Comparing Apples to Oranges?

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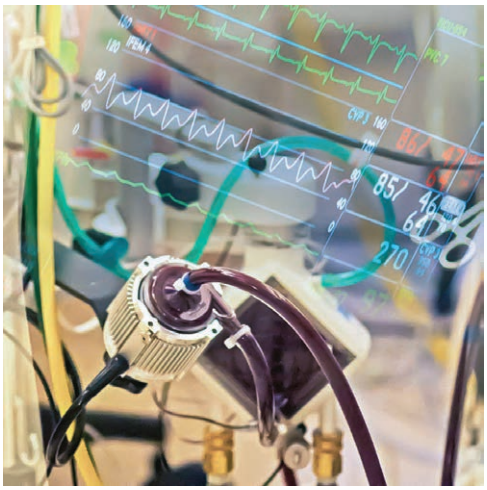
Extracorporeal membrane oxygenation is a lifesaving intervention used for patients with severe forms of the acute respiratory distress syndrome (ARDS), often when clinicians believe that other less invasive therapies have failed to improve severe hypoxemia.[1,2] While the use of extracorporeal membrane oxygenation has rapidly increased around the world in recent years,[3,4] the focus has been on survival as the primary outcome of interest. Despite the enthusiasm in the critical care community for studying long-term outcomes after critical illness, there are few long-term follow-up data, including functional outcomes, in patients who received extracorporeal membrane oxygenation for ARDS.[5]



"[Beyond survival]…there are few long-term follow-up data, including functional outcomes, in patients who received extracorporeal membrane oxygenation for [acute respiratory distress syndrome]."

In this issue, Grasselli *et al.* report the long-term outcomes of survivors of extracorporeal membrane oxygenation at 1 yr after discharge from a single center.[6] Over a 3-yr period they measured patient outcomes, including lung function, 6-min walk distance, and health-related quality of life. They compared the outcomes of 34 patients who received extracorporeal membrane oxygenation for ARDS with 50 non–extracorporeal membrane oxygenation–treated patients with ARDS. At baseline, there were notable differences between the groups. Extracorporeal membrane oxygenation patients were more severely hypoxemic, with worse respiratory system compliance, although with fewer major comorbidities. This may be like comparing apples to oranges, as extracorporeal membrane oxygenation is likely to be considered for use in patients with severe forms of ARDS refractory to other therapies. In addition, major comorbidities are usually exclusion criteria for consideration of extracorporeal membrane oxygenation. Despite the baseline differences between the groups, survival, lung function, chest computed tomography, and 6-min walk distance were reasonably comparable between the groups at 1 yr. Of note, the authors report that lung function was nearly normal at 1 yr, while reporting numerous abnormalities, particularly in the chest computer tomography in both groups. Nonetheless, patients in both groups appeared to have had a reasonable recovery at one year from a pulmonary perspective.

Patients who received extracorporeal membrane oxygenation had better health-related quality of life and lower risk of post-traumatic stress at 1 yr, despite having worse ARDS. This is different from previous reports of health-related quality of life after extracorporeal membrane oxygenation, and clinicians should be cautious interpreting these results.[7] There are several limitations to comparing extracorporeal membrane oxygenation and non–extracorporeal membrane oxygenation ARDS patients who were not matched at baseline and who were not randomly allocated. First, major comorbidities have an effect on the trajectory of recovery.[8] As the non–extracorporeal membrane oxygenation group had significantly more comorbidities at baseline compared with the extracorporeal membrane oxygenation group, it is unsurprising that their quality of life was also lower at 1 yr. Second, there was no baseline measure of health-related quality of life in either group, so it is unclear if the differences at 1 yr reflect baseline differences. This is an ongoing limitation in evaluating outcomes of critically ill patients admitted in an emergency. In such cases, the options to

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Corresponding article on page 572.

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assess pre-intensive care unit function and health-related quality of life are to ask the patient, family, or other surrogates at the time of admission to the hospital, or to ask the patient at the time of follow-up. Unfortunately, both methods have inherent risk of bias.

We note with interest the lower risk of posttraumatic stress in the extracorporeal membrane oxygenation survivors, measured with the Impact of Event Score-Revised, despite the higher severity of their acute illness. Extracorporeal membrane oxygenation patients have previously been reported as high risk for posttraumatic stress due to the combination of younger age, heterogeneous conditions, profound illness severity, and prolonged intensive care unit stay.[9] This is a key area for future research.

It is important to mention that in this study, there was 35% loss to follow-up in those who survived to discharge, with three patients in the extracorporeal membrane oxygenation group not surviving the year post hospitalization, and with the investigators unable to contact other patients or patients choosing not to participate in the study. The main reported reason for declining to participate in the follow-up at 1 yr was the distance to travel to the hospital. These patients may have been too unwell to travel, or perhaps were back at work and too busy to travel. Either way, a large loss to follow-up is an important limitation of many studies evaluating long-term outcomes, and it is unclear how these patients may have influenced the results.[10] Sensitivity analyses may reassure the reader that the missing data has not determined the main findings.

We congratulate the authors on an important contribution to the growing, yet still quite limited, literature on long-term outcomes in patients who have received extracorporeal membrane oxygenation for ARDS or other indications. However, this study also speaks to the urgent need for larger, multicenter, rigorously conducted studies, in order to tease out the role extracorporeal membrane oxygenation may be playing in long-term functional, neurocognitive, and psychiatric outcomes.

Competing Interests

Dr. Brodie is currently on the Trial Steering Committee for the VENT-AVOID (Extracorporeal CO2 Removal With the Hemolung RAS for Mechanical Ventilation Avoidance During Acute Exacerbation of COPD) trial sponsored by ALung Technologies (Pittsburgh, Pennsylvania). He was previously on the medical advisory board of ALung Technologies. All compensation for these activities was paid to Columbia University, New York, New York. He is currently on the medical advisory boards for Baxter (Deerfield, Illinois) and BREETHE (Halethorpe, Maryland).

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