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ABSTRACT
The ongoing COVID-19 pandemic has placed pressure on health care systems and intensive care unit capacity worldwide. Respiratory insufficiency is the most common reason for hospital admission in patients with COVID-19. The most severe form of respiratory failure is acute respiratory distress syndrome (ARDS), which is associated with significant morbidity and mortality. Patients with ARDS are often have been admitted to clinical environments where teams and physicians have less experience with ARDS management. This article is intended to provide a pragmatic guide for nonintensivist practitioners who care for patients with ARDS requiring mechanical ventilation (MV). In the absence of MV trials specifically in patients with COVID-19-associated ARDS, the information presented is on the basis of general ARDS trials. We encourage readers to supplement this report with the evolving literature on management of COVID-19-specific ARDS.

Defining ARDS
The Berlin definition of ARDS requires all of the following criteria to be present: (1) symptoms or known clinical insult within 1 week; (2) bilateral opacities on chest imaging, not fully explained by effusions, nodules, or atelectasis; (3) respiratory failure not fully explained by cardiac failure or hypervolemia; (4) arterial oxygen tension (PaO2)/fraction of inspired oxygen (FiO2) ≤ 300 with positive end expiratory

RÉSUMÉ
La pandémie de COVID-19 qui sévit toujours exerce des pressions sur les systèmes de soins de santé et les unités de soins intensifs partout dans le monde. L’insuffisance respiratoire est la cause la plus fréquente d’admission à l’hôpital des patients atteints de COVID-19. La forme la plus grave d’insuffisance respiratoire est le syndrome de détresse respiratoire aiguë (SDRA), qui est associé à des taux élevés
treated with invasive mechanical ventilation according to established evidence-based and guideline recommended management strategies. With growing strain on critical care capacity, clinicians from diverse backgrounds, including cardiovascular specialists, might be required to help care for the growing number of patients with severe respiratory failure and ARDS. The aim of this article is to outline the fundamentals of ARDS diagnosis and management, including mechanical ventilation, for the nonintensivist. In the absence of mechanical ventilation trials specifically in patients with COVID-19-associated ARDS, the information presented is on the basis of general ARDS trials.

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Basic Management of MV in Patients With ARDS

Although a detailed review of respiratory and MV physiology is beyond the scope of this article, a working understanding of a basic MV pressure waveform is required to understand the stepwise algorithm presented. MV breaths are delivered in either a spontaneous or mandatory mode. In a mandatory mode, the ventilator delivers a set number of breaths per minute, defined as the respiratory rate (RR), regardless of patient effort. These delivered breaths are either volume controlled (VC) whereby a set tidal volume ($V_T$) is delivered, or pressure controlled whereby a set inspiratory pressure is delivered. A mandatory VC pressure waveform is presented in Figure 1. The peak pressure is the highest pressure reached during the respiratory cycle and represents alveolar pressure and resistance to air flow. The plateau pressure is measured during an inspiratory hold, and as such, represents alveolar pressure alone without a resistance component. Isolated high peak pressures can be seen with high resistance in the circuit, bronchospasm, secretions, or endotracheal tube obstruction. High peak and plateau pressures can be seen in parenchymal lung disease (pulmonary edema, ARDS, consolidation, pneumothorax) or secondary to extrapulmonary causes such as pleural effusions, intra-abdominal hypertension, and morbid obesity (Supplemental Fig. S1).

After inspiration to the peak inspiratory pressure, expiration begins with a predetermined termination signal (flow or pressure) and is characterized by an exponential decrease in airway pressure back to the set PEEP. PEEP improves oxygenation, in part, by mitigating alveolar collapse and increasing the surface area for gas exchange at the alveolar level. The driving pressure is a measure of "lung shear stress" (or cyclical lung strain) and is calculated by subtracting the plateau pressure from the total PEEP.

An algorithmic approach to managing MV in ARDS patients is provided in Figure 2 and the evidence underpinning these recommendations is outlined in Supplemental Table S1. When initiating low $V_T$ ventilation (LTVV), the first decision involves choosing the mode of MV. VC will deliver a consistent $V_T$ and is a reasonable initial choice. Additionally, VC provides the option of setting a 0.2-second inspiratory hold, which gives a real-time plateau pressure measurement. Next, the $V_T$ and RR are set, which together determine the total minute ventilation and, therefore, $CO_2$ clearance and pH. We suggest using 6 mL/kg predicted body weight $V_T$ as an initial setting. The RR is set to meet the patient’s minute ventilatory demands while allowing for permissive hypercapnia (ie, pH 7.25-7.35 and arterial oxygen tension [PaCO$_2$] > 45 mm Hg). It is reasonable to set the initial RR at 20 breaths per minute and subsequently adjust it to maintain an arterial pH > 7.25. We suggest setting an initial PEEP of 10 cm H$_2$O and FiO$_2$ of 1.0. We suggest weaning the FiO$_2$ as soon as possible to target an arterial oxygen saturation of 88%-95% or a PaO$_2$ of 55-80 mm Hg.

After MV initiation, the PEEP and FiO$_2$ can be adjusted using the ARDSNet PEEP table in Figure 2. We favour the low PEEP table as the initial strategy because routine higher PEEP strategies have not been associated with improved outcomes. Importantly however, lung injury is often heterogeneous, and clinicians must individualize MV settings accordingly.

Additional MV physiologic goals include monitoring the plateau and driving pressures and avoiding hypervolemia. A plateau pressure < 30 cm H$_2$O is the generally accepted target on the basis of the ARDSNet trial, which showed reduced de morbidité et de mortalité. Les patients atteints de SDRA sont souvent traités par une méthode de ventilation artificielle invasive, conformément aux stratégies de prise en charge recommandées fondées sur des données probantes et sur les lignes directrices établies. En raison des tensions croissantes exercées sur les ressources en soins intensifs, les cliniciens de différents domaines, y compris les spécialistes en soins cardiovasculaires, pourraient être appelés en renfort pour soigner les patients de plus en plus nombreux à présenter une insuffisance respiratoire grave et un SDRA. Nous résumons ici les fondements du diagnostic et de la prise en charge du SDRA, notamment la ventilation artificielle, à l’intention des non-intensivistes. En l’absence d’études sur le recours à la ventilation artificielle en cas de SDRA dû à la COVID-19, les renseignements fournis reposent sur les études portant sur le SDRA en général.
mortality and increased ventilator-free days in the LTVV arm. Higher pressures are associated with barotrauma and ventilator-induced lung injury. If the plateau pressure exceeds 30 cm H₂O, the V₉ should be decreased in 1 mL/kg predicted body weight increments to a minimum of 4 mL/kg. Higher driving pressure (plateau pressure – PEEP) is independently associated with mortality in patients with moderate and severe ARDS. We suggest a driving pressure goal of ≤ 14 mm Hg. A starting central venous pressure goal of 4-8 mm Hg is reasonable. A lower central venous pressure target can be considered in the more hypoxic patient, whereas a higher target might be needed if intravascular volume is considered inadequate.

If hypoxemia persists (PaO₂/FiO₂ < 150 and FiO₂ > 0.6 with PEEP > 5 mm Hg) despite optimization of initial LTVV ventilator settings, prone (face down) ventilation has been shown to reduce mortality. Prone positioning involves moving a patient from the supine position to the prone position for 12- to 16-hour cycles per day. This manoeuvre, in part, redistributes perfusion to the better ventilated ventral lung regions, thereby improving gas exchange and oxygenation. Proning results in decreased mortality when initiated early in patients with severe ARDS. Because of the unique patient care required during proning, we suggest consultation with a critical care medicine specialist.

Management in Refractory Cases
Most patients will be adequately managed with the aforementioned ARDS MV management principles; however, some patients might require advanced treatment for refractory hypoxemia or hypercapnia (Supplemental Table S1). These patients should be managed in collaboration with a critical care medicine specialist. It is important to acknowledge that the therapies discussed in this section have not been definitively shown to improve mortality. Continuous neuromuscular blockade (NMB) has the potential benefit of reducing patient-ventilator dysynchrony and/or work of breathing in patients with ARDS; however, the efficacy of routine NMB in ARDS in randomized trials is conflicting (Supplemental Table S1). Because of the potential adverse consequences of NMB, such as intensive care unit weakness, we do not routinely use this in our practice. Indications to consider NMB include patient-ventilator dyssynchrony despite deep sedation and refractory hypoxemia or hypercapnia. Recruitment manoeuvres are transient increases in transpulmonary pressure performed in a deeply sedated patient with a goal to improve oxygenation. Many different protocols exist, such as applying 30-40 cm H₂O for 20-30 seconds. If oxygenation improves, clinicians can consider increasing PEEP. The main adverse consequences of recruitment manoeuvres are hemodynamic instability and barotrauma such as pneumothorax and should only be performed in consultation with an intensivist. Inhaled prostacyclin or nitric oxide can improve oxygenation by selectively vasodilating well ventilated zones and therefore improving ventilation and perfusion matching. Additionally, these inhaled agents decrease pulmonary vascular resistance and right ventricular afterload. Despite these effects, no clear mortality benefit exists. Less commonly, some patients with ARDS experience refractory hypercapnia and respiratory acidosis (pH < 7.25). In well sedated and paralyzed patients, ventilatory strategies include increasing the RR and modestly increasing the V₉ provided that goals of plateau pressures and driving pressures are maintained. These strategies might result in dynamic expiratory flow trapping (auto-PEEP), which can be quantified with an end-expiratory hold.

If patients continue to have refractory hypoxemia or hypercapnia, a consultation for veno-venous extracorporeal membrane oxygenation, depending on regional local availability and patient candidacy, can be considered. The Murray score is composed of 4
Figure 2. Algorithmic approach to MV in patients with ARDS. ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; FiO2, fraction of inspired oxygen; H2O, H2O; MV, mechanical ventilation; PaO2, arterial oxygen tension; PBW, predicted body weight; PEEP, positive end expiratory pressure; SpO2, arterial oxygen saturation (indirect measurement); VT, tidal volume; VV-ECMO, veno-venous extracorporeal membrane oxygenation.
variables (hypoxemia, respiratory compliance, chest x-ray findings, and PEEP) and is used to grade the severity of lung injury in ARDS. A Murray score > 3.0 or a pH < 7.20-7.25 during optimized therapy, should prompt early notification to the extracorporeal membrane oxygenation team.

**Conclusion**
Cardiovascular specialists who routinely care for patients requiring MV without ARDS are well positioned to care for critically ill patients. It is imperative that clinicians understand and feel comfortable with the basic management of ARDS, which can be applied to patients with respiratory failure due to COVID-19.

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