines on the Management of C Coronavirus Disease 2019 (COVID-19)

For more information on the management of children, see Information for Pediatric Healt Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock a Dysfunction in Children .

Investigational Therapeutics

No FDA-approved drugs have demonstrated safety and efficacy in randomized controlled COVID-19. Use of investigational therapies for treatment of COVID-19 should ideally be do in randomized controlled trials. Several clinical trials are underway testing multiple drugs against SARS-CoV-2 and/or immunomodulatory effects that may have clinical benefit. For Information for Clinicians on Therapeutic Options for COVID-19 Patients. For the informat U.S., see ClinicalTrials.gov .

Discontinuation of Transmission-Based Precaution Isolation

Patients who have clinically recovered and are able to discharge from the hospital but wh their Transmission-Based Precautions may continue isolation at their place of residence under recommendations on discontinuation of Transmission-Based Precautions or home isolatic recovered from COVID-19 illness, please see: Interim Guidance for Discontinuation of Transmission of Hospitalized Patients with COVID-19, Interim Guidance for Discontinua

Patients with COVID-19, and Discontinuation of In-Home Isolation for Immunocompromis

Additional resources:

- Information for Pediatric Healthcare Providers
- Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19)
- Frequently Asked Questions on COVID-19 Testing at Laboratories
- Healthcare Professionals: Frequently Asked Questions and Answers
- Interim Infection Prevention and Control Recommendations for Patients with Suspections Disease 2019 (COVID-19) or in Healthcare Settings
- World Health Organization. Interim Guidance on Clinical management of severe acut novel coronavirus (nCoV) infection is suspected

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- Surviving Sepsis Campaign: Guidelines on the Management of Critically III Adults with (COVID-19)
- Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and 5
- Surviving Sepsis Campaign International Guidelines for the Management of Septic Sł
 Organ Dysfunction in Children
- Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Officia the American Thoracic Society and Infectious Diseases Society of America
- ◆ ACR Recommendations for the use of Chest Radiography and Computed Tomograph
 Infection
- Infectious Diseases Society of America Guidelines on the Treatment and Managemer
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- National Institutes of Health: Coronavirus Disease 2019 (COVID-19) Treatment Guide

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