Respiratory Management of Patients with COVID-19

During the SARS-CoV-2 pandemic, respiratory management of hospitalized patients diagnosed with COVID-19 is an important aspect of their clinical care. As with any new pathogen or disease, staying up-to-date with new information and expert opinions is critical to adapt clinical management protocols. Initial descriptions of the clinical course of COVID-19 disease reported patients with acute respiratory distress syndrome (ARDS) suffering high morbidity and mortality on mechanical ventilation, but investigations and clinician accounts of patient physiology propose this original opinion may not be entirely accurate.

To support clinical care, we want to share about current knowledge regarding the pathophysiology and management of patients presumed infected with SARS-CoV-2 throughout its clinical course and to specifically review the role of non-invasive ventilation (NIV) options in the treatment of patients presenting with early-stage COVID-19 disease.

Vyaire Medical is not seeking to promote, endorse or advise the off-label use of its products. However, we recognize the unusual and acute circumstances created by the COVID-19 pandemic and the needs of health care professionals to consider modifications to standard clinical practices in an effort to address the needs of patients with respiratory exacerbations.

IMPORTANT: The information presented here is based on the current understanding of the potential risks and functionality of mechanical ventilation systems based on a literature review and clinical experience. The selection and use of systems must first be reviewed and evaluated by each facility's medical and administrative staff, in consultation with manufacturers' instructions for use with its respective machinery, before implementation. As care for patients diagnosed with COVID-19 evolves, Vyaire will update information on our web site, so please bookmark it for easy access: US: **www.vyaire.com/Covid-19**; International: **intl.vyaire.com/Covid-19**.

Pathophysiology of COVID-19

Upwards of 14 percent of patients manifesting clinical symptoms of COVID-19 experience severe disease requiring hospitalization and 5 percent require critical care admission.[1] Of those requiring hospitalization, new reports demonstrate that two broad phenotypes are seen: an early hypoxemic stage followed by a severe late-stage acute respiratory failure associated with high mortality rates.[2]

SARS-CoV-2 enters the human host primarily via the upper respiratory tract and migrates to the lung, which supports the hypothesis that the initial infection leads to a modest local subpleural interstitial edema with disruption of normal regulation of pulmonary vascular tone.[3] The result is a loss of hypoxic pulmonary vasoconstriction leading to hypoxemia, without hypercarbia, from ventilation-perfusion mismatch (particularly shunt) typical in the differing West zones of the lung.[4] Clinicians call this "silent hypoxia," as the patient does not seem to notice their respiratory insufficiency and may not have the sensation of dyspnea or breathlessness despite increases in respiratory rate or minute ventilation (MV) or both.[5] This early "L-type" phase is characterized by low elastance (high compliance), low lung weight (as calculated on CT), and low response to positive end-expiratory pressure (PEEP).[6]

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As the disease progresses, oxygenation declines and MV increases. Increased respiratory drive may intensify tidal strains and energy loads applied to vulnerable lung tissues.[7]

This increased strain and expanding parenchymal damage leads to increased lung permeability from inflammation, which ultimately results in lung edema, described as "patient self-inflicted lung injury (P-SILI)." Progression of this vicious cycle leads to acute respiratory distress syndrome (ARDS). The "H-type" phase of disease consolidates alveolar air spaces to manifest high elastance (low compliance) and high lung weight secondary to decreased gas volumes and increased edema, and high PEEP response and recruitability because of increased amount of non-aerated tissue.[8,9]

Table 1. Progression of COVID-19 Disease Pathophysiology

	Early	Late
Elastance	Low *(high compliance)*	High *(low compliance)*
Lung weight	Low *(minimal alveolar edema)*	High *(increased alveolar edema)*
PEEP	Low	High
Non-aerated tissue	Low	Increased
Recruitability of collapsed alveoli	Low	High

Management

With such divergent pathophysiologic features between early and late-stage COVID-19 disease, it is appropriate that specific respiratory management goals may also differ.

L-Type Disease

Slowing disease progression and avoiding mechanical ventilation are key to treating patients with early stage COVID-19. Among patients who are critically ill, 71 to 79 percent require mechanical ventilation and of those, mortality is upwards of 81 percent.[10,11,12]

The need for mechanical ventilation is high when ICU capacity in regional pandemic "hot-spots" is stressed, raising concern that supply of critical care beds and ventilators may not be sufficient for the number of patients. NIV may offer a reasonable middle-ground between supplemental oxygen and mechanical ventilation, if used properly.

The first step in treatment, therefore, is reversing hypoxemia through an increase in inspired oxygen concentration (FiO_2). The goal in this early stage is the avoidance of further P-SILI from excessive inspiratory efforts associated with increased MV.

For these reasons, therapy should focus on minimizing excessive inspiratory efforts in response to hypoxemia. If supplemental oxygen alone is insufficient, NIV should be considered.

Three types of NIV are used today:

- continuous positive airway pressure (CPAP),
- high-flow nasal oxygen (HFNO), and
- high FiO_2/PEEP nasal positive airway pressure via the SuperNO_2VA device.[13]

These therapies improve oxygenation and decrease work of breathing in patients with respiratory distress, thereby potentially halting further progression of P-SILI in early-stage COVID-19 disease.[14,15,16,17]

Table 2. Advantages and Disadvantages of SuperNO$_2$VA, CPAP and HFNO

	Advantages	Disadvantages	Special Considerations
SuperNO$_2$VA	• High FiO_2 • Low flow rates equivalent to supplemental oxygen • Airtight mask seal • Allows for talking, eating, drinking, oral hygiene, etc. • Titratable PEEP • Can place surgical mask over mouth • Inexpensive and readily available • Single patient use	• Minimal inspiratory support *(may be advantage to limit stretch/P-SILI).*	• Does not need special equipment • Can be deployed anywhere a standard oxygen source exists (wall or tank)
CPAP	• High FiO_2 • Decreased work of breathing (L/Her) • Heated/humidified for prolonged use. • Positive inspiratory and expiratory pressure	• Leak-prone mask seal • Requires capital equipment • Expensive • Requires high-flow rates • Difficult to cover with surgical mask	• Increased VT may lead to P-SILI from increased inspiratory pressures (Frat x 2).[11]
HFNO	• High FiO_2 • Tolerated well by patients • Decreased work of breathing • Heated/humidified for prolonged use • Can cover with surgical mask • Allows for talking, eating, drinking, oral hygiene, etc.	• Loose interface seal • Requires capital equipment • Expensive • Requires high-flow rates	• Limited positive pressure delivery

The use of NIV has limitations to consider. Transmission of SARS-CoV-2 is primarily by virions contained in respiratory droplets, but significant risk of aerosol transmission to healthcare providers (HCPs) and patients exists during certain procedures or settings.[18] Therefore, delivery of treatment options for patients with COVID-19 should not increase transmission risk to others.

Whether aerosols from NIV modalities can transmit SARS-CoV-2 has not been validated yet and may not pose as large a threat as previously imagined. For other coronaviruses, previous evaluations of NIV use by HCPs has not identified significant infection transmission risks. When HCPs used proper Personal Protective Equipment (PPE), no significant association occurred between the use of NIV or HFNO and increased transmission of severe acute respiratory syndrome (SARS) virus during the outbreak of the early 2000s, although such risk did increase with endotracheal intubations.[19]

Regardless, all would agree that appropriate PPE for HCPs is required, including N95 respirator masks, gowns, gloves, eye protection, and aprons.[20] Ideally patients requiring hospitalizations for treatment of COVID-19 would be placed in a negative pressure room with frequent air turnover to minimize the risk of aerosolized viral particles infecting others. Aerosolization studies also confirm that a loose fitting NIV interface increases exhaled air dispersion as well as use of increased flow rate and/or pressures.[21,22,23]

Recommendations: Ensure adequate fit of any NIV interface and to limit flow and pressure to the lowest possible setting required to improve oxygenation and reduce the risk of P-SILI. Have caution using conventional CPAP or HFNO because of the high fresh gas flows required, whereas SuperNO$_2$VA PAP uses flows consistent with supplemental oxygen. Where possible, connect to a bacterial/viral filter, a surgical mask placed over the device, mouth, and nose may further reduce spread of aerosolized viral particles during NIV use.

Best Practices for SuperNO$_2$VA use

- Lower a surgical or N95 mask just below the nostrils but still cover the patient's mouth.
- Place SuperNO$_2$VA nasal mask over the patient's nose and adjust straps to ensure there are no leaks around the mask. Some clinicians place gauze near the ears for protection.
- Train the patient how to adjust the straps for comfort.
- Attach one end of a bacterial/viral filter to the hyperinflation bag and the other end to the SuperNO$_2$VA.
- Connect the oxygen tubing to the wall and set flows between 8-15 L/min.
- Partially or completely close the adjustable pressure limiting (APL) valve to generate PEEP.
- Train patient how to adjust the APL valve for comfort.
- A clinician should monitor the patient's oxygen saturation to ensure therapy is effective.

Recommendations for use

- Areas where wall or tank supplemental oxygen is available;
- COVID-19 patient with oxygen saturation (SpO_2) less than 92 percent on nasal cannula or non-rebreather;
- To prolong the apneic period during laryngoscopy and endotracheal intubation;
- Respiratory support post-extubation; or
- Step-down units post respiratory insufficiency.

If you have any additional questions, please reach out to your local Vyaire representative.

As a world leader in respiratory care, we take our critical role in the response to this global health crisis seriously. At Vyaire, our goal is to meet the demand as best we can and ensure our customers have the products they need. We are truly proud to partner with you on the frontlines of the COVID-19 global health crisis. The work you are doing is improving outcomes for patients around the world.

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