

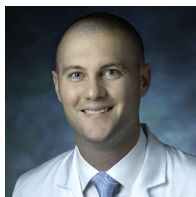
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REPLY: SPLITTING OVER LUMPING IN MECHANICAL SUPPORT FOR ACUTE RESPIRATORY DISTRESS SYNDROME Reply to the Editor:



Amid the present pandemic, clinical researchers are once again confronted with the challenge posed by patients with acute respiratory distress syndrome (ARDS). As of this writing, more than 2.6 million people in the United States have been diagnosed and 127,000 have died as a result of severe acute respiratory syndrome coronavirus 2, the virus that causes coronavirus 2019 (COVID-19).¹ Although hospitalization rates are difficult to track, models forecast admissions to potentially crest at about 15,000 per day domestically,² with a significant percentage of those patients requiring mechanical ventilation due to ARDS. It is often said that adversity breeds innovation and given both the volume and acuity of the moment, opportunity for advancement in our understanding of the management of this vexing disease is undeniable.

In this context, the letter by Joyce³ introduces a provocative, if not potentially visionary, approach to the treatment of ARDS. The letter summarizes the experience at the Medical College of Wisconsin, where multidisciplinary teams are utilizing the transcatheter Protek Duo Right Ventricular Assist Device (LivaNova PLC, Houston, Tex) to not only support the right ventricle, which is commonly implicated when hemodynamic instability results, but also as a means to facilitate extubation, avoiding the known harmful effects of mechanical ventilation in this population. The rationale for the approach has merit and early results among 9 consecutive patients are compelling.

The inherent hypothesis of the piece was nonetheless striking in its generality, namely that offloading the right ventricle will mitigate cardiopulmonary compromise. Although this mechanism may contribute to the clinical dilemma,⁴ our understanding of COVID-19 is ever-evolving. Some have proposed that the pulmonary effects may be represented by multiple phenotypes that respond differently to hallmark lung-protective ventilation strategies.⁵⁻⁷ Furthermore, ARDS has a wide spectrum of presentations and severity.⁸ Concomitant neurologic impairment, multiorgan dysfunction, and coagulopathy are wide ranging and unpredictable. When considering the care of COVID-19 patients, teams should guard against the impulse to cast generalizations and assign interventions in broad swaths. Rather, this disease calls for the development of precise definitions and inclusion criteria to properly classify patients and assign therapies.

It is encouraging to read that the team in Wisconsin is preparing to conduct a multicenter prospective trial, and the devil of such study remains in the details. Recall that extracorporeal membrane oxygenation (ECMO) for ARDS—although theoretically ideal as a tool to avoid positive pressure ventilation and ensure lung rest and recovery—remains controversial, in part due to the challenges of conducting appropriate clinical trials. Promising early results suggesting improved mortality with ECMO for ARDS were criticized due to inconsistencies in care among control patients.⁹ Unfortunately, a more recent study with improved standardization could not recreate this mortality benefit, potentially the result of high crossover due to the use of ECMO for rescue therapy.¹⁰ Put simply, the management of ARDS is complicated and study of ECMO is messy. Although the solution will almost certainly be the result of splitting rather than lumping, centers with adequate resources and expertise are encouraged to leverage this moment to translate innovative anecdotes into new standards of care.

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REPLY: PROTECTING THE RIGHT VENTRICLE IN COVID-19 ACUTE RESPIRATORY DISTRESS SYNDROME—MORE



**DATA REQUIRED
Reply to the Editor:**

Coronavirus disease 2019 (COVID-19) is a multisystem disease prominently associated with acute respiratory distress syndrome (ARDS). Anecdotal observations suggest high rates of right ventricular (RV) failure in these patients, perhaps partially attributable to venous thromboembolic disease; however, the precise incidence and significance of COVID-19–associated RV failure remains unknown. Importantly, RV failure is also common in patients with ARDS without COVID-19.¹ Extracorporeal membrane oxygenation (ECMO) has demonstrated mortality benefit in patients with severe forms of ARDS^{2,3} and has been demonstrated to decrease pulmonary pressures rapidly in patients with severe ARDS.⁴ If RV failure is more common in COVID-19–associated ARDS, then targeted extracorporeal therapy supporting the RV would be worthy of exploration.

In this issue of the *Journal*, Joyce⁵ reports a single-center experience with an oxygenator and right ventricular assist device (oxy-RVAD) in 9 patients with COVID-19–

associated ARDS.⁵ The significance of the report lies not in the patient outcomes, which were incomplete at the time of reporting. Rather, the significance lies in the hypothesis that an oxy-RVAD, in contrast with venovenous ECMO alone, may provide greater support for the failing RV, and that this is particularly applicable in COVID-19.

Without greater detail regarding patient selection, severity of illness, comorbidities, complications, and other factors, and without a control group, Joyce’s letter⁵ simply demonstrates feasibility of this approach. The introduction of a second variable, endotracheal extubation, may complicate the ability to assess the direct effect of the primary intervention. Nonetheless, Joyce⁵ reports favorable, if partial, outcomes in the cohort. Pressor requirements were eliminated, and 6 of the 9 patients were decannulated.

If the oxy-RVAD approach is rational and feasible, is it advisable? One issue raised by Joyce⁵ is cost. Clearly, any future study of an oxy-RVAD in this setting, as with ECMO, should be accompanied by detailed cost-benefit analyses.

Notably, Joyce⁵ couples the technology with extubation, with avoidance of ventilator-induced lung injury as the central theme of the letter (in the title and introduction). This issue therefore merits independent comment. Extubation alone is no guarantee of safe passage for the lungs. Without mitigating large pleural pressure swings, liberation from invasive mechanical ventilation, although assuredly eliminating ventilator-induced lung injury, may nonetheless result in lung injury if the patient is air hungry and working hard to breathe, so-called patient self-inflicted lung injury.⁶ So although this too may be feasible, it must be seen as an additional experiment.

As Joyce⁵ says, “Anecdotal evidence should always be viewed with a degree of skepticism.” We agree. The experience described is intriguing but preliminary, with insufficient data to guide clinical practice or broader recommendations. As we learn more about COVID-19–associated RV failure, the specific need in this context may become clearer. Notwithstanding the separate issue of extubating patients during ECMO (or oxy-RVAD) support, the broader hypothesis may be applicable to any severe patient with ARDS with concomitant severe RV dysfunction. Clearly, more data are needed, and we look forward to Joyce’s planned multicenter, randomized clinical trial.

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