

The Case for Prolonged ECMO for COVID-19 ARDS as a Bridge to Recovery or Lung Transplantation

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Clinical guidelines for managing patients with severe acute respiratory syndrome coronavirus 2 infection have evolved significantly since the first patients with coronavirus 2019 (COVID-19) were reported. The use of extracorporeal membrane oxygenation (ECMO) in patients with acute respiratory distress syndrome (ARDS) as a result of COVID-19 was met initially with some skepticism because of (1) concerns of limited resource availability and the need to focus these resources in other areas of the critical care management of these patients and (2) early studies reporting that the use of ECMO in patients with COVID-19 was associated with high mortality in small cohorts.¹ As the international experience grew, an initial experience of ECMO use in patients with COVID-19 was published in 2020 using data from the Extracorporeal Life Support Organization Registry. In this report, the estimated cumulative incidence of in-hospital mortality was 37.4% at 90 d after ECMO initiation, which was deemed comparable with outcomes after ECMO use in patients with ARDS unrelated to COVID-19.^{2,3} In a more recent analysis of the Extracorporeal Life Support Organization Registry, which was published in 2021 and included 4812 patients with COVID-19 who received ECMO at 1 of 349 centers in 41 countries, the mortality rate of ECMO-supported patients with COVID-19 significantly increased worldwide throughout the pandemic, and the duration of ECMO support also increased.⁴ These dynamic outcomes are reflective of changes in practices, the addition of new ECMO centers, calls for continued surveillance that facilitated awareness of local and regional mortality rates, the duration of ECMO support, and resource constraints.

As physicians became more experienced with the use of ECMO in patients with COVID-19, ECMO practices

evolved, often accompanied by functional and physiological improvement. It became evident that pulmonary recovery frequently lagged behind that typically seen for ARDS of other etiologies, and for that reason, the duration of ECMO support continued to increase during subsequent waves of the pandemic. Barbaro et al reported an increase in the median time of ECMO support in patients with COVID-19 ARDS from 14d to 20 d between a cohort of COVID patients supported with ECMO before May 2, 2020, and a cohort of patients treated from May 2, 2020, to December 31, 2020. Median ECMO support was also significantly longer than the 10–14 d of support seen in patients who required ECMO for non-COVID ARDS.⁴ Lung transplantation has been offered as a life-saving therapy for some patients with COVID-19 who present with persistent lung failure despite several weeks or months of support in the intensive care unit and who face an uncertain recovery. To date, only a few cases of lung transplant due to lung failure caused by COVID-19 have been reported, however.^{5,6} Early outcomes were acceptable for the severely ill patients in these initial reports.

There are no clear guidelines on candidate selection for lung transplantation necessitated by COVID-19–associated ARDS. However, Cypel et al put forth some recommended considerations when assessing these complex patients regarding their potential candidacy for lung transplantation.⁷ These recommendations included that (1) candidates should be younger than 65 y of age; (2) they should have only single-organ dysfunction; (3) sufficient time to allow lung recovery should be provided and lung transplantation should not be considered sooner than 4–6 wks after the initial clinical signs of respiratory failure; (4) there should be radiological evidence of irreversible lung disease; and (5) the patient should exhibit adequate neurological status and be awake and able to participate in physical rehabilitation while on the transplant waiting list. Other standard criteria for lung transplant candidacy must also be met. The International Society for Heart and Lung Transplantation COVID-19 Task Force put forth similar recommendations on recipient selection for cardiothoracic transplantation during the COVID-19 pandemic.⁸

In this issue of Transplantation, Mohanka et al reported the outcomes of 20 patients with COVID-19 ARDS supported on ECMO.⁹ They compared the outcomes of patients who required <30 d of ECMO support and patients with prolonged ECMO support (>30 d). They found that 60% of the patients who required prolonged ECMO support were eventually discharged from the hospital, and 1 patient received a lung transplant. In this group, the median ECMO support duration was 86 d (range 42–201). The

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overall survival of the patients supported for >30 d with ECMO, who the authors refer to as ECMO long-haulers, was 70% and was significantly better than the 20% overall survival in patients supported with ECMO for <30 d, despite higher rates of complications, such as renal failure, pleural space complications, infections, and frailty, in the “long haulers.” The authors concluded that despite worse pulmonary physiology, frequent complications, and a tortuous hospital course, patients supported with ECMO for >30 d for COVID-19-associated ARDS have the potential to recover and be weaned off ECMO without the need for a lung transplant. They advocate that a customized approach with a more conservative timeline for the consideration of lung transplant may be prudent when caring for these patients.

ECMO is a resource-intensive form of lung support that requires significant institutional commitment and a well-trained team to ensure good outcomes. As we have seen increasing duration of ECMO support as this COVID-19 pandemic progresses, it has become evident that an important burden is imposed on the treating teams and institutions when caring for these patients. One of the most vexing questions is the timing to initiate a lung transplant evaluation. Although cases of some patients recovering some pulmonary functional after months on ECMO have been reported, these cases are anecdotal.¹⁰ Until recently, the limited experience in lung transplant for COVID-19-associated ARDS suggested that consideration for transplant in the absence of radiological and functional recovery after 6–8 wks of ECMO support is reasonable. One of our concerns in delaying this evaluation is that the risks associated with prolonged ECMO support, including infections, bleeding, and vascular complications, could preclude patients from becoming lung transplant candidates.

It is unclear in this study if patients treated with prolonged ECMO support were not considered for lung transplantation more frequently because of the complications that developed, and if extended support was the result of an absence of other options in patients with single-organ failure. Aside from this, the functional recovery observed in 6 of 10 patients after an average of 85 d of ECMO was remarkable. Although recovery may not have been complete, it was sufficient to allow successful ECMO weaning. The long-term outcomes in this patient population are unknown, but conceptually knowing that weaning and transplantation are possible after prolonged support could allow a semiselective transplant evaluation, as needed.

Further work is needed in the lung transplantation specialty to redefine “irreversible” lung failure and create decision-making pathways for ECMO as a bridge to transplant for patients who are not yet listed for lung transplantation. We feel that patients with COVID-19 ARDS supported on ECMO should have access to and be evaluated by a multidisciplinary team with expertise in ECMO and pulmonary management to identify risk factors for irreversible lung injury and define the appropriate timing for referral to a specialized lung transplant center. Research on biomarkers and lung recovery in ECMO patients is needed to predict which patients will benefit the most from ECMO as a bridge to transplant when recovery is not an option.

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