2. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, *et al*.; LUNG SAFE Investigators; ESICM Trials Group. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA* 2016;315: 788–800.
3. Al-Samkari H, Karp Leaf RS, Dzik WH, Carlson JCT, Fogerty AE, Waheed A, *et al*. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. *Blood* 2020;136:489–500.
4. Mazzeffi M, Kon Z, Menaker J, Johnson DM, Parise O, Gelsomino S, *et al*. Large dual-lumen extracorporeal membrane oxygenation cannulas are associated with more intracranial hemorrhage. *ASAIO J* 2019;65:674–677.
5. Rubino A, Vuylsteke A, Jenkins DP, Fowles JA, Hockings L, Valchanov K. Direct complications of the Avalon bicaval dual-lumen cannula in respiratory extracorporeal membrane oxygenation (ECMO): single-center experience. *Int J Artif Organs* 2014;37:741–747.
6. Wichmann D, Sperhake JP, Lutgehetmann M, Steurer S, Edler C, Heinemann A, *et al*. Autopsy findings and venous thromboembolism in patients with COVID-19. *Ann Inter Med* [online ahead of print] 6 May 2020; DOI: 10.7326/M20-2003.
7. Kuhl T, Michels G, Pfister R, Wendt S, Langebartels G, Wahlers T. Comparison of the avalon dual-lumen cannula with conventional cannulation technique for venovenous extracorporeal membrane oxygenation. *Thorac Cardiovasc Surg* 2015;63:653–662.
8. Amato MBP, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, *et al*. Driving pressure and survival in the acute respiratory distress syndrome. *N Engl J Med* 2015;372:747–755.
9. Combes A, Hajage D, Capellier G, Demoule A, Lavoué S, Guervilly C, *et al*.; EOLIA Trial Group, REVA, and ECMONet. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *N Engl J Med* 2018;378:1965–1975.

Reply to Wengenmayer *et al.*

From the Authors:

We read with interest the correspondence from Wengenmayer and colleagues. The authors suggested that we should have adjusted our ventilation strategy under extracorporeal membrane oxygenation (ECMO) to be more protective. As recommended in the Extracorporeal Life Support Organization (ELSO) guidelines (1), we maintained a high positive end-expiratory pressure (PEEP) and reduced V_T to maintain a plateau pressure (PP) under 25 cm H_2O, but we did not drastically reduce the respiratory rate and the driving pressure (ΔP). The measure of these two parameters are indeed associated with mortality at Day 1 of acute respiratory distress syndrome (ARDS) (2) but not the ΔP in patients with obesity (most of our patients) (3). Thus, reducing ΔP by decreasing V_T in patients with obesity could probably not be the main goal when PP remains acceptable. Indeed, the LUNG SAFE (Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure) study (2) did not show any superiority of the ΔP to predict mortality. Furthermore, even if the ΔP value at day 1 was associated with mortality, to date, optimizing this parameter during the following days is not correlated with survival. Knowing the specificity of coronavirus disease (COVID-19)–related ARDS (4) and the high rate of patients with obesity treated in our small cohort (58.8%), one could advance that our strategy might be more protective by preventing overdistension.

Our cannulation strategy is much more a matter of debate: the double-lumen cannulas are indeed not recommended in first intension by ELSO (1) because their positioning can be longer and require the use of an ultrasound system. Regarding oxygenation and decarboxylation, this type of cannula is as efficient as conventional cannulation (5). Our team is experienced in this type of cannulation, limiting the adverse events during cannulation. In view of the morphotype of our patients, a single jugular cannulation facilitated their half-seated position and nursing. Moreover, these cannulas have the advantage of encouraging patient mobilization (5) and potentially limiting the consumption of sedatives, which is not insignificant in the context of a period with work overload. Because this type of cannula is associated with more bleeding (6), we wondered if the high rate of bleeding in our series is facilitated by the cannula, anticoagulation, or the transfusion strategy. Our transfusion target is consistent with ELSO guidelines (1). Concerning the anticoagulation, neither of the two patients with serious hemorrhagic events were overanticoagulated, and the five other patients were transfused on minor bleedings or hemolysis without a negative impact on patient prognosis. On the other hand, we reported two oxygenator thrombosis and three thromboembolic events. Considering the high incidence of thrombotic events in patients with COVID-19 and the ELSO guidelines (1), our anticoagulation target seems to be reasonable.

In our series, two patients died of refractory ARDS with pulmonary fibrosis making the respiratory weaning impossible after decannulation. Two patients developed refractory septic shock with a predominance of vasoplegia, making conversion to venoaterial ECMO (VA-ECMO) ineffective. One patient died during cannulation of cardiac tamponade, and one was on VA-ECMO. Thus, optimizing the support during the time either by converting to VA-ECMO or adding a second cannula would not have modified the mortality of our case series. It is important to note that the context of pandemic-induced work overload and the patients' management by interim intensivists who were not used to taking care of patients with ARDS with ECMO may explain some intensive care management difficulties and suboptimal ventilator settings.

In conclusion, in the context of the pandemic, we have chosen a mastered management of our patients. However, ECMO implantation in refractory ARDS related to COVID-19 allowed more protective ventilation parameters, improving patient status. Our results highlighted a preference for an adaptation of ventilator parameters on the PP and moderate PEEP in this specific series characterized by more obese patients and 65% survival in the ICU. ■

Originally Published in Press as DOI: 10.1164/rccm.202007-2670LE on August 14, 2020

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

Alexandra Monnier, M.D.
Pierre-Emmanuel Falcoz, M.D., Ph.D.
Strasbourg University Hospital
Strasbourg, France

Julie Helms, M.D., Ph.D.
Ferhat Meziani, M.D., Ph.D.*
Strasbourg University Hospital
Strasbourg, France

and

University of Strasbourg
Strasbourg, France

*Corresponding author (e-mail: ferhat.meziani@chru-strasbourg.fr).

References

1. Shekar K, Badulak J, Peek G, Boeken U, Dalton HJ, Arora L, *et al*.; ELSO Guideline Working Group. Extracorporeal Life Support Organization COVID-19 interim guidelines. *ASAIO J* [online ahead of print] 29 Apr 2020; DOI: 10.1097/MAT.0000000000001193.
2. Laffey JG, Bellani G, Pham T, Fan E, Madotto F, Bajwa EK, *et al*.; LUNG SAFE Investigators and the ESICM Trials Group. Potentially modifiable factors contributing to outcome from acute respiratory distress syndrome: the LUNG SAFE study. *Intensive Care Med* 2016;42:1865–1876.
3. De Jong A, Cossic J, Verzilli D, Monet C, Carr J, Conseil M, *et al*. Impact of the driving pressure on mortality in obese and non-obese ARDS patients: a retrospective study of 362 cases. *Intensive Care Med* 2018;44:1106–1114.
4. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L, *et al*. COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med* 2020;46:1099–1102.
5. Kuhl T, Michels G, Pfister R, Wendt S, Langebartels G, Wahlers T. Comparison of the avalon dual-lumen cannula with conventional cannulation technique for venovenous extracorporeal membrane oxygenation. *Thorac Cardiovasc Surg* 2015;63:653–662.
6. Falcoz PE, Monnier A, Puyraveau M, Perrier S, Ludes PO, Olland A, *et al*. Extracorporeal membrane oxygenation for critically ill patients with COVID-19-related acute respiratory distress syndrome: worth the effort? [letter]. *Am J Respir Crit Care Med* 2020;202:460–463.

Acute Respiratory Distress Syndrome in COVID-19: Do All These Patients Definitely Require Intubation and Mechanical Ventilation?

To the Editor:

We have read "Respiratory Pathophysiology of Mechanically Ventilated Patients with COVID-19: A Cohort Study" by Ziehr and colleagues with great interest (1). In this letter, the authors described characteristics and outcomes in 66 patients with coronavirus disease (COVID-19) managed with mechanical ventilation. It is a great pleasure to see that 62.1% of these patients were successfully extubated after 2–3 weeks of mechanical ventilation. However, a few questions arose after reading the paper.

First, did all these patients definitely require intubation? Unfortunately, the authors didn't specify in their letter the indications they had used for intubation, as the higher proportion of successfully weaned patients might be explained by lower severity of COVID-19 pneumonia. As we can see from given data, the respiratory parameters at the ICU admission and during the first 5 days were not so critical.

1. Median Pa_{O_2}/FI_{O_2} was 182 mm Hg and even reached 245 mm Hg at Day 1 (more than 300 mm Hg in some patients, and one patient had Pa_{O_2}/FI_{O_2} about 600 mm Hg). Recent randomized controlled trials and meta-analyses that included adult patients with acute hypoxemic respiratory failure have shown that patients with even more severe hypoxemia can be successfully managed by high-flow oxygen therapy or noninvasive ventilation (2, 3). For example, in the randomized controlled trial by Frat and colleagues, mean Pa_{O_2}/FI_{O_2} on inclusion was about 150 mm Hg, and all those patients were treated with standard oxygen, high-flow oxygen, or noninvasive ventilation (2).
2. Median plateau pressure was about 21 cm H_2O and median positive end-expiratory pressure (PEEP) was about 10 cm H_2O; therefore, the calculated driving pressure was only 11 cm H_2O, which is close to driving pressure in healthy lungs. This means that the patients' lungs had only multilocal alveolar damage and possibly low recruitability (so-called L-phenotype) (4).

Second, why did 95% of patients receive vasopressors? A possible explanation can be seen in Figure 1 by Ziehr and colleagues. A high proportion of patients had PEEP levels exceeding 14 (14–20) cm H_2O despite low recruitability demonstrated in COVID-19–associated acute respiratory distress syndrome (ARDS) (4): 15 patients at Day 1 (22.7%), 20 patients at Day 2 (30%), and 21 patients at Day 5 (36.8%). This can lead to lung overdistension and acute cor pulmonale. On the contrary, the reduced PEEP levels in patients with COVID-19 resulted in an increase in lung compliance and a decrease in dead space ventilation in a small observational study (5). Deep sedation can be another possible explanation of the high usage of vasopressors (data not presented).

Third, why did the authors so often use neuromuscular blockade (in 42% of patients)? The benefit of neuromuscular blockers was shown in the ACURASYS trial, in which they were used in patients with Pa_{O_2}/FI_{O_2} less than 150 mm Hg in the first 48 hours of mechanical ventilation (6). If we look at Figure 1 by Ziehr and colleagues, we can see that only six patients (9%) had Pa_{O_2}/FI_{O_2} less than 150 mm Hg on Day 2. The neuromuscular blockade can lessen ventilator-induced lung injury by decreasing transpulmonary pressure swings in dependent lung regions in severe ARDS, but it is not the case for mild or moderate ARDS.

Finally, we have a question about the prone position during mechanical ventilation. The authors declared that median PEEP was 13 (interquartile range, 12–15) cm H_2O while supine and 14 (interquartile range, 12–15) cm H_2O while prone, so the PEEP levels in prone position did not decrease and even increased. This seems useless because a prone position that decreases the lung superimposed pressure must lead to a decrease in the PEEP levels.

Author Contributions: All authors contributed equally to the conception, drafting, and final editing of this manuscript.

Originally Published in Press as DOI: 10.1164/rccm.202007-2713LE on August 18, 2020