

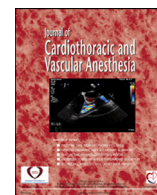


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Editorial

Long-Term Outcomes Are Important: Extracorporeal Membrane Oxygenation for COVID-19

The authors read with great interest the work by Biancari et al. in *The Journal of Cardiothoracic and Vascular Anesthesia* titled “Six-month Survival after Extracorporeal Membrane Oxygenation for Severe COVID-19.”¹ Published are the results of their international multicenter retrospective review of 132 patients with severe coronavirus disease 2019 (COVID-19)–related acute respiratory distress syndrome (ARDS). Their cohort included patients supported with both venovenous (VV) and venoarterial (VA) extracorporeal membrane oxygenation (ECMO). The primary indication for ECMO cannulation was COVID-19–related ARDS, with most patients (83%) supported with VV ECMO. The study’s primary endpoint was mortality at six months, with a reported six-month mortality of 53% (70 of 132). From the 132-patient cohort, ten patients were supported with VA ECMO, making it challenging to draw conclusions from this subgroup. The importance of this work goes beyond the presentation of six-month outcomes; the authors also were able to identify pre-ECMO cannulation determinants of six-month outcomes. Age and arterial pH before cannulation for ECMO were associated with an increased risk of mortality at six months. Patients ≥ 60 years of age and patients with a pH < 7.23 were found to have a higher six-month mortality. This work offered much needed insight into the long-term outcomes (six months) of patients requiring ECMO for COVID-19–related ARDS.

When a patient or family member asks us “How will my life be different in six months, how close to baseline will I be?” regarding ECMO, it is frustratingly difficult to answer this question. ECMO has been used for more than 30 years; yet, unfortunately, very little is known about long-term outcomes such as physical capability, daily life, life expectancy, neurologic outcomes, psychiatric outcomes, and overall quality of life. When initiating mechanical ventilation, beginning renal replacement therapy, deploying ECMO, or using other major life support interventions, what the patient will be capable of in the long term after surviving their critical illness always should be considered.

Large cohorts of formerly hospitalized non-ECMO patients with COVID-19 who subsequently were discharged alive are

being studied for long-term effects; these patients are also known as “long haulers”. In one large review by Huang et al. of 1,733 patients queried for symptoms six months after hospital discharge, 63% continued to have fatigue or muscle weakness, 26% had difficulty with sleep, and 23% percent reported psychiatric symptoms of anxiety or depression.² In the same study, Huang et al. found that many patients remained physically compromised, with more than 20% displaying below-normal performance on a six-minute walk test.²

In contrast, most literature on ECMO outcomes, particularly in relation to COVID-19, focuses on survival to discharge, or a short period thereafter (30 days). A recent study by Barbaro et al. examined the ECMO outcomes in COVID-19 from the Extracorporeal Life Support Organization international database; a mortality of 39% (survival of 61%) was noted in patients with complete data for their hospitalization.³ In the same study, Barbaro et al. noted a tracheostomy rate of 444 of 1,003 patients or 44.3%.³ Another database review by Shaefi et al. of 190 patients supported with ECMO for COVID-19 found that 66.8% of patients survived to hospital discharge or were still alive at 60 days.⁴ Both the works by Barbaro et al. and Shaefi et al. are important and served as the foundation of understanding the immediate short-term outcomes of patients with COVID-19 who require ECMO. However, data on life after hospitalization, at six months, at one year, or beyond, are extremely scant, because they are not recorded in most databases. Data on the long-term effects of severe COVID-19 requiring ECMO are difficult to obtain given that the disease first was recognized in late 2019.

Beyond survival, quality of life data rarely are available on a large scale and are limited to smaller reviews of data. To obtain a deeper and more meaningful understanding of life after ECMO, longer-term follow-up is required to paint a realistic picture to patients and their family members. Long-term survival, especially with good functional status, for any major intervention during hospitalization should be one of the most important metrics to define a success rate. Retaining near-baseline functional status is most reflective of a meaningful and successful intervention. Long-term survival after VV ECMO in cohorts requiring support for indications other than COVID-19 has been described, but

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further work certainly is needed.^{5,6} To that end, in a retrospective review of 255 patients, von Bahr et al. found a survival to discharge of 64%, 90-day survival of 55%, and a one-year survival of 52%.⁶ In a similar review of ECMO long-term outcomes in 84 patients (33 of whom received VV ECMO for respiratory failure), 66.7% of ECMO patients were alive at one year.⁵ It appeared that the survival reported by Biancari et al. was in-line with that of von Bahr in the pre-COVID-19 era.

With thousands of patients already having undergone ECMO support for COVID-19 pneumonia, the contribution by Biancari et al. was the first of what the authors hope to be a series of works that shed light on the important subject of life after ECMO for COVID-19. Many questions remain regarding long-term recovery from ECMO for the most critically ill patients who survive. COVID-19 is a multisystem disease and as such has multiple sequelae. For example, preliminary work on COVID-19 patients in the early period after recovery from hospitalization found that pulmonary function tests frequently displayed a pattern of a restrictive defect.^{7,8} Given that the lung function of patients on ECMO for refractory hypoxemia due to COVID-19 pneumonia is among the most compromised, these patients should be followed to better characterize the frequency and extent of lingering lung pathology. Additionally, understanding the time scale of tracheostomy decannulation is important as a means of informing patients and family members about what to expect.

Extrapulmonary effects of COVID-19 require better long-term understanding, as well. The risk of thromboembolic phenomenon in patients with COVID-19 may be higher than other critically ill patients, and as such, understanding the duration of this hypercoagulable state is an important and unanswered question.⁹ It especially is relevant to understand the long-term sequelae of this thrombotic state in decannulated ECMO patients because of the high risk of cannula-associated deep vein thrombosis in all ECMO patients, let alone those with COVID-19. Renal dysfunction is common in ECMO patients; understanding the frequency, recovery, and the effects on outcome will be important for prognostication in patients with COVID-19 supported by ECMO. Finally, posttraumatic stress disorder and chronic pain are common among patients recovering from critical illness; the added difficulty of limited visitation takes an enormous toll on patients and their families' mental wellbeing.¹⁰ Understanding the long-term psychiatric effects of critical illness in the COVID-19 ECMO population will be extremely important to inform practices for prevention and treatment.

Another aspect of the COVID-19 ECMO patient population that has not been explored thoroughly is the duration of VV ECMO support and its effects on long-term mortality. Biancari et al. reported a mean duration of ECMO support of 14.6 days; the duration of support did not differ between the six-month survivors and nonsurvivors. This reported duration of 14.6 days was similar to the pre-COVID ARDS ECMO duration of 15 days.¹¹ These new data potentially can help answer the question of what is a reasonable amount of time to keep COVID-19 patients on ECMO support.

The COVID-19 pandemic continues to exert significant stress on healthcare systems worldwide. Although patients

undergoing ECMO represent a very small percentage of those infected with COVID-19, they represent an important population at the extremes of illness due to this novel disease. Although it was a relatively small study, Biancari et al. nonetheless have taken an important step toward describing the long-term outcomes of patients requiring ECMO for COVID-19. It is very likely that the work by Huang et al. represented a less-severe glimpse of what will be found in patients with COVID-19 supported with ECMO; the authors expect more patients with physical compromise, psychiatric abnormalities, and other multisystem dysfunction.² As the COVID-19 pandemic continues to evolve, the authors hope to see more research detailing the chronic effects of COVID-19 in the unique subgroup of patients requiring ECMO support.

Conflicts of interest

A.A.D. consults for Edwards Lifesciences.

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