Clinical Management Guideline

Optimizing respiratory care in coronavirus disease-2019: A comprehensive, protocolized, evidence-based, algorithmic approach

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INTRODUCTION

Respiratory management of patients with coronavirus disease 2019 (COVID-19) is both complex and highly nuanced.[1] Although most patients with COVID-19 develop mild or no symptoms, a smaller proportion (up to 15%) experience progressive hypoxic respiratory failure requiring escalating levels of oxygen support.[2] Significant accumulated experience in caring for patients with SARS-CoV-2 pulmonary illness resulted in the recognition of major respiratory failure patterns, the benefits of early proning, and the importance of a step-wise escalation in levels of invasiveness across the entire spectrum from nasal cannula to extracorporeal support.[3‑4] Given substantial heterogeneity among various algorithmic approaches to oxygen therapy and the need for both standardization and optimization of clinical management methodologies, the Joint ACAIM-WACEM COVID-19 Clinical Management Taskforce (CCMT) set out to establish and publish a unified approach to the patient who presents with SARS-CoV-2 lower respiratory tract infection (LRTI). In addition, the CCMT hopes that a protocol-driven strategy will lead to conservation of precious healthcare resources, such as intensive care beds and ventilators, by eliminating unnecessary interventions and various other process inefficiencies.

Clinical rationale

The Joint ACAIM-WACEM CCMT is a multidisciplinary group with participants from multiple countries and significant collective expertise in clinical management of COVID-19. Based on our shared experiences, we set

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out to design and optimize a uniform approach toward patients suffering from SARS-CoV-2 LRTI. The primary goal of the CCMT was to ensure broad applicability of the resultant treatment algorithms across diverse clinical settings, regardless of resource availability [Table 1]. The secondary goal was to produce a comprehensive, evidence-based resource that will provide clinicians with an easy-to-use and powerful set of tools to manage COVID-19 patients with LRTI and respiratory failure. Multiple sources were utilized when compiling this collection of algorithms and tables.[2,5,20]

The working hypothesis adopted by the CCMT is that in COVID-19, the disease caused by SARS-CoV-2 manifests primarily as an oxygen diffusion problem rather than as alterations involving ventilation-perfusion (V/Q) mismatch, low fraction of inspired oxygen (FiO2), or hyperventilation.[11,3,4,11] Consequently, we advocate that initial attempts to address the oxygenation-related impairment should include low-flow nasal cannula (LFNC) and reservoir masks, with progressive escalation to high-flow nasal cannula (HFNC) before implementing awake proning or non-invasive positive pressure ventilation (NIPPV).[11,14,15,21,22] If these maneuvers and strategies are ineffective, we advocate that a prompt transition is made toward invasive mechanical ventilatory support.[14,22,23] Cumulatively, the above approach serves to optimize and standardize the overall management of COVID-19 patients with LRTI. The rationale for applying different oxygen therapies to different primary pathophysiologic respiratory problems is presented in Table 2.

### Patient history and clinical assessment

Infection with COVID-19 should be suspected in patients presenting with “typical” signs and symptoms including fever, cough, and various degrees of hypoxia,[24] although clinical manifestations can take a number of other forms, particularly in the elderly population.[2] Patients with elevated risk of severe disease are older, immunocompromised, morbidly obese, male, or have two or more chronic comorbid conditions.[2,24-26] Additional clinical signs and symptoms associated with severe illness include tachycardia, hyperthermia (≥39°C), encephalopathy, and hemodynamic instability.[2,27] While a “typical” COVID-19 presentation is seen in the vast majority of cases,[2] additional specific “red flags” such as the presence of “silent hypoxia” must be kept in mind.[27-30] Reliable oxygen saturation measurement (SpO2) is the cornerstone of initial risk stratification and disease severity assessment. Patients with normal (or “baseline,” if preexisting pulmonary disease exists) SpO2 are stratified as “low risk,” whereas patients with an initial SpO2 < 93% (or similar decline below “baseline” levels) require immediate supplemental oxygen therapy.

In addition to a comprehensive COVID-19 laboratory workup,[2,31] specific factors associated with severe respiratory disease have been identified, including the presence of myalgias, elevated hemoglobin levels, and elevated alanine aminotransferase.[2] Specific risk assessment tools may be considered including the MuLBSTA[32] and BCRSS scores.[2,33] Moreover, laboratory findings of a neutrophil-to-lymphocyte ratio of >3.3,

### Table 1: Comparison between resource-abundant and resource-limited health-care settings

| Setting/environment/safety | Resource abundant + patient centered | Resource limited + HCP centered |
|------------------------------|-------------------------------------|---------------------------------|
| Phase of pandemic            | 1, 2                                | 3, 4                            |
| Infrastructure               | Adequate                            | Average                         |
| Hospital occupancy           | Low                                 | High                            |
| Surge ICU beds               | No                                  | Yes                             |
| Regular health-care providers | Yes                                 | No                              |
| Dedicated CCM services       | Yes                                 | No                              |

The joint ACAIM-WACEM COVID-19 Clinical management Taskforce recognizes that there exist significant regional variations in terms of health-care resources, including considerations related to infrastructure, capacity, clinical skillset, equipment, access/availability, and other resources essential for patient care. ICU: Intensive care unit, HCP: Health-care provider, CCM: Critical care medicine, COVID-19: Coronavirus disease 2019

### Table 2: Oxygen therapies and respiratory pathophysiology, including evidence-based support

| Oxygenation | Ventilation | WOB | Solves diffusion | Solves V/Q mismatch | Solves recruitment |
|-------------|-------------|-----|------------------|---------------------|-------------------|
| LFNC        | +           | -   | -                | +                   | -                 |
| Reservoir mask | + +       | -   | +/-              | +                   | -                 |
| HFNC       | + +        | +/+ | +/+              | +/+                 | -                 |
| Awake proning | +        | +   | +/+              | +                   | -                 |
| HFNC + awake proning | + + + | +   | +               | +/(H)               | +/(H)             |
| CPAP (no O₂) | -         | +/+ | +/+              | -                   | +                 |
| CPAP (with O₂) | +        | +/+ | +/+              | +                   | +                 |
| NIPPV (no O₂) | -        | +   | +                | +/-                 | +                 |
| NIPPV (with O₂) | +        | +   | +                | +                   | +                 |
| IMV        | +          | +   | +                | +                   | +                 |
| IMV + proning | + +      | +   | +                | +                   | +                 |
| ECLS       | + +        | +   | +                | +                   | +                 |

H: Based on past evidence, but largely hypothetical in the context of COVID-19 lower respiratory disease. WOB: Work of breathing. LFNC: Low-flow nasal cannula, HFNC: High-flow nasal cannula, V/Q mismatch: Ventilation-perfusion mismatch, CPAP: Continuous positive airway pressure, NIPPV: Noninvasive positive pressure ventilation, IMV: Invasive mechanical ventilation, ECLS: Extracorporeal life support, COVID-19: Coronavirus disease 2019, + / +/+ / +++ Denotes the level of available evidence, with * +/+ and *- denoting insufficient or lack of supporting evidence, respectively
thrombocytopenia, markedly elevated D-dimer, and early elevations in highly sensitive troponin, are all linked to severe disease and poorer prognosis.\cite{2,34-37} Severe COVID-19 may also be associated with elevated risk of thromboembolic events.\cite{38}

**Pertinent diagnostic and clinical monitoring criteria**

Radiographic workup is an important part of the overall COVID-19 patient assessment. The initial chest radiograph shows “typical” diagnostic changes in >67% of patients, and this may increase to >95% in cases of severe disease.\cite{39} Noncontrast computed tomography (NCCT) of the chest may correlate with both the diagnosis and severity of COVID 19, and has a reported sensitivity of >90% at 2–5 days post-onset of symptoms and 97% sensitivity thereafter.\cite{2,39,40} If the NCCT findings are suspicious for COVID-19,\cite{41} low-molecular-weight heparin administration and hospital admission should be considered. If the NCCT is not suggestive of COVID-19, then contrast-enhanced
Finally, important considerations and Resource abundant
Resource limited

On arrival

Indicated.

Necessitating tube thoracostomy placement when patients on prolonged positive pressure ventilation, the risk of pneumothorax may be elevated in

Specific clinical monitoring criteria, as directly relevant to the current manuscript, can be stratified according to patient/assessment location as well as the overall resource availability [Table 3]. Within this larger paradigm, several assessment tools need to be introduced, including the SCRUB-60 tool [Table 4][43-45] and the SBC tool [Table 5][46-48].

Finally, the risk of pneumothorax may be elevated in patients on prolonged positive pressure ventilation, necessitating tube thoracostomy placement when indicated.[49]

**CT of the chest or V/Q scanning may be considered to rule out other causes of hypoxia.**

**Specific note**

A full discussion regarding the complex issue of monitoring and maintaining adequate oxygenation in the outpatient/home setting is beyond the scope of this
IBW Formula[3]
Male: 50 kg + 2.3 kg per inch over 5 feet
Female: 46 kg + 2.3 kg per inch over 5 feet

Critical Care Consult.
Management of secretions.
Targets:
$\text{pO}_2 \geq 80$ | $\text{pCO}_2 \leq 45$ | $\text{pH} \geq 7.3$

Initial Ventilator Settings
$\text{FiO}_2 \geq 60\%$ | $\text{PEEP} \geq 5$ | $\text{P/F} < 200$
$\text{RR} = 20$ | $\text{I:E} = 1.2$
$\text{Vt} = 7 \text{ml/kg IBW}$

Conservative fluid strategy
Liberal use of NMB
Target $\text{SpO}_2 \geq 92$
Attach closed suction

Optimize pharmacotherapy
Organ injury assessment
Cardiovascular assessment
Chest imaging

Determine $\text{Pplat}$ by inspiratory hold for 0.5 – 2 sec

Treatment Escalation Plan
Early determination and standardized documentation of ceiling of care, with review by experienced clinician

Figure 2: Management algorithm for coronavirus disease 2019 patients with respiratory failure requiring mechanical ventilation. IBW: Ideal body weight, $\text{FiO}_2$: Fraction of inspired oxygen, PEEP: Positive end expiratory pressure, P/F: $\text{PaO}_2/\text{FaO}_2$, RR: Respiratory rate, Vt: Tidal volume, $\text{SpO}_2$: Peripheral capillary oxygen saturation, DP: Driving pressure, Cstat: Static compliance, iNO: inhaled nitrous oxide, Pplat: Plateau pressure, ABG: Arterial blood gas, See references[56,57] for ARDSnet original sources.

| Table 6: Summary of key correlates with patient response to specific levels of oxygenation strategy/support |
|---|
| **Modality** | Continue HFNC Improves oxygenation and provides some added PEEP effect | Attempt awake proning for | Assisted ventilation for |
| **Response to oxygen** | Good response | Poor response | Inadequate response or increased WOB |
| Probable primary pathophysiology | Diffusion abnormality | V/Q mismatch | Collapsed alveoli or shunt or fragile |
| Caveats | Aerosolization risk | Ensure no contraindications to proning | Ensure no contraindications to NIPPV (always factor device considerations of max. $\text{FiO}_2$) |
| Patient tolerability | | | |

NIPPV: Noninvasive positive pressure ventilation, HFNC: High-flow nasal cannula, PEEP: Positive end expiratory pressure, WOB: Work of breathing.

document; however, a dedicated Joint ACAIM-WACEM COVID-19 Clinical Management Taskforce guideline is forthcoming with recommendations specific to the implementation of home-based oxygenation strategy in patients with isolated hypoxia and clinically mild disease.
Figure 3: Management algorithm for patients with severe coronavirus disease 2019 respiratory failure. NMBA: Neuromuscular blocking agents, ECLS: Extracorporeal life support, CCM: Critical care medicine, FiO2: Fraction of inspired oxygen, PEEP: Positive end expiratory pressure, Vt: Tidal volume, DP: Driving pressure, Cstat: Static compliance, HCP: Health-care provider, PPE: Personal protective equipment, P/F: PaO2/FiO2, SAPS-II: Simplified Acute Physiology score-II, APACHE-II: Acute Physiology and Chronic Health Evaluation

Table 7: Summary of important escalation points that will provide a clinically applicable framework for objective therapeutic approach transitions

| Modality     | Ceiling of therapy | ROX at (Hs) SpO2/FiO2/RR | Failure  | Success |
|--------------|--------------------|--------------------------|----------|---------|
| HFNC[19,20,48,49] | ROX index < 3.85 | 2                        | < 2.85   | > 4.88  |
|              |                    | 6                        | < 3.47   | > 4.88  |
|              |                    | 12                       | < 3.85   | > 4.88  |
| LFNC         | S/F ratio          |                          |          |         |
| NIPPV        | P/F ratio          |                          |          |         |
| Prone        | SCRB-60            |                          |          |         |
|              | SBC                |                          |          |         |

ROX index: Ratio of pulse oximetry/fraction of inspired oxygen to respiratory rate.[20] HFNC: High-flow nasal cannula, LFNC: Low-flow nasal cannula, NIPPV: Noninvasive positive pressure ventilation, S/F ratio: SpO2/FiO2, P/F ratio: PaO2/FiO2, SBC: Single breath count
Table 8: Summary of mechanical ventilation and proning strategies utilized in coronavirus disease-19

| Ventilator strategy<sup>1,2,16,20,22,34</sup> | Proning strategy<sup>10,21,30</sup> |
|-----------------------------------------------|-------------------------------------|
| Measure driving pressure                      | Indications                          |
| Driving pressure                              | P/F < 50                              |
| <15 cmH<sub>2</sub>O                           | Driving pressure > 15 cmH<sub>2</sub>O |
| >15 cmH<sub>2</sub>O                           | Compliance < 40 ml/cmH<sub>2</sub>O   |
| Tidal volume                                  | Limited resources (PPE)               |
| 8 ml/kg                                       | Proning expertise not available       |
|                                               | Avoid if                              |
| If inadequate response, consider rescue measures: NMBa, diuretic, FiO<sub>2</sub> ≥ 80% |
| Compliance                                    | Escalate PEEP                         |
| >40 ml/cmH<sub>2</sub>O                       | Optimize NMBa                         |
| <40 ml/cmH<sub>2</sub>O                       | Settings                              |
| Actions                                       |                                |
| Continue same ventilatory strategy.           | Tidal volume 6 ml/kg                  |
| Low tidal volume                              | FiO<sub>2</sub> ≥ 60%, PEEP ≥ 5       |
| High PEEP                                     | Within 6 h for patients with good prognosis |
| Prone positioning                             | Within 24 h for patients with poor prognosis |
|                                               |                                      |
| Phenotype                                      | Type L                               |
|                                               | Type H                               |

PPE: Personal protective equipment, NMBa: Neuromuscular blocking agents, PEEP: Positive end expiratory pressure, P/F: PaO<sub>2</sub>/FiO<sub>2</sub> ratio

Table 9: Important considerations and limitations related to proning therapy

| Condition                                      | Ceiling of therapy for (awake) prone positioning (repeated assessments every 30 min-2 h) |
|------------------------------------------------|------------------------------------------------------------------------------------------|
| Absolute                                       | Relative                                                                                 |
| Unstable spine                                 | Unstable spine                                                                          |
| Raised ICP                                     | Unstable spine                                                                          |
| Thoracic or abdominal injuries                 | Unstable spine                                                                          |
| Morbid obesity                                 | Morbid obesity                                                                          |
| Pregnancy                                      | Morbid obesity                                                                          |
| Inability to tolerate procedure                | Inability to tolerate procedure                                                         |
| Increased work of breathing                    | Increased work of breathing                                                              |
| Tachypnea                                      | Tachypnea                                                                                |
| Hemodynamic instability                        | Hemodynamic instability                                                                  |
| Deterioration in SCRB-60 or SBC                | Deterioration in SCRB-60 or SBC                                                          |

SBC: Single breath count [Table 5], SCRB-60: Clinical risk stratification score [Table 4]

Figure 4: Treatment escalation plan checklist. ED: Emergency department, HDU: High-dependency unit, CCM: Critical care medicine, IMV: Invasive mechanical ventilation, ECLS: Extracorporeal life support, LFNC: High-flow nasal cannula, HFNC: High-flow nasal cannula, NIPPV: Noninvasive positive pressure ventilation

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There are no conflicts of interest.

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