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).

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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.

We believe that the authors used invasive ventilation instead of noninvasive respiratory support in many cases because of known

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concerns about airborne transmission of COVID-19 during noninvasive strategies. We consider that the results of this trial should be carefully reviewed and interpreted with caution. ■

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Andrey I. Yaroshetskiy, M.D.*
Sechenov First Moscow State Medical University (Sechenov University)
Moscow, Russia
and
Pirogov Russian National Research Medical University
Moscow, Russia

Sergey N. Avdeev, M.D.
Sechenov First Moscow State Medical University (Sechenov University)
Moscow, Russia

Vasily D. Konanykhin, M.D.
Pirogov Russian National Research Medical University
Moscow, Russia

ORCID ID: 0000-0002-5999-2150 (S.N.A.).

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

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Reply to Yaroshetskiy *et al.*

From the Authors:

We conducted a retrospective observational cohort study focused solely on intubated patients with coronavirus disease (COVID-19) respiratory failure at two tertiary medical centers (1). It was not a clinical trial and did not include a nonintubated comparator cohort. Dr. Yaroshetskiy and colleagues raise important questions about the use of noninvasive respiratory support for COVID-19, but these are questions that our study was not designed to answer. We can only say that measures of gas exchange, respiratory system compliance, and positive end-expiratory pressure application in our patients were similar to those from prior large cohorts of acute respiratory distress syndrome (ARDS), as detailed in our manuscript. Patients were intubated according to standard clinical criteria and received established evidence-based care for ARDS at the discretion of the treating physician. This included prone positioning for patients with persistent hypoxemia or elevated airway pressures. Measures of gas exchange in patients receiving prone ventilation in our cohort were similar to those in published trials of prone ventilation for ARDS. Neuromuscular blockade was provided at the discretion of the treating physician, and shock was defined as the presence of any inotropes or vasopressors, regardless of level. ■

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David R. Ziehr, M.D.*
Massachusetts General Hospital
Boston, Massachusetts
and
Beth Israel Deaconess Medical Center
Boston, Massachusetts

Jehan Alladina, M.D.*‡
Massachusetts General Hospital
Boston, Massachusetts

Camille R. Petri, M.D.
Jason H. Maley, M.D.
Massachusetts General Hospital
Boston, Massachusetts
and
Beth Israel Deaconess Medical Center
Boston, Massachusetts

Ari Moskowitz, M.D.
Beth Israel Deaconess Medical Center
Boston, Massachusetts

Benjamin D. Medoff, M.D.
Kathryn A. Hibbert, M.D.
B. Taylor Thompson, M.D.§
C. Corey Hardin, M.D., Ph.D.
Massachusetts General Hospital
Boston, Massachusetts

ORCID IDs: 0000-0002-8029-7259 (D.R.Z.); 0000-0003-0136-6859 (J.A.).

*These authors contributed equally to this work.
‡Corresponding author (e-mail: jalladina@mgh.harvard.edu).
§B.T.T. is Associate Editor of *AJRCCM*. His participation complies with American Thoracic Society requirements for recusal from review and decisions for authored works.

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