Integrating Mechanical Ventilation and Extracorporeal Membrane Oxygenation in Severe Acute Respiratory Distress Syndrome

To the Editor:

We read with great interest the study of Araos and colleagues (1), who elegantly demonstrated that near-apneic ventilation decreases lung injury and early fibroproliferation in an animal model of extracorporeal membrane oxygenation (ECMO)-supported acute respiratory distress syndrome (ARDS). Although minimizing risks of ventilator-induced lung injury on venovenous ECMO is paramount, the risks/benefits of strategies employed to minimize ventilator-induced lung injury also merit due consideration.

First, a demonstration that near-apneic ventilation with moderate positive end-expiratory pressure does not promote atelectasis and worsen intrapulmonary shunt fraction in this study may have been particularly helpful. Blood flow through the diseased pneumonic lung or lungs or parts of the lung that have collapsed will contribute to intrapulmonary shunting, also referred to as venous admixture. The shunt fraction is the calculated estimate of how much hypoxic blood should return to the arterial side after passing through the shunt to produce the measured arterial oxygen results, for a given Q. The lung is a mixture of heterogeneous units, each with a different V/Q ratio that can be severely affected by the loss of hypoxic vasoconstriction on venovenous ECMO. In addition, hypoventilation induced by extracorporeal carbon dioxide removal can lower the global V/Q ratio of the native lungs and results in reabsorption atelectasis, therefore worsening hypoxemia (2). During near-apneic ventilation in severe ARDS, the contribution of native lungs to oxygenation is obviously significantly reduced. This makes the patient near-total ECMO dependent for oxygenation, often requiring high ECMO blood flows in the setting of a high Q state.

Second, as reported by the authors, the very low respiratory rate contributed significantly to the marked decrease in mechanical power observed in the near-apneic group. It should be noted that our understanding of the complex heart–lung–ventilator ECMO interactions are still evolving. Given that venovenous ECMO is a therapy delivered over weeks to months, the benefits of extreme lung protection should be balanced against risks associated with such strategies. We need to ensure that ventilation strategies employed on ECMO do not limit our ability to provide evidence-based supportive measures such as fluid restriction, minimization of sedation, and pharmacologic paralysis and early rehabilitation. To date, potential clinical benefits have only been demonstrated with a ventilation strategy that employed moderate positive end-expiratory pressure and limited plateau pressures \( \leq 24 \text{ cmH}_2\text{O} \) (3, 4). Last, moving forward, there is a sound physiologic rationale to reinforce the ventilator strategy employed in the EOLIA (ECMO to Rescue Lung Injury in Severe ARDS) trial with prone positioning. Although ECMO provides lung protection, prone positioning may further improve respiratory system compliance and V/Q matching (5, 6). This may minimize reliance on higher ECMO blood flows with such extreme mechanical ventilation reduction strategies until the risk/benefit ratio of such strategies is clearly established.

References

1. Bhavani SV, Carey KA, Gilbert ER, Afshar M, Verhoef PA, Churpek MM. Identifying novel sepsis subphenotypes using temperature trajectories. Am J Respir Crit Care Med [online ahead of print] 21 Feb 2019; DOI: 10.1164/rccm.201806–1197OC.

2. van Lier D, Geven C, Leijte GP, Pickkers P. Experimental human endotoxemia as a model of systemic inflammation. Biochimie 2018; 159:99–106.

Copyright © 2019 by the American Thoracic Society
Reply to Shekar and Schmidt

From the Authors:

We thank Dr. Shekar and Dr. Schmidt for their letter regarding our recent publication (1). They raise important questions about the clinical impact and potential drawbacks of the near-apneic protocol tested in our study.

Regarding intrapulmonary shunt, we measured it at the end of the experiment (data not shown) and found no differences between the near-apneic group and the group ventilated with conventional protective ventilation, which suggests that near-apneic ventilation did not promote further atelectasis. Moreover, in the near-apneic ventilation, the contribution of the native lungs to oxygenation was significant by the end of the experiment, as indicated by oxygen tensions of 78 ± 4 mm Hg in the mixed venous blood and 300 ± 31 mm Hg in the arterial blood.

As pointed out in the Discussion of our study, we agree with Dr. Shekar and Dr. Schmidt in that applying very low respiratory rates and VT during near-apneic ventilation may require deep sedation and neuromuscular blockade, which ideally should be avoided. However, observational studies have shown that during the first 3 days after connection to extracorporeal membrane oxygenation, most patients with acute respiratory distress syndrome are deeply sedated and paralyzed, even if they are not receiving near-apneic ventilation (2, 3).

To overcome these controversies, we now need clinical studies to identify the optimal ventilatory strategies for patients with acute respiratory distress syndrome connected to extracorporeal membrane oxygenation.

Copyright © 2019 by the American Thoracic Society

References

1. Araos J, Alegria L, Garcia P, Cruces P, Soto D, Erranz B, et al. Near-apneic ventilation decreases lung injury and fibroproliferation in an acute respiratory distress syndrome model with extracorporeal membrane oxygenation. Am J Respir Crit Care Med 2019;199:603–612.
2. Schmidt M, Stewart C, Bailey M, Nieszkowska A, Kelly J, Murphy L, et al. Mechanical ventilation management during extracorporeal membrane oxygenation for acute respiratory distress syndrome: a retrospective international multicenter study. Crit Care Med 2015;43: 654–664.
3. Del Sorbo L, Goffi A, Goligher E, Fan E, Slutsky AS. Setting mechanical ventilation in ARDS patients during VV-ECMO: where are we? Minerva Anestesiol 2015;81:1369–1376.

Copyright © 2019 by the American Thoracic Society

Author disclosures are available with the text of this letter at www.atsjournals.org.

Joaquin Araos, D.V.M., Ph.D.
Pontificia Universidad Católica de Chile
Santiago, Chile

and

Cornell University
Ithaca, New York

Alejandro Bruhn, M.D., Ph.D.*
Pontificia Universidad Católica de Chile
Santiago, Chile

ORCID IDs: 0000-0002-9805-9769 (J.A.); 0000-0001-8034-1937 (A.B.).

*Corresponding author (e-mail: alejandrobruhn@gmail.com).