Training/Practice
Contemporary Issues in Cardiology Practice

The Basics of ARDS Mechanical Ventilatory Care for Cardiovascular Specialists

Erin Rayner-Hartley, MD,[a,b] P. Elliott Miller, MD,[c] Barry Burstein, MD,[d,e] Lior Bibas, MD,[f]
Michael Goldfarb, MD,[g] Penelope Rampersad, MD, MSc,[h] and Sean van Diepen, MD, MSc[i]

[a] Department of Critical Care Medicine, Respiratory Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA

[b] Division of Cardiology, Royal Columbian Hospital, University of British Columbia, New Westminster, British Columbia, Canada

[c] Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, Connecticut, USA

[d] Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, Minnesota, USA

[e] Division of Cardiology, Trillium Health Partners, University of Toronto, Mississauga, Ontario, Canada

[f] Division of Cardiology and Critical Care, Pierre-Boucher Hospital, Longueuil, Quebec, Canada

[g] Azrieli Heart Centre, Division of Cardiology, Jewish General Hospital, McGill University, Montreal, Quebec, Canada

[h] Department of Cardiovascular Medicine, Heart, Vascular, and Thoracic Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA

[i] Department of Critical Care Medicine and Division of Cardiology, Department of Medicine, University of Alberta, Edmonton, Alberta, Canada

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

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

The outbreak of COVID-19 has spread globally since it was first reported in December 2019. Although a variety of clinical manifestations have been reported, the primary reason for morbidity and mortality is hypoxemic respiratory failure.[1] Among hospitalized patients, the published mortality is approximately 5% and is commonly due to refractory respiratory failure and shock.[1] Epidemiological studies report that acute respiratory distress syndrome (ARDS) is common among hospitalized patients with COVID-19 and represents the primary indication for transfer to intensive care units.[1] Recently published guidelines summarize the current recommendations in this rapidly evolving field.[2] As health care systems become increasingly strained, patients with COVID-

19 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 (PaO_2)/fraction of inspired oxygen (FiO_2) $\leq$ 300 with positive end expiratory

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.

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.

pressure (PEEP) ≥ 5 cm H_2O. ARDS is further classified according to severity on the basis of arterial blood gas analysis: mild (PaO_2/FiO_2 201-300), moderate (PaO_2/FiO_2 101-200), and severe ($PaO_2/FiO_2 \leq 100$).[3] ARDS is commonly associated with various infectious, traumatic, and inflammatory conditions, all of which are associated with direct and indirect lung injury; however, a clear pathophysiological mechanism has not been elucidated. Importantly, many patients with these associated conditions will not develop ARDS, suggesting that other pathophysiological mechanisms might play an inciting role. Cardiovascular specialists should be aware of ARDS mimickers, such as heart failure and alveolar hemorrhage.

Advances in supportive strategies, including MV with invasive positive pressure ventilation via endotracheal intubation, have improved outcomes for patients with ARDS; however, mortality remains high. Death might result as a consequence of the underlying illness, refractory hypoxia with or without progressive right ventricular dysfunction, due to multiple organ failure, and/or critical illness complications.

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_2O 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_2O is the generally accepted target on the basis of the ARDSNet trial, which showed reduced

Rayner-Hartley et al.
Basics of ARDS Mechanical Ventilation

1677
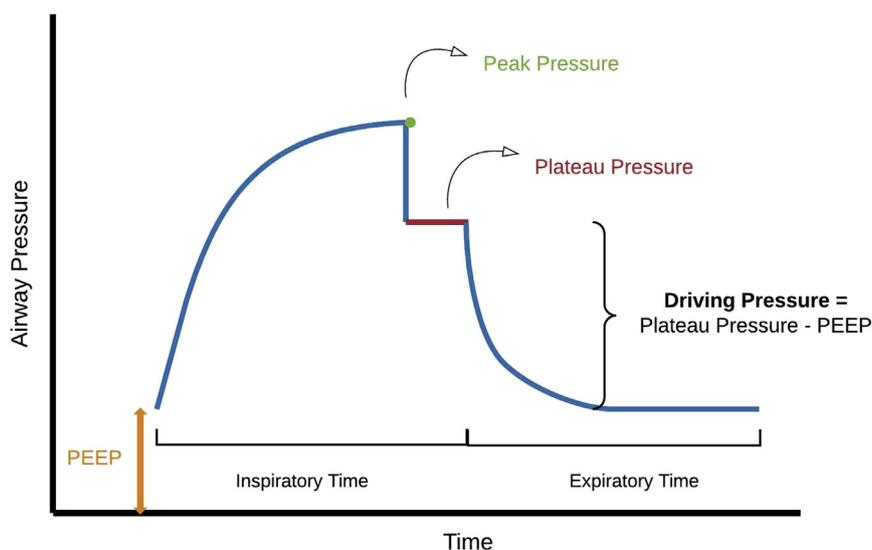
Respiratory System Compliance = Tidal Volume / (Plateau Pressure - PEEP)

Figure 1. Volume control pressure waveform. PEEP, positive end expiratory pressure.

mortality and increased ventilator-free days in the LTVV arm.[3] Higher pressures are associated with barotrauma and ventilator-induced lung injury. If the plateau pressure exceeds 30 cm H_2O, the V_T 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.[3] We suggest a driving pressure goal of ≤ 14 mm Hg. Last, a substantial body of evidence supports a conservative fluid management strategy to limit translocation of fluid into the pulmonary interstitium and alveoli.[4] 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 hypoxemic patient, whereas a higher target might be needed if intravascular volume is considered inadequate.
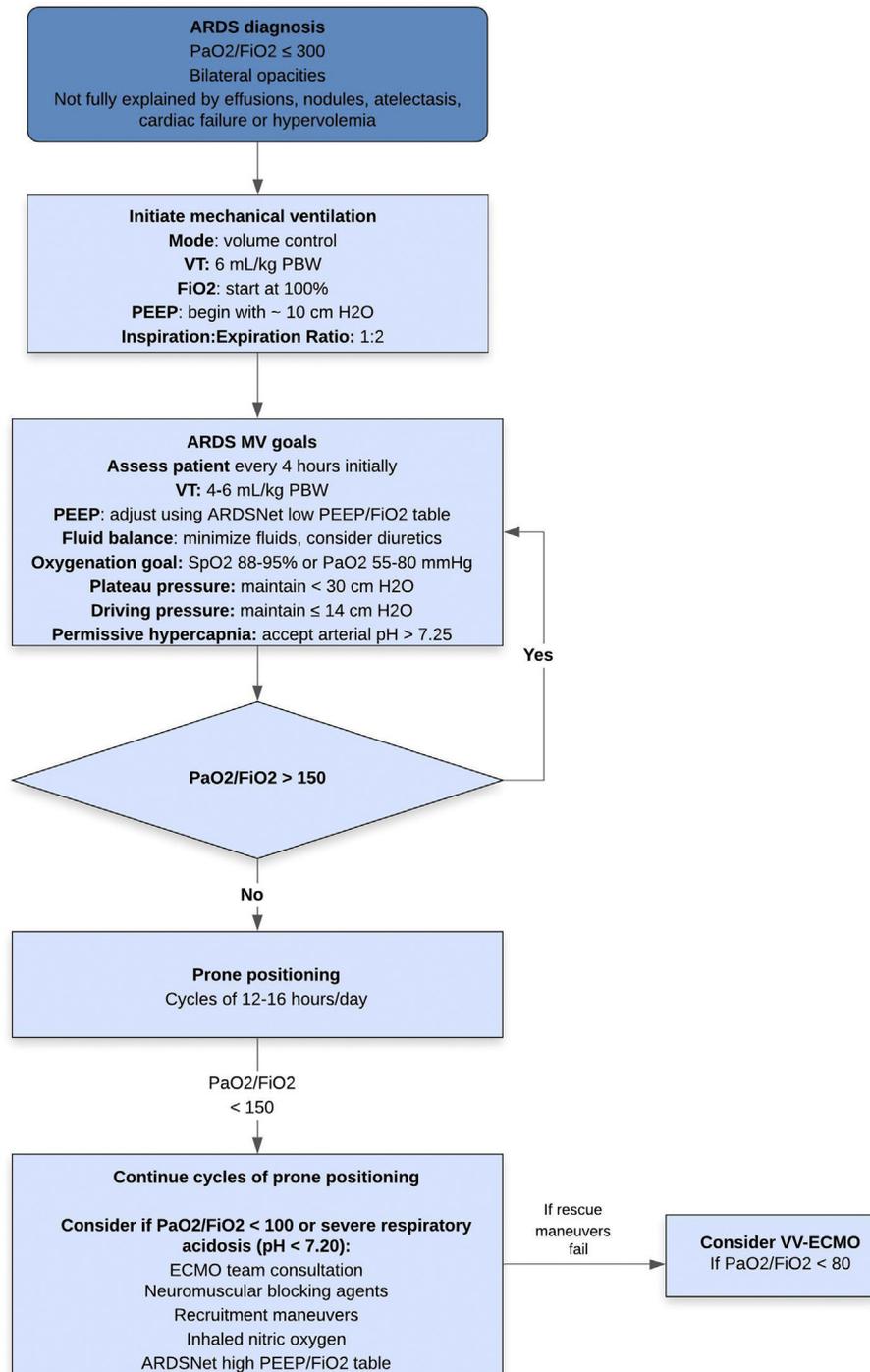
If hypoxemia persists ($PaO_2/FiO_2 < 150$ and $FiO_2 > 0.6$ with PEEP > 5 mm Hg) despite optimization of initial LTVV ventilator settings, prone (face down) ventilation has been shown to reduce mortality. Prone positioning involves moving a patient from the supine position to the prone position for 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.[3] 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 dyssynchrony 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).[5] 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 H_2O 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 V_T 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

ARDS diagnosis
PaO2/FiO2 ≤ 300
Bilateral opacities
Not fully explained by effusions, nodules, atelectasis,
cardiac failure or hypervolemia

↓

Initiate mechanical ventilation
Mode: volume control
VT: 6 mL/kg PBW
FiO2: start at 100%
PEEP: begin with ~ 10 cm H2O
Inspiration:Expiration Ratio: 1:2

↓

ARDS MV goals
Assess patient every 4 hours initially
VT: 4-6 mL/kg PBW
PEEP: adjust using ARDSNet low PEEP/FiO2 table
Fluid balance: minimize fluids, consider diuretics
Oxygenation goal: SpO2 88-95% or PaO2 55-80 mmHg
Plateau pressure: maintain < 30 cm H2O
Driving pressure: maintain ≤ 14 cm H2O
Permissive hypercapnia: accept arterial pH > 7.25

↓

PaO2/FiO2 > 150 — Yes →

No ↓

Prone positioning
Cycles of 12-16 hours/day

PaO2/FiO2
< 150

↓

Continue cycles of prone positioning

Consider if PaO2/FiO2 < 100 or severe respiratory acidosis (pH < 7.20):
ECMO team consultation
Neuromuscular blocking agents
Recruitment maneuvers
Inhaled nitric oxygen
ARDSNet high PEEP/FiO2 table

If rescue maneuvers fail →

Consider VV-ECMO
If PaO2/FiO2 < 80

ARDSNet Low PEEP/FiO2 Table												
FiO2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	12	14	14	14	16	18	20

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, H_2O; 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 extra-corporeal membrane oxygenation.

Rayner-Hartley et al.
Basics of ARDS Mechanical Ventilation

1679

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.

Funding Sources

The authors have no funding sources to declare.

Disclosures

The authors have no conflicts of interest to disclose.

References

1. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323:1061-9.

2. Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Crit Care Med 2020;48:e440-69.

3. Fan E, Del Sorbo L, Goligher EC, et al. An official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine clinical practice guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2017;195:1253-63.

4. Grissom CK, Hirshberg EL, Dickerson JB, et al. Fluid management with a simplified conservative protocol for the acute respiratory distress syndrome. Crit Care Med 2015;43:288-95.

5. Moss M, Huang DT, Brower RG, et al. Early neuromuscular blockade in the acute respiratory distress syndrome. N Engl J Med 2019;380:1997-2008.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2020.07.011.