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# Management of COVID-19 Respiratory Distress

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**A**cute respiratory distress syndrome (ARDS) can originate from either the gas or vascular side of the alveolus. Although the portal for coronavirus disease 2019 (COVID-19) is inhalational, and alveolar infiltrates are commonly found on chest x-ray or computed tomography (CT) scan, the respiratory distress appears to include an important vascular insult that potentially mandates a different treatment approach than customarily applied for ARDS. Indeed, the wide variation in mortality rates across different intensive care units raises the possibility that the approach to ventilatory management could be contributing to outcome.<sup>1-3</sup>

COVID-19 is a systemic disease that primarily injures the vascular endothelium. If not expertly and individually managed with consideration of the vasocentric features, a COVID-19 patient with ARDS ("CARDS") may eventually develop multiorgan failure, even when not of advanced age or predisposed by preexisting comorbidity.

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## Standard Approaches to Ventilating ARDS

Normally, ARDS is characterized by noncardiogenic pulmonary edema, shunt-related hypoxemia, and reduced aerated lung size ("baby lung"), which accounts for low respiratory compliance.<sup>4</sup> In such settings, increasing lung size by recruiting previously collapsed lung units is often achieved through the use of high levels of positive end-expiratory pressure (PEEP), recruiting maneuvers, and prone

positioning. Because high transpulmonary pressure induces stress across the lung that is poorly tolerated in ARDS, relatively low tidal volumes, together with tolerance for modest (permissive) hypercapnia, facilitate the goal of minimizing ventilator-induced lung injury (VILI). Indeed, in the early phases of ARDS, before a patient has fatigued or been sedated, the high transpulmonary pressures associated with spontaneous vigorous inspiratory effort may contribute to damage (so-called patient self-induced lung injury [P-SILI]).<sup>5</sup>

## Clinical Features of CARDS

Soon after onset of respiratory distress from COVID, patients initially retain relatively good compliance despite very poor oxygenation.<sup>1,2</sup> Minute ventilation is characteristically high. Infiltrates are often limited in extent and, initially, are usually characterized by a ground-glass pattern on CT that signifies interstitial rather than alveolar edema. Many patients do not appear overtly dyspneic. These patients can be assigned, in a simplified model, to "type L," characterized by low lung elastance (high compliance), lower lung weight as estimated by CT scan, and low response to PEEP.<sup>6</sup> For many patients, the disease may stabilize at this stage without deterioration while others, either because of disease severity and host response or suboptimal management, may transition to a clinical picture more characteristic of typical ARDS. These can be defined as "type H," with extensive CT consolidations, high elastance (low compliance), higher lung weight, and high PEEP response. Clearly, types L and H are the conceptual extremes of a spectrum that includes intermediate stages, in which their characteristics may overlap. Another feature consistently reported is a highly activated coagulation cascade, with widespread micro- and macro-thromboses in the lung and in other organs (eFigure 1 in the [Supplement](#)); very elevated serum D-dimer levels are a consistent finding associated with adverse outcomes.<sup>7</sup>

These observations indicate the fundamental roles played by disproportionate endothelial damage that disrupts pulmonary vasoregulation, promotes ventilation-perfusion mismatch (the primary cause of initial hypoxemia), and fosters thrombogenesis. In addition, remarkably increased respiratory drive may, if unchecked, intensify tidal strains and energy loads from a patient's respiratory effort applied to highly vulnerable tissue, adding P-SILI to the mix of the lung's inflammatory assault.<sup>5,8</sup> When confronting such an unfamiliar and rapidly evolving environment, only certain aspects of well-accepted lung-protective approaches to ARDS remain rational at these different stages. More important, inattention to the vascular side (eg, avoidance of fluid overload, reduction of cardiac output demands) could inadvertently promote counterproductive responses (eg, edema) and iatrogenic damage.

## Protecting the CARDS Lung

Patients with type L CARDS, having good lung compliance, accept larger tidal volumes (7-8 mL/kg ideal body weight) than those customarily prescribed for ARDS without worsening the risk of VILI. Actually,

in a 70-kg man, with respiratory system compliance of 50 mL/cm H<sub>2</sub>O and PEEP of 10 cm H<sub>2</sub>O, a tidal volume of 8 mL/kg yields a plateau pressure of 21 cm H<sub>2</sub>O and driving pressure of 11 cm H<sub>2</sub>O, both well below the currently accepted thresholds for VILI protection (30 and 15 cm H<sub>2</sub>O, respectively). Higher VT could help avoid reabsorption atelectasis and hypercapnia due to hypoventilation with lower tidal volumes.

The key issue in this early stage is disrupted vasoregulation, where the pulmonary vasoconstriction that normally occurs in response to hypoxia fails to occur because of an endothelial assault that mismatches perfusion to ventilation and may result in profound hypoxemia. The clinician's first response, boosting F<sub>IO<sub>2</sub></sub>, may indeed prove effective early on. If insufficient, noninvasive support (eg, high-flow nasal O<sub>2</sub>, CPAP, Bi-PAP) may stabilize the clinical course in mild cases, provided that the patient does not exert excessive inspiratory efforts. However, if respiratory drive is not reduced by oxygen administration and noninvasive support, persistently strong spontaneous inspiratory efforts simultaneously increase tissue stresses and raise pulmonary transvascular pressures, vascular flows, and fluid leakage (ie, P-SILI).<sup>8-10</sup> Progressive deterioration of lung function (a VILI vortex) may then rapidly ensue. Early intubation, effective sedation, and/or paralysis may interrupt this cycle. Targeting lower PEEP (8-10 cm H<sub>2</sub>O) is appropriate. Raising mean transpulmonary pressures by higher PEEP or inspiratory-expiratory ratio inversion redirects blood flow away from overstretched open airspaces, accentuating stresses on highly permeable microvessels and compromising CO<sub>2</sub> exchange without the benefit of widespread recruitment of functional lung units.

If lung edema increases in the type L patient, either because of the disease itself and/or P-SILI, the baby lung shrinks further, and the type H phenotype progressively develops. Concentrating the entire ventilation workload on an already overtaxed baby lung increases its power exposure and blood flow, thereby accentuating its potential for progressive injury.

There are 2 major contributors to this VILI vortex of shrinking the baby lung: airspace VILI<sup>8</sup> and intensified stresses within the vessels that perfuse it<sup>9,10</sup> (eFigure 2 in the [Supplement](#)). Over time, superimposed VILI and unchecked viral disease incite inflammation and edema, promoting local and generalized thrombogenesis, intense cytokine release, right ventricular overload, and systemic organ dysfunction. In this advanced state, it is advisable to apply a more conventional lung-protective strategy: higher PEEP (≤15 cm H<sub>2</sub>O), lower tidal volume (6 mL/kg), and prone positioning while minimizing oxygen consumption. Whichever the disease type, weaning should be undertaken cautiously ([Table](#)).



### **Table. Time Course and Treatment Approach to Ventilation Support for Patients With CARDS**

**Table. Time Course and Treatment Approach to Ventilation Support for Patients With CARDS**

Time period	Objective	Respiratory support options	Rationale
Before intubation	Adequate gas exchange Avoid P-SILI	Supplemental oxygen, CPAP, NIV, HFNC Awake prone positioning, Target nonvigorous breathing	Powerful respiratory effort can cause reinforcing lung and vascular stress, resulting in injury
During mechanical ventilation	Avoid pulmonary deterioration and VILI vortex	Minimize PEEP, frequency and tidal volume Adjust to acceptable gas exchange Maintain fluid balance Reduce O <sub>2</sub> demand Consider ECMO	Minimize transpulmonary and vascular stresses
After intubation	Minimize pulmonary stress Optimize O <sub>2</sub> Avoid VILI vortex	Type L <sup>a</sup> : use lower PEEP (<10 cm H <sub>2</sub> O) Use more liberal tidal volume (7-9 mL/kg) as needed Reduce O <sub>2</sub> demand Consider prone positioning	Lower tidal volumes are unnecessary Higher PEEP is ineffective, creates dead space, and adversely redirects blood flow
	Reduce and evenly distribute lung and vascular stresses Optimize O <sub>2</sub> Avoid VILI vortex	Type H <sup>a</sup> : use higher PEEP (<15 cm H <sub>2</sub> O) Lower tidal volume (5-7 mL/kg) Reduce O <sub>2</sub> demand Implement prone positioning	More closely behaves and responds like typical ARDS
Weaning phase	Avoid reversion to previously worsened pulmonary state by causing VILI and worsening edema	Make transitions cautiously Avoid abrupt changes Spontaneous trials only at the very end of the weaning process	Strong spontaneous efforts raise O <sub>2</sub> demand, increase edema, and promote P-SILI

Abbreviations: ARDS, acute respiratory distress syndrome; CARDS, COVID-19 with ARDS; CPAP, continuous positive airway pressure; ECMO, extracorporeal membrane oxygenation; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; P-SILI, patient self-inflicted lung injury; PEEP, positive end-expiratory pressure; VILI, ventilator-induced lung injury.

<sup>a</sup> Type L: Scattered ground-glass infiltrates, higher compliance (>50 mL/cm H<sub>2</sub>O), not PEEP responsive; less dyspnea. Type H: Extensive infiltrates of atelectasis and edema, lower compliance, PEEP responsive, overtly dyspneic.

COVID-19 causes unique lung injury. It may be helpful to categorize patients as having either type L or H phenotype. Different ventilatory approaches are needed, depending on the underlying physiology.

## Article Information

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