Management Algorithm for Subclinical Hypoxemia in Coronavirus Disease-2019 Patients: Intercepting the “Silent Killer”

INTRODUCTION

The presence of asymptomatic hypoxemia (AH) in patients with coronavirus disease (COVID-19) is well described.[1] AH is thought to be responsible for the phenomenon of rapid clinical deterioration and mortality in the hospital setting.[2] and is frequently associated with the delayed escalation of care.[3] In addition, at-home mortality is thought to be elevated among those with AH who are discharged from the emergency department following an apparently low-acuity ambulatory evaluation.[4,5] Such patients may have profound hypoxemia without significant dyspnea, with the initial sign of deterioration being confined to escalating oxygen requirement.[8]

CLINICAL RATIONALE

Following similar experiences across our institutions, spanning three continents and highly diverse patient populations, this working group of the combined American College of Academic International Medicine and World Academic Council of Emergency Medicine (ACAIM-WACEM) COVID-19 Taskforce arrived at an algorithm intended to establish a unified approach to this insidious and potentially lethal clinical problem [Figure 1]. Regardless of the algorithm utilized in the diagnosis and treatment of COVID-19, the evaluation of each patient should always begin with, and be based on, careful medical history and detailed clinical exam. Building on this foundation, the managing health-care provider (HCP) should obtain appropriate laboratory and radiographic tests to help confirm the diagnosis, to determine disease severity, and to accurately triage the patient.

PATIENT HISTORY AND BEDSIDE EVALUATION

The presence of COVID-19 should be suspected in patients who present with characteristic symptoms among which fever and cough are the most common.[6,7] Patients at higher risk of severe clinical course tend to be older, frail, immunocompromised, morbidly obese, carrying two or more chronic comorbid conditions, and male.[7,10] Additional correlates of severe illness may include tachycardia, hyperthermia of >39°C, encephalopathy, and hemodynamic instability. Although “typical” symptoms of COVID-19 are present in the vast majority of cases,[7] additional specific “red flags” must be kept in mind by the managing HCP. These warning signs may be subtle and include the appearance of ≥3%–5% drop in SpO2 after approximately 60 s of mild activity/ambulation, SpO2/FiO2 ratio <300, SpO2 <93% on room air, and the presence of hypoxemia without tachypnea or other signs of respiratory compromise [Figure 1].[4,11,12]

LABORATORY ASSESSMENT

Initial diagnostics include complete blood count with differential and platelets; comprehensive metabolic panel (inclusive of liver function tests); coagulation profile (e.g., prothrombin time, partial thromboplastin time [PTT], international normalized ratio [INR], see below); C-reactive protein; D-dimer; high sensitivity (hs) Troponin; procalcitonin; ferritin, lactate, venous or arterial blood gas analysis; blood cultures; and nasal and pharyngeal viral swabs.[7,13] Electrocardiogram may be considered based on the HCP’s level of suspicion.[7,13] Laboratory findings of a neutrophil-to-lymphocyte ratio of >3.3; markedly elevated D-dimer; and early elevations in hs-Troponin, are significantly associated with severe disease and poorer prognosis.[7,14-16] Coagulation abnormalities may also be seen among patients with more severe COVID-19 presentations.[17] More specifically, HCP’s may see thrombocytopenia, increased INR, prolonged activated PTT, and abnormal levels of fibrin degradation products. Associated with the above findings is the elevated risk of venous thromboembolism, prompting recommendations for thromboprophylaxis.[18]

RADIOGRAPHY ASSESSMENT

Initial chest radiograph shows typical COVID-19 diagnostic changes in approximately two-thirds of patients; however, this may increase to >95% in those with severe disease.[13] Noncontrast computed tomography (NCCT) of the chest is characterized by good correlation with both the diagnosis and severity of COVID-19, providing an overall sensitivity of >90% at 2–5 days after the onset of symptoms and 97% sensitivity thereafter.[7,19,20] If the NCCT findings are highly suspicious for COVID-19,[21] the patient should be considered for thromboprophylaxis with low molecular weight heparin administration[18,22] and for the hospital admission. If the NCCT does not show findings characteristic of COVID-19, additional testing with contrast-enhanced computed tomography of the chest or ventilation/perfusion scanning may be considered to rule out other causes of hypoxia (e.g., pulmonary embolism) as per managing HCP’s index of clinical suspicion. The decision regarding patient admission should be made on a case-by-case basis under such circumstances.
**Important clinical considerations:**

- Coronavirus disease-2019 appears to have significant pro-thrombotic effects,[23,24] D-Dimer levels are elevated under these circumstances
- Contrast computed tomographic angiography chest after a negative noncontrast computed tomography is not usually an option in a pandemic situation due to limited resources
- Dehydration and acute kidney injury can exist hence cautious use of intravenous contrast is recommended[25,26]
- Perform computed tomographic pulmonary angiography only if suspicion of pulmonary embolism (PE) is high. If contrast nephropathy risk is high, consider appropriate renal risk remediation or other imaging modalities (e.g. ventilation/perfusion scan when ruling out pulmonary embolism)
• Surrogate findings on point-of-care ultrasound cardiac and thoracic/pulmonary ultrasound are important.[27,28]
• Post-admission empiric therapeutic doses of low molecular weight heparin appear to be both effective and preventive in the context of elevated PE risk.[29]


**Summary and Conclusions**

In the early stages of COVID-19 clinical illness, the ability to oxygenate is impaired. However, the patient does not necessarily display the conventionally expected signs or symptoms of respiratory failure, including shortness of breath. Given the above, HCP’s must remain vigilant and proactively look for ‘red flags’ described herein, such as the appearance of ≥3%–5% drop in SpO2 after approximately 60 s of mild activity/ambulation, SpO2/FiO2 ratio <300, SpO2 <93% on room air, and the presence of hypoxemia without tachypnea [Figure 1].[4,11,12] In summary, this expert group views AH as the proverbial “canary in the coalmine” and the first harbinger of future respiratory deterioration in COVID-19 patients.

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**References**