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Posthospitalization outcomes after extracorporeal membrane oxygenation (ECMO) for COVID-19

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ABSTRACT

Background: Critical illness from COVID-19 is associated with prolonged hospitalization and high mortality rates. Extracorporeal membrane oxygenation is used for refractory severe acute respiratory distress syndrome in COVID-19 with outcomes comparable to other indications for extracorporeal membrane oxygenation. However, long-term functional outcomes have yet to be fully elucidated.

Methods: We performed a retrospective chart review of 24 consecutive patients who required extracorporeal membrane oxygenation due to COVID-19 associated severe acute respiratory distress syndrome and survived to hospital discharge. After hospitalization, we contacted patients and administered the Patient-Reported Outcomes Measurement Information System (PROMIS) Global-10 tool to assess longer-term outcomes. We abstracted demographics, clinical course, outcomes, and disposition variables from the electronic medical record. Descriptive statistical analysis was used on the retrospective data collection.

Results: Inpatient data were analyzed for 24 patients, and 21 of 24 (88%) patients completed the Patient-Reported Outcomes Measurement Information System tool at an average of 8.8 months post-hospitalization. At hospital discharge, 62.5% of patients had ongoing oxygen requirements (nasal cannula, trach collar, or mechanical ventilation); 70.8% were discharged to a location other than home. However, at the time of follow-up, only 9.5% of patients required supplemental oxygen, all tracheostomies had been removed, and all patients resided at home. Patients reported relatively high levels of global physical function, and though there was a high reported incidence of fatigue, overall pain scores were low.

Conclusion: Long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome from coronavirus disease 2019 are promising. Extracorporeal membrane oxygenation therapy may confer morbidity benefits in patients with coronavirus disease and remains a valuable modality with excellent functional outcomes and preserved quality of life for survivors.

Introduction

Since 2019, there have been over 200 million infections and over 5 million deaths worldwide due to COVID-19.[1] Despite initial improvements in daily infection and hospitalization rates from an efficient deployment of highly effective vaccines in late 2020, the emergence and spread of the delta variant resulted in increased infections and record hospitalizations across the United States among the unvaccinated population.[2] Although the incidence of COVID-19 infection requiring intensive care unit (ICU) admission is relatively low, for some patients there remains associated high healthcare resource utilization, prolonged hospitalizations, and high mortality rates.[3] One meta-analysis found a pooled in-hospital mortality rate of approximately 40% in patients with COVID-19 with acute respiratory distress syndrome (ARDS), although reported rates varied substantially by country and ranged between 13% to 73%.

Extracorporeal membrane oxygenation (ECMO) is an effective supportive therapy for patients with COVID-19 who develop severe ARDS that is refractory to conventional mechanical ventilation, prone positioning, and paralytics.[4,5] Currently, the Extracorporeal Life Support Organization (ELSO) reports an in-hospital mortality rate of 48% in over 7,000 patients with COVID-19 who received

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ECMO.[6] A recent systematic review of 69 studies reported an average case fatality rate of 45% amongst patients with COVID-19 who required invasive mechanical ventilation and did not receive ECMO.[7] The comparable mortality rates between these 2 groups suggest a potential mortality benefit with ECMO in COVID-19.

In the ELSO COVID-19 cohort, among the survivors, there was a high incidence of discharge to either an inpatient rehabilitation facility, long-term acute care hospital, or another inpatient hospital. This finding is attributable to critical illness deconditioning and the need for prolonged ventilatory wean after severe ARDS.[4] Prior quality of life studies in patients after hospitalization with non–COVID-associated ARDS requiring ECMO show a lack of severe disability at 6 months compared to similar patients managed with conventional ventilation alone. Currently, there is a lack of information regarding the long-term outcomes after ECMO for severe COVID-19–associated ARDS.[4,8,9] We hypothesized that there would be significant mental and physical deficits noted by patients or their caregivers in the posthospitalization period in patients after COVID-19–associated ARDS requiring ECMO. We, therefore, analyzed survivors of severe ARDS from COVID-19 that required venovenous (VV) ECMO at our institution and performed a survey after hospitalization to evaluate quality of life and functional status.

Methods

The University of North Carolina at Chapel Hill medical center is a 900-bed academic tertiary care hospital. It is also a high-volume ECMO center, averaging around 60 cannulations per year before COVID-19. Since early 2020, the ECMO volume has increased substantially, and over the past 19 months, 152 patients with severe ARDS from COVID-19 have received ECMO. We followed the standard, pre-COVID-19 ELSO guidelines for appropriate patient selection,[10] though since this was a novel virus and much was unknown regarding best practices for this specific patient population, we were more aggressive at cannulating patients if they were young or had a short duration of intubation before progression to severe/refractory ARDS. More specifically, patients were considered candidates for ECMO with the following criteria after ventilator optimization: severe ARDS with severe hypoxia (Pa_{O_2}:F_{IO_2} < 100 for several hours; Pa_{O_2}:F_{IO_2} < 150 with concern for progressive/quick clinical decline); hypercarbia causing severe respiratory acidosis (pH < 7.0) despite ventilator optimization; severe ARDS and/or severe hypercarbia and progressive clinical decline despite the use of adjunctive therapies, such as prone positioning, paralysis, advanced ventilator settings, and inhaled vasodilators; requiring high/damaging plateau pressures (>35) on the ventilator to maintain adequate oxygenation; and ventilation with or without the presence of barotrauma. We considered older age (>70 years), progressive acute multi-system organ failure, extensive medical comorbidities, prolonged duration of mechanical ventilation (>7–10 days), irreversible neurologic injury, and profound immunosuppression (ie, acquired immunodeficiency virus, active cancer) as contraindications. Currently, the overall survival to hospital discharge after ECMO for COVID at our institution is 40%. For reference, the survival of all patients with COVID-19 admitted to the ICU at our institution is 60%, though this includes a substantial number of non-intubated and non-ARDS patients.

We performed a retrospective chart review to identify all patients who underwent VV ECMO for COVID-19 from April 1, 2020, to April 10, 2021. We included all patients that were successfully decannulated from ECMO and were discharged or transferred from our hospital in the analysis ($n = 24$). During the study period, 54 patients ultimately died while on ECMO or after decannulation but before hospital discharge. Follow-up with post-ECMO survivors ranged from 2 months to a year post-decannulation, with a mean time of 8.8 months since hospital discharge. We excluded all patients that died while on ECMO or expired before hospital discharge. We abstracted demographics, clinical course, outcomes, and disposition variables from the electronic medical record for each patient.

To assess functional status and quality of life, we utilized the Patient-Reported Outcomes Measurement Information System (PROMIS) Global-10 tool. This tool is a validated global health assessment created to measure symptoms, functional status, and quality of life. This short survey asks 10 questions related to physical/mental/social health, pain, fatigue, and overall quality of life. The benefit of this survey is that each question has individual utility in assessing various aspects of functional status in addition to a calculated total score (T-score) assessing global physical and mental health. A lower T-score correlates with worse physical or mental

Table I
Patient clinical data

	Total N = 24
Demographics	
Age, y	41.0 (35.5–51.5)
Sex, n (%)	
Male	15 (63)
Female	9 (38)
Race, n (%)	
Black or African American	7 (29)
Hispanic or Latino	12 (50)
White or Caucasian	5 (21)
BMI	35.6 (31.7–44.9)
Charlson comorbidity index (CCI)	1.0 (0.0–1.0)
History of asthma, n (%)	3 (13)
History of diabetes, n (%)	9 (38)
History of hyperlipidemia, n (%)	4 (17)
History of hypertension, n (%)	5 (21)
History of sleep apnea, n (%)	2 (8)
Prior To ECMO cannulation	
Paralyzed, n (%)	18 (75)
Proned, n (%)	16 (67)
Cardiac arrest, n (%)	1 (4)
Renal failure, n (%)	3 (13)
P/F ratio	64.0 (50.0–93.0)
Murray score	3.8 (3.8–4.0)
Adjuvant therapies, n (%)	
Convalescent plasma	11 (46)
Remdesivir	20 (83)
Dexamethasone	19 (79)
Monoclonal antibody	6 (25)
Antiviral	2 (8)
Time from intubation to cannulation, d	1.5 (0.6–5.5)
Total cannulation time, d	9.1 (5.6)
Total ventilated days	23.0 (16.0–51.0)
Tracheostomy, n (%)	13 (57)
ICU length of stay, d	35.0 (20.6)
Hospital length of stay, d	49.1 (34.1)
Complications, n (%)	
New need for dialysis	4 (17)
Stroke during admission	2 (8)
Major bleeding during admission	2 (8)
DVT At discharge	10 (42)
On anticoagulation For DVT	8 (33)
Oxygen at discharge, n (%)	
None	9 (38)
Nasal cannula	9 (38)
Trach collar	3 (13)
Ventilator	3 (13)
Discharge disposition, n (%)	
Home	7 (29)
Long-term acute care hospital	3 (13)
Rehab	11 (46)
Transfer	3 (13)

BMI, body mass index; *CCI,* Charlson comorbidity index; *DVT,* deep vein thrombosis; *ECMO,* extracorporeal membrane oxygenation; *ICU,* intensive care unit.

Table II
Results from PROMIS survey

	Poor	Fair	Good	Very Good	Excellent
In general, would you say your health is:	4.8%	4.8%	71.4%	19.1%	0.0%
In general, would you say your quality of life is:	4.8%	19.1%	38.1%	9.5%	28.6%
In general, how would you rate your physical health?	9.5%	19.1%	57.1%	14.3%	0.0%
In general, how would you rate your mental health, including your mood and your ability to think?	9.5%	14.3%	23.8%	14.3%	38.1%
In general, how would you rate your satisfaction with your social activities and relationships?	9.5%	19.1%	28.6%	28.6%	14.3%
In general, please rate how well you carry out your usual social activities and roles.	9.5%	19.1%	33.3%	23.8%	14.3%

	Not at all	A little	Moderately	Mostly	Completely
To what extent are you able to carry out your everyday physical activities such as walking, climbing stairs, carrying groceries, or moving a chair?	14.3%	9.5%	33.3%	19.1%	23.8%

	Never	Rarely	Sometimes	Often	Always
In the past 7 days, how often have you been bothered by emotional problems such as feeling anxious, depressed or irritable?	52.4%	9.5%	9.5%	28.5%	0.0%

	None	Mild	Moderate	Severe	Very Severe
In the past 7 days, how would you rate your fatigue on average?	9.5%	28.6%	38.1%	19.1%	4.8%

	0 = No Pain	1	2	3	4	5	6	7	8	9	10 = Worst Pain
How would you rate your pain on average	33.3%	9.5%	0.0%	9.5%	4.8%	9.5%	14.3%	4.8%	4.8%	9.5%	0.0%

PROMIS, Patient-Reported Outcomes Measurement Information System.

health. The average T-score for the United States population is 50 points, with a range of 16.2 to 67.6.[11] We administered the survey over the phone with each survivor from June 2021 to July 2021. The major benefit of this questionnaire is that it is facile, decreasing the respondent burden and increasing the response rate. The study personnel administered the survey to all eligible participants. Additionally, we queried each participant about current supplemental oxygen usage, the presence of a tracheostomy, and the use of tube feeds for nutrition.

Descriptive statistical analysis was used on the retrospective data collection. We report means with standard deviations for parametric variables and medians with interquartile ranges for non-parametric variables. We used Stata 17.1 (StataCorp: College Station, TX) for all statistical analyses. The University of North Carolina Institutional Review Board approved this study.

Results

A total of 24 patients met the inclusion criteria for this study (Table I). The median age was 41 (interquartile range [IQR]: 35.5–51.5), and 63% were male patients. The median body mass index was 35.6 (IQR: 31.7–44.9). At least 1 pre-existing significant medical comorbidity (diabetes, hypertension, asthma, reflux, hyperlipidemia, or obstructive sleep apnea) was present in 58.3% of patients. All patients were on maximal ventilator settings at the time the ECMO team was consulted; 75% of these patients received paralytics, and 67% had been proned before ECMO cannulation. The median time from intubation to ECMO cannulation was 1.5 days (IQR: 0.6–5.5), with a median P/F ratio at the time of cannulation of 64.0 (IQR: 50.0–98.0). Total time on ECMO was 9.1 days (standard deviation: 5.6). All patients were cannulated with 2 cannulas, either in the internal jugular/femoral veins or bi-femoral veins configuration. All patients were deeply sedated during their course of ECMO, with a goal Richmond Agitation and Sedation Scale of −4 to −5, and no patients ambulated while on ECMO. Fifty-seven percent of patients received a tracheostomy. The median length of stay at our institution was 42 days (IQR: 26–63). Significant bleeding events ($n = 2$; 8.3%) and stroke ($n = 2$; 8.3%) while on ECMO were rare. Most patients were discharged to an inpatient rehabilitation facility ($n = 11$; 45.8%) or were transferred to another hospital ($n = 6$; 25.0%). Additionally, at the time of discharge, most were on low-flow nasal cannula for oxygen supplementation or room air ($n = 18$; 75%); 6 patients (26%) required ongoing full ventilatory support or were undergoing ventilatory wean. All patients received inpatient physical and occupational therapy after resolution of acute/severe critical illness.

Survey responses were collected for 21 out of 24 (88%) of all ECMO survivors (Table II). For native Spanish speakers, the survey was translated into Spanish and then administered. Physical health was described as good or very good in 71.7% of participants. The ability to carry out daily physical activities (walking, climbing stairs, carrying groceries, or moving a chair) was mostly or entirely carried out by the patient in 42.9% of participants. Although 62% of patients reported ongoing moderate to severe fatigue, overall pain was low in most participants on a scale of 0 to 10 with a median of 3 (IQR: 0–6). The average physical health T-score for the group was 42.5 (standard error: 4.2), and the average mental health T-score was 50.8 (standard error: 3.7). At the time of survey follow-up, only 2 patients (9.5%) remained on supplemental oxygen. All patients with a tracheostomy had been decannulated, and no patients had tube feed requirements.

Discussion

In this single-institution patient-related outcomes study in a cohort of ECMO survivors of COVID-19–associated ARDS, we show that overall average physical health T-scores were only slightly lower than the national average (42.5 compared to 50, respectively), but mental health scores were essentially the same (50.8 compared to 50, respectively). Although most patients did report ongoing fatigue, they reported a relatively high level of physical function and minimal pain. Furthermore, there was a very low incidence of ongoing supplemental oxygen requirement. All patients who had been discharged with a tracheostomy had been

successfully decannulated, and all patients were residing at home at the time of follow-up.

There is a paucity of studies on quality of life and functional outcomes after ECMO in general. In the early 2000s, the CESAR trial evaluated patients 6 months after hospitalization for severe ARDS and compared patients randomized to receive ECMO versus conventional ventilatory management only. Quality of life assessments revealed a reduced long-term risk of death and severe disability in patients treated with ECMO compared to those in the conventional management group. However, a higher percentage of patients in the ECMO group reported ongoing problems with mobility, self-care, pain, and anxiety. Despite these differences, overall quantitative health scores were similar between the 2 groups of survivors.[9] Based on the results of this study, it seems that patient-reported outcomes after severe ARDS requiring ECMO are at least comparable to similarly critically ill patients managed without ECMO.

Posthospitalization evaluation of survivors of severe ARDS from COVID-19 requiring ECMO is even more limited. Our findings suggest that many survivors of COVID-19 have prolonged illness after ECMO decannulation or significant morbidities from their hospitalization requiring ongoing medical intervention and rehabilitation. A recent article by Horwitz et al evaluated 6-month outcomes in 126 patients hospitalized with severe COVID-19, including 9 patients who received ECMO. They found that 74% of patients reported that their health had not returned to baseline 6 months after hospitalization. There was also a high incidence of fatigue (85%) and shortness of breath (63%), although only 9% of patients without pre-COVID oxygen requirements were still requiring oxygen therapy. The specific details of the ECMO patient's responses and how those compared to other patients with similar levels of critical illness were not delineated.[12] There is a clear association between COVID-19–associated critical illness and prolonged debilitating symptoms regardless of the need for ECMO.

Global physical and mental health T-scores averages on the PROMIS Global tool for the patients in our study were 42.5 and 50.8, respectively. In a recently published cohort of patients hospitalized with COVID-19 requiring at least 6 liters of oxygen supplementation, 6-month post-discharge global physical and mental health T-scores on the PROMIS Global tool were 45.3 and 47.0, respectively.[12] Importantly, only a small minority of patients (7%) in this cohort required ECMO. The T-scores between our study and this more heterogeneous cohort are similar, even though all patients in our study had severe ARDS that was refractory to conventional ventilatory management. This is suggestive of a potential morbidity benefit to ECMO in the COVID-19 population, though extensive further study is needed.

Similar to data reported by ELSO, we noted a high incidence of hospital discharge to another facility, though 29.2% of our patients were discharged directly home with outpatient services. The remaining 70.8% of patients were discharged to a long-term acute care hospital (12.5%), inpatient rehab (45.8%), or were transferred to another acute care hospital (12.5%); at the time of the survey completion, all patients were residing at home, with 19% still requiring outpatient physical and occupational therapy. Other recent studies focusing on survivors of COVID-19–associated critical illness in patients who did not require ECMO found ongoing debilitating symptoms that affected the patient quality of life and were associated with increased utilization of outpatient resources.[13,14] At this time, it is unclear whether the residual symptoms experienced by many survivors of COVID-19 are related to the virus itself or instead are repercussions of severe critical illness.[12]

The limitations of this study include the relatively small number of participants and the lack of standardization in time from hospitalization to survey follow-up. Overall, however, this study is the first to our knowledge to precisely evaluate the functional and quality of life outcomes in patients with severe ARDS from COVID-19 who required ECMO.

In conclusion, our findings suggest that critically ill patients with severe ARDS from COVID-19 who require ECMO have outcomes comparable to those reported from a less severely ill cohort of hospitalized COVID-19 patients. Although residual symptoms and continued need of outpatient therapy were noted months after hospitalization in many patients, most reported high levels of function and few mental health issues. Long-term outcomes after hospitalization with severe ARDS from COVID-19 requiring ECMO are promising, and ECMO may confer morbidity benefits compared to conventional ventilator support. ECMO therapy in COVID patients remains a valuable modality with excellent functional outcomes and preserved quality of life for survivors.

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Conflict of interest/Disclosure

The authors collectively have no conflicts of interest to disclose.

References

1. World Health Organization. WHO coronavirus (COVID-19) dashboard; 2021. https://covid19.who.int/. Accessed December 1, 2021.
2. Kupferschmidt K, Wadman M. Delta variant triggers new phase in the pandemic. *Science*. 2021;372:1375–1376.
3. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA*. 2020;323:1574–1581.
4. Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. *Lancet*. 2020;396:1071–1078.
5. Bartlett RH, Ogino MT, Brodie D, et al. Initial ELSO guidance document: ECMO for COVID-19 patients with severe cardiopulmonary failure. *ASAIO J*. 2020;66:472–474.
6. Extracorporeal Life Support Organization. ECLS ELSO-Ea. Full COVID-19 registry dashboard; 2021. https://www.elso.org/Registry/FullCOVID-19RegistryDashboard.aspx. Accessed December 1, 2021.
7. Lim ZJ, Subramaniam A, Ponnapa Reddy M, et al. Case fatality rates for patients with COVID-19 requiring invasive mechanical ventilation. A meta-analysis. *Am J Respir Crit Care Med*. 2021;203:54–66.
8. Knudson KA, Gustafson CM, Sadler LS, et al. Long-term health-related quality of life of adult patients treated with extracorporeal membrane oxygenation (ECMO): an integrative review. *Heart Lung*. 2019;48:538–552.
9. Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet*. 2009;374:1351–1363.
10. Extracorporeal Life Support Organization. ELSO guidelines for cardiopulmonary extracorporeal life support (Version 1.4); 2017. https://www.elso.org/Portals/0/ELSO%20Guidelines%20For%20Adult%20Respiratory%20Failure%201_4.pdf. Accessed December 1, 2021.
11. Rothrock NE, Amtmann D, Cook KF. Development and validation of an interpretive guide for PROMIS scores. *J Patient Rep Outcomes*. 2020;4:16.
12. Horwitz LI, Garry K, Prete AM, et al. Six-month outcomes in patients hospitalized with severe COVID-19. *J Gen Intern Med*. 2021;36:3772–3777.
13. Halpin SJ, McIvor C, Whyatt G, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *J Med Virol*. 2021;93:1013–1022.
14. Cellai M, O'Keefe JB. Characterization of prolonged COVID-19 symptoms in an Outpatient Telemedicine Clinic. *Open Forum Infect Dis*. 2020;7:ofaa420.