

OPEN

One-Year Functional, Cognitive, and Psychological Outcomes Following the Use of Extracorporeal Membrane Oxygenation in Coronavirus Disease 2019: A Prospective Study

OBJECTIVES: To prospectively describe 1-year outcomes, with a focus on functional outcome, cognitive outcome, and the burden of anxiety, depression, and post-traumatic stress disorder, in coronavirus disease 2019 patients managed with extracorporeal membrane oxygenation.

DESIGN: Prospective case series.

SETTING: Tertiary extracorporeal membrane oxygenation center in the United States.

PATIENTS: Adult coronavirus disease 2019 acute respiratory distress syndrome patients managed with extracorporeal membrane oxygenation March 1, 2020, to July 31, 2020.

INTERVENTIONS: Baseline variables, treatment measures, and short-term outcomes were obtained from the medical record. Survivors were interviewed by telephone, a year following the index intensive care admission. Functional outcome was assessed using the modified Rankin Scale and the World Health Organization Disability Assessment Scale 2.0. Cognitive status was assessed with the 5-minute Montreal Cognitive Assessment. The Hospital Anxiety and Depression Scale was used to screen for anxiety and depression. Screening for post-traumatic stress disorder was performed with the Posttraumatic Stress Disorder Checklist 5 instrument.

MEASUREMENTS AND MAIN RESULTS: Twenty-three patients were managed with extracorporeal membrane oxygenation, 14 (61%) survived to hospital discharge. Thirteen (57%) were alive at 1 year. One patient was dependent on mechanical ventilation, another intermittently required supplemental oxygen at 1 year. The median modified Rankin Scale score was 2 (interquartile range, 1–2), median World Health Organization Disability Assessment Scale 2.0 impairment score was 21% (interquartile range, 6–42%). Six of 12 previously employed individuals (50%) had returned to work, and 10 of 12 (83%) were entirely independent in activities of daily living. The median Montreal Cognitive Assessment score was 14 (interquartile range, 13–14). Of 10 patients assessed with Hospital Anxiety and Depression Scale, 4 (40%) screened positive for depression and 6 (60%) for anxiety. Four of 10 (40%) screened positive for post-traumatic stress disorder.

CONCLUSIONS: Functional impairment was common a year following the use of extracorporeal membrane oxygenation in coronavirus disease 2019, although the majority achieved independence in daily living and about half returned to work. Long-term anxiety, depression, and post-traumatic stress disorder were common, but cognitive impairment was not.

KEY WORDS: acute respiratory distress syndrome; cognitive impairments; coronavirus disease 2019; extracorporeal membrane oxygenation; functional dependence; post-traumatic stress disorder

Venkatakrisna Rajajee, MBBS,
FNCS, FCCM^{1,2}

Christopher Mon-Chee Fung, MD³

Katharine Surella Seagly, PhD⁴

Pauline Kyonsook Park, MD,
FACS, FCCM⁵

Krishnan Raghavendran, MBBS⁵

David Antonio Machado-Aranda,
MD⁵

Jonathan William Scott, MD⁵

Matthew Joseph Delano, MD⁵

Ashraf Shaaban Abdel Aziz
Abou El Ela, MBBCH⁶

Jonathan William Haft, MD⁶

Craig Andrew Williamson, MD^{1,2}

Jakob Israel McSparron, MD⁷

Ross Blank, MD⁸

Lena Marie Napolitano, MD,
FACS, FCCP, FCCM⁵

Copyright © 2021 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of the Society of Critical Care Medicine. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/CCE.000000000000537

As of June 2021, it is estimated that over 177 million patients have developed coronavirus disease 2019 (COVID-19) worldwide and over 3.8 million patients have died (1). COVID-19 patients with acute respiratory distress syndrome (ARDS) and respiratory failure refractory to conventional measures may be supported with extracorporeal membrane oxygenation (ECMO). The Extracorporeal Life Support Organization (ELSO) has published guidelines for the use of ECMO in COVID-19 (2). A systematic review prior to the COVID-19 pandemic concluded that ECMO decreases mortality in ARDS (3); however, cost-efficacy is likely dependent on long-term outcomes in the specific population receiving the intervention (4). The role of ECMO in the COVID-19 pandemic has been a matter of debate. An early report from China suggested a very low survival rate (1/6, 17%) with the use of ECMO (5). Subsequent reports have demonstrated higher rates of short-term survival, at 39–67% (6–10). A multicenter study of 132 patients from Europe revealed 6-month survival of 47% (11). Persistent impairment in respiratory function (12), in addition to neurologic complications (13), may limit long-term functional recovery following COVID-19–related ARDS. Survivors of critical illness are at risk for the Post-Intensive Care Syndrome (PICS), with long-term cognitive, functional, and psychologic impairments (14–17). Long-term PICS data in the COVID-19 ECMO population is critical for appropriate patient selection, informed counseling of families, accurate analyses of cost-efficacy, and understanding the true burden of disease. No studies, to our knowledge, have yet reported 1-year ECMO outcomes in COVID-19 ARDS.

Our objective was to prospectively describe 1-year outcomes, with a focus on functional outcome, cognitive outcome, and the burden of anxiety, depression, and post-traumatic stress disorder (PTSD), in COVID-19 patients managed with ECMO at our institution.

METHODS

This is a prospective case series. Approval of the Institutional Review Board of the University of Michigan Medical School was obtained (HUM00187958). A partial HIPAA waiver was granted to access the electronic medical record to screen for eligibility and contact patients for potential participation. Eligible patients or legally authorized representatives (LARs) were contacted by telephone and verbal informed consent

obtained after subjects reviewed a consent form sent to them by e-mail. All adult (age > 18 yr) patients with COVID-19–induced ARDS managed with ECMO March 1, 2020, to July 31, 2020, at our institution were eligible. Patients met the Berlin definition of ARDS (18). The diagnosis of COVID-19 was based on appropriate symptoms (19) and a positive reverse transcriptase polymerase chain reaction test. Information related to the index admission was obtained through electronic data capture supplemented by manual review and abstraction. This included demographics, physiologic variables, laboratory values, therapeutic measures, neurologic complications, and short-term outcomes. Neurologic complications included delirium, acute ischemic stroke, intracranial hemorrhage, hypoxic/ischemic brain injury, seizures, and severe (less than antigravity power while briskly following commands) neuromuscular weakness of any cause. Short-term outcome measures included inhospital mortality, duration of mechanical ventilation, duration of ECMO, ICU length of stay (LOS), and discharge location.

Long-term outcomes were obtained through telephone interview of survivors between April 23, 2021, and May 31, 2021. The primary author (V.R.), who is certified in the administration of modified Rankin Scale (mRS) and Montreal Cognitive Assessment (MoCA), conducted the interviews. Information was obtained on the need for supplemental oxygen, other respiratory support, readmissions, and the use of inpatient rehabilitation services after the index admission. Functional outcome was determined using the 12-item version of the World Health Organization (WHO) Disability Assessment Scale 2.0 (WHODAS 2.0) applicable to a 1-month period prior to the interview (20) and the mRS using the mRS 9Q questionnaire (21, 22). The WHODAS 2.0 is the scale used by the WHO for reporting of long-term disability following COVID-19 (23). It measures disability across six domains—cognition, mobility, self-care, interpersonal relationships, work/household roles, and participation in society—which can be administered via telephone, has been validated concurrently against multiple other measures of functional impairment, and has been used in a variety of conditions such as PICS, psychiatric disease, trauma, surgery, neurologic illness, and chronic disease (16, 20, 24–28). A multidisciplinary group comprising representatives of the international ECMO network and the ELSO recently recommended the mRS

as the most appropriate long-term disability measurement tool in patients managed with ECMO (29). Cognitive outcome was determined with the 5-minute MoCA instrument, which has been validated for telephone use (30). Screening for anxiety and depression was performed using the Hospital Anxiety and Depression Scale (HADS), with a score of 11 or above in either the depression or anxiety components considered abnormal and 8, 9, or 10 considered borderline (31). The Society of Critical Care Medicine recently provided strong recommendations for the use of MoCA to screen for long-term cognitive impairment and the use of HADS to screen for long-term psychologic well-being after critical illness, regardless of etiology (15). Screening for PTSD was performed with the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition's Posttraumatic Stress Disorder Checklist (PCL-5) for the 1-month period prior to the interview (32). A PCL-5 score greater than 30 indicates potential benefit from treatment of PTSD. The PCL is the most well-established screening measure for detecting PTSD following any potential adverse event and has shown good reliability and concurrent validity with other measures of PTSD in post-ICU patients (33). Free-response statements from subjects regarding their ability to function and quality of life were recorded.

ECMO: Patient Selection and Management Protocol

COVID-19 patients with ARDS were considered for venovenous ECMO if they met the following criteria—persistent severe hypoxemia despite maximal mechanical ventilation and rescue approaches and no absolute contraindications present. Contraindications included irreversible pulmonary disease, severe multiple organ failure, severe comorbidities, contraindication to anticoagulation, and anoxic brain injury. In addition to low tidal volume high positive end-expiratory pressure (PEEP) ventilation, all patients with COVID-19-induced ARDS were managed with deep sedation, prone position, neuromuscular blockade, fluid restrictive therapy with liberal use of diuretics, and renal replacement therapy for acute kidney injury prior to consideration for venovenous ECMO. Venoarterial ECMO was performed for patients with cardiovascular collapse or cardiogenic shock with no absolute contraindications present. All patients received therapeutic anticoagulation while on ECMO. Survivors who chose to

follow-up at our institution were seen at a post-ICU clinic staffed by two of the authors—a pulmonary critical care specialist (J.I.M.) and a rehabilitation neuropsychologist (K.S.S.).

Statistical Analysis

Descriptive statistics were calculated using proportions for categorical variables and median with interquartile range (IQR) for continuous variables. Associations between variables and outcomes of interest were tested using the chi-square or Fisher exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. Correlation between continuous variables and WHODAS-2.0 scores was examined using Spearman rank correlation (ρ), with 95% CI. The threshold for statistical significance was a two-sided *p* value of less than 0.05. Subjects with missing data were excluded from the specific analysis performed. Analysis was not performed when greater than 20% of subjects had missing data. Statistical analyses were performed using MedCalc for Windows, Version 20.0 (MedCalc Software, Ostend, Belgium).

RESULTS

A flow diagram of the 236 mechanically ventilated patients admitted to our institution between March 1, 2020, and July 31, 2020, is in **Figure S1** (Supplement, <http://links.lww.com/CCX/A788>). Of these, 23 (9.7%) were managed with ECMO. Four (17%) of these 23 were admitted through the emergency department and 19 (83%) admitted directly to inpatient units. The median age was 47 years (IQR, 37–52 yr), 18 (35%) were female. The median $\text{PaO}_2/\text{FiO}_2$ (P/F) ratio on 96 mm Hg (IQR, 71–133 mm Hg) at admission and 69 mm Hg (IQR, 57–79 mm Hg) immediately prior to initiation of ECMO. Twenty (87%) underwent venovenous ECMO and 3 (13%) venoarterial ECMO. Median ICU LOS was 47 days (IQR, 24–54 d). Baseline variables are in **Table 1**, respiratory status and support provided are in **Table 2**. Therapeutic interventions and in-hospital outcomes of all patients are in **Table 3**. Eight patients died (35%) while on ECMO, including two of three patients (67%) on venoarterial ECMO and six of 20 (30%) on venovenous ECMO. For the two venoarterial ECMO patients, comfort care was initiated within 24 hours of cannulation for severe multiple organ failure. Of the six patients who died while on venovenous ECMO,

TABLE 1.
Distribution of Baseline and Inhospital Variables

Variable	All Patients, <i>n</i> = 23	Dead at Discharge, <i>n</i> = 9	Alive at Discharge, <i>n</i> = 14	<i>p</i>
Age, yr, median (IQR)	47 (37–52)	49 (40–56)	41 (30–52)	0.21
Sex female, <i>n</i> (%)	18 (35)	2 (22)	6 (43)	0.32
Race, <i>n</i> (%)				0.12
Black	14 (61)	4 (44)	10 (71)	
White	7 (30)	3 (33)	4 (29)	
Hispanic	2 (9)	2 (22)	0 (0)	
Ethnicity Hispanic, <i>n</i> (%)	2 (9)	2 (22)	0 (0)	1.00
Body mass index, kg/m ² , median (IQR)	33 (27–37)	29 (27–34)	34 (30–38)	0.23
Charlson comorbidity index, median (IQR)	2 (1 to 4)	3 (1–4)	2 (1–3)	0.68
Sequential Organ Failure Assessment score, median (IQR)	12 (10–14)	12 (11–14)	11 (10–14)	0.34
Physiologic variables at admission				
Heart rate, beats/min, median (IQR)				
Maximum	115 (102–132)	119 (93–134)	114 (109–124)	0.86
Minimum	75 (63–84)	63 (54–85)	80 (70–84)	0.13
Systolic blood pressure, mm Hg, median (IQR)				
Maximum	137 (120–166)	137 (133–154)	137 (114–171)	0.84
Minimum	101 (90–109)	90 (86–95)	107 (94–121)	0.02*
Respiratory rate, breaths/min, median (IQR)				
Maximum	33 (28–40)	29 (25–36)	35 (32–40)	0.09
Minimum	13 (10–19)	15 (10–19)	12 (10–19)	0.86
Temperature, °F, median (IQR)				
Maximum	99.8 (98.7–100.6)	99.8 (99–100.3)	99.8 (98.7–100.8)	0.95
Minimum	97.7 (97.2–98.2)	97.5 (96.9–98.0)	97.8 (97.3–98.4)	0.29
Laboratory variables at admission, median (IQR)				
Absolute lymphocyte count, ×10 ³ cells/mcL	0.9 (0.5–1.7)	0.6 (0.5–0.8)	1.2 (0.5–1.83)	0.13
C-reactive protein, mg/L	21 (14–29)	17 (6–27)	22 (16–31)	0.32
Creatinine, mg/dL	1.18 (0.77–2.78)	1.05 (0.77–2.05)	1.31 (0.80–2.91)	0.59
D-dimer, µg/mL	3.85 (1.29–6.45)	1.63 (1.02–4.68)	5.03 (2.28–6.75)	0.25
Ferritin, ng/mL	1,453 (1,132–2,895)	1,453 (1,310–2,603)	1,514 (595–3,583)	0.60
Lactate dehydrogenase, U/L	676 (512–871)	634 (538–903)	716 (500–854)	0.82
Lactate, mmol/L	1.9 (1.28–2.43)	1.4 (1.23–2.15)	1.95 (1.30–2.50)	0.65

n = sample size, IQR = interquartile range.

three had comfort care initiated at family request, two died related to complications during ECMO support, and one had no return of native lung function. One venovenous ECMO patient with return of native lung function and successful decannulation subsequently died due to necrotizing infected pancreatitis during

hospitalization. Fifteen patients (65%), including one of three (33%) on venoarterial ECMO and 14 of 20 (70%) on venovenous ECMO, were successfully decannulated and survived the inhospital stay. One patient died of recurrent bacterial pneumonia and septic shock shortly after hospital discharge.

TABLE 2.
Respiratory Status and Support

Variable	All Patients, <i>n</i> = 23	Dead at Discharge, <i>n</i> = 9	Alive at Discharge, <i>n</i> = 14	<i>p</i>
P/F ratio at admission in mm Hg, median (IQR)	96 (71–133)	98 (66–113)	94 (75–140)	0.80
pH at admission, median (IQR)	7.31 (7.27–7.40)	7.29 (7.23–7.47)	7.31 (7.28–7.37)	0.74
Respiratory support at admission, highest, <i>n</i> (%)				0.29
None	1 (4)	0 (0)	1 (7)	
Nasal cannula	1 (4)	0 (0)	1 (7)	
Heated high-flow nasal cannula	2 (9)	0 (0)	1 (7)	
Mechanical ventilation, invasive	18 (78)	9 (100)	11 (79)	
FiO ₂ at admission, median (IQR)				
Maximum, %	100 (100–100)	100 (100–100)	100 (100–100)	1.00
Minimum, %	73 (55–80)	68 (53–80)	78 (55–85)	0.51
Compliance static in mL/cm H ₂ O at admission, median (IQR)	27 (20–38)	28 (21–36)	25 (19–38)	0.59
P/F ratio immediately prior to ECMO initiation in mm Hg, median (IQR)	69 (57–79)	70 (56–83)	69 (61–76)	0.73
Positive end-expiratory pressure immediately prior to ECMO initiation, median (IQR)	18 (16–20)	16 (15–20)	20 (17–20)	0.30
Compliance static in mL/cm H ₂ O immediately prior to ECMO initiation, median (IQR)	22 (19–26)	20 (18–29)	22 (19–25)	0.91
Symptom onset to intubation, d, median (IQR)	7 (4–15)	15 (6–17)	5 (3–10)	0.05
Symptom onset to ECMO, d, median (IQR)	14 (10–22)	18 (12–24)	14 (9–21)	0.35
Intubation to ECMO, d, median (IQR)	7 (4–10)	6 (2–10)	7 (6–11)	0.41
ECMO duration, d, median (IQR)	16 (8–32)	13 (< 1–44)	16 (12–20)	0.85
Mechanical ventilation, d, median (IQR)	40 (16–50)	31 (6–51)	43 (35–50)	0.31

ECMO = extracorporeal membrane oxygenation, IQR = interquartile range, *n* = sample size, P/F = Pao₂/FiO₂.

Fourteen of 15 survivors (93%) of the in-hospital stay and six of nine (67%) who died in-hospital were diagnosed with delirium (*p* = 0.26). Three patients died without an adequate evaluation off sedation. Two patients suffered neurologic complications other than delirium. One patient on venovenous ECMO suffered bilateral femoral neuropathy and leg weakness from bilateral psoas hematomas associated with anticoagulation. Another patient on venovenous ECMO was found to have a persistently poor mental status off sedation, and MRI revealed multifocal small (< 1 cm) acute ischemic strokes in all major vascular distributions consistent with an embolic shower. A source of emboli was not established.

The remaining 13 patients (57%) were alive at the time of the 1-year follow-up interview. All 13, or their LARs, were reached by telephone. One patient and one LAR were willing to provide information on return to

work and activities of daily living but did not complete the assessment scales. Another patient was ventilator dependent at a long-term facility and unable to complete the assessment scales; her LAR provided information on her level of functioning. The remaining 10 patients were interviewed directly over the telephone. The median time from index admission for COVID-19 to telephone interview was 381 days (IQR, 378–385 d). None of the other long-term survivors had previously been diagnosed with dementia, major depression, or anxiety. None required home oxygen prior to the COVID-19 diagnosis.

Long-Term Respiratory Support

At the 1-year mark from the index admission, one of 13 survivors remained on mechanical ventilation at a long-term facility. One other patient used 2 L/min

TABLE 3.
Distribution of Therapeutic Interventions and Inhospital Outcomes

Variable	All Patients, <i>n</i> = 23	Dead at Discharge, <i>n</i> = 9	Alive at Discharge, <i>n</i> = 14	<i>p</i>
Therapeutic interventions				
Continuous renal replacement therapy, <i>n</i> (%)	16 (70)	8 (89)	8 (57)	1.00
Hemodialysis, <i>n</i> (%)	9 (39)	8 (89)	1 (4)	0.02
Vasopressor days, median (IQR)	16 (9–32)	29 (3–34)	16 (10–32)	1.00
Vasopressors, <i>n</i> (%)				1.0
Norepinephrine	23 (100)	9 (100)	14 (100)	
Vasopressin	16 (70)	7 (78)	9 (64)	
Epinephrine	3 (13)	3 (33)	0 (0)	
Phenylephrine	1 (4)	0 (0)	1 (7)	
Angiotensin 2	1 (4)	1 (11)	1 (7)	
Glucocorticoids, <i>n</i> (%)	8 (35)	4 (44)	4 (29)	0.45
Dexamethasone Randomized Evaluation of Covid-19 Therapy protocol	2 (9)	2 (22)	0 (0)	
Methylprednisolone acute respiratory distress syndrome protocol	3 (13)	0 (0)	3 (21)	
Both	3 (13)	2 (22)	1 (7)	
Tocilizumab, <i>n</i> (%)	5 (22)	1 (11)	4 (29)	0.33
Remdesivir, <i>n</i> (%)	2 (9)	1 (11)	1 (7)	1.00
Inhospital outcomes				
ICU length of stay, d, median (IQR)	47 (24–54)	30 (7–51)	51 (40–60)	0.07
Hospital length of stay, d, median (IQR)	47 (28–54)	30 (6–61)	51 (43–60)	0.06
Discharge location, <i>n</i> (%)				NA
Dead	9 (39)	9 (100)	0 (0)	
Long-term acute care	4 (17)	NA	4 (29)	
Subacute rehabilitation/skilled nursing facility	1 (4)	NA	1 (7)	
Inpatient acute rehabilitation	5 (22)	NA	5 (36)	
Home	4 (17)	NA	4 (29)	

n = sample size, NA = not applicable, IQR = interquartile range.

supplemental oxygen with unusual exertion outside the home only. All other patients required no respiratory support at any time, although one required continuous positive airway pressure for newly diagnosed obstructive sleep apnea.

Rehabilitation

The patient who suffered multifocal ischemic strokes was at a long-term ventilator facility, all others were at home at the time of telephone interview. Three of 13 long-term survivors were admitted to acute inpatient

rehabilitation following their index admission. Two were first discharged to a long-term acute care facility for weaning (where they stayed for 28 and 42 d) then underwent inpatient rehabilitation for 21 and 35 days, respectively. The third was at inpatient rehabilitation for 14 days.

Functional Outcome and Return to Work

Twelve of 13 long-term survivors had been independent to all activities of daily living and were employed full-time prior to the diagnosis of COVID-19. One patient

with mild developmental delay required minimal assistance for activities of daily living prior to developing COVID-19 and was not previously employed full-time. Six of 12 (50%) previously employed long-term survivors had returned to work. Five were working to the same extent as before COVID-19, while one was employed in a less intense capacity. The remaining six patients who were not employed all stated that physical or psychologic impairments related to COVID-19 were the reason they could not work. Excluding the patient with mild developmental delay, 10 of 12 (83%) previously independent long-term survivors were entirely independent to all activities of daily living (mRS < 3). One survivor remained ventilator dependent (mRS 5, WHODAS impairment score 100%) and the other required assistance only for shopping and groceries because she had stopped driving (mRS 3, WHODAS impairment score 62.5%). Other than the patient with long-term ventilator dependence, all other survivors (11/12, 92%) were independent within the home.

The median mRS score of long-term survivors was 2 (IQR, 1–2). The median WHODAS impairment score was 21% (IQR, 6–42%). A summary of responses to mRS and WHODAS-2.0 questions are in **Tables 4** and **5**, respectively. A significant positive correlation was found between age and WHODAS-2.0 impairment score ($\rho = 0.63$; 95% CI, 0.12–0.88; $p = 0.02$); however, no significant correlation was observed between impairment score and days on ECMO ($p = 0.33$), ventilator days ($p = 0.94$), or ICU LOS ($p = 0.62$). Of the two patients with neurologic complications, the patient with bilateral psoas hematomas had mild residual knee weakness at 1 year and had returned to work in a less intense role but was unable to resume hobbies (mRS 2, WHODAS 8.33%). The patient with multifocal ischemic strokes was ventilator dependent and not consistently following commands at 1 year but able to localize bilaterally (mRS 5, WHODAS 100%).

Cognitive Outcome

The patient with long-term ventilator dependence and inability to follow commands was profoundly cognitively impaired and could not be interviewed for a MoCA score. Among the 10 patients who completed the 5-minute telephone MoCA, the median score was 14 (IQR, 13–14; lowest score, 13) out of a total possible 15 points. Median language fluency score was 3 (IQR, 2–4) out of 4, median orientation score 6 (IQR, 6–6)

out of 6, and median recall score 5 (IQR, 4–5) out of 5. The median years of education among individuals who underwent cognitive assessment was high at 16 years (IQR, 14–16 yr). Adjustment of MoCA scores for education was not performed since this has primarily been described with low education levels and may adversely impact sensitivity (34).

Anxiety, Depression, and PTSD

Of 10 patients who could be assessed with HADS, 4 (40%) screened positive for both depression and anxiety. Additionally, one patient (10%) screened positive for anxiety alone and one patient (10%) was borderline for anxiety. Of the 6 (60%) who scored borderline or abnormal on either the anxiety or depression scale, four were receiving counseling at the time of interview. Two were receiving medication for depression and anxiety and one for anxiety alone. The two subjects not already receiving treatment were referred to counselors. The median HADS anxiety score was 9.5 (IQR, 2–14) and the median depression score was 2 (IQR, 1–11). Four of 10 patients (40%) scored 31 or above on the PCL-5 screener, indicating they would likely benefit from treatment for PTSD. Of these, three were already under treatment (two with medication and counseling, one with counseling alone) and the fourth was referred to a counselor. The median PCL-5 score was 24 (IQR 17–37).

Free-Response Answers

Four respondents said they were “...no longer comfortable in groups of people...” and were worried about reinfection. Two survivors with WHODAS-2.0 impairment greater than 50% and positive screening for anxiety, depression, and PTSD stated they were grateful to be alive and for the medical care provided. Two other long-term survivors stated that they were able to enjoy the things they used to enjoy more than they could prior to COVID-19 in response to the corresponding question on the HADS questionnaire.

DISCUSSION

Our prospective case series of COVID-19 patients managed with ECMO has several encouraging findings. Long-term survival was 57%, and all but one of the patients who survived the in-hospital stay were alive at 1 year. Only one long-term survivor failed

TABLE 4.
Responses to Modified Rankin Scale 9 Question Questionnaire, 11 Respondents

Question No.	Question	Yes, n (%)	No, n (%)
1	Do you have any symptoms that are bothering you?	10 (91)	1 (9)
2	Are you able to do the same work as before?	5 (45)	6 (55)
3	Are you able to keep up with your hobbies?	5 (45)	6 (55)
4	Have you maintained your ties to friends and family?	10 (91)	1 (9)
5	Do you need help making a simple meal, doing household chores, or balancing a checkbook?	1 (9)	10 (91)
6	Do you need help with shopping or traveling close to home?	2 (18)	9 (82)
7	Do you need another person to help you walk?	1 (9)	10 (91)
8	Do you need help with eating, going to the toilet, or bathing?	1 (9)	10 (91)
9	Do you stay in bed most of the day and need constant nursing care?	1 (9)	10 (91)

TABLE 5.
Responses to 12-Item World Health Organization Disability Assessment Scale 2.0 Questionnaire for the Prior Month, 11 Respondents

Please Note: When Scoring World Health Organization Disability Assessment Scale, the Following Numbers Are Assigned to Responses:

- 0 = No difficulty
- 1 = Mild difficulty
- 2 = Moderate difficulty
- 3 = Severe difficulty
- 4 = Extreme difficulty or cannot do

Question No.	Question	Median Score (IQR)
S1	Standing for long periods such as 30 min?	0 (0–3)
S2	Taking care of your household responsibilities?	1 (0–2)
S3	Learning a new task, e.g., learning how to get to a new place?	0 (0–1)
S4	How much of a problem did you have in joining in community activities (e.g., festivities, religious, or other activities) in the same way as anyone else can?	0 (0–3)
S5	How much have you been emotionally affected by your health problems?	3 (2–4)
S6	Concentrating on doing something for ten minutes?	0 (0–2)
S7	Walking a long distance such as a kilometer (or equivalent)?	1 (0–3)
S8	Washing your whole body?	0 (0–2)
S9	Getting dressed?	0 (0–1)
S10	Dealing with people you do not know?	2 (0–3)
S11	Maintaining a friendship?	0 (0–1)
S12	Your day-to-day work/school?	1 (0–4)
	Total impairment score (%)	21 (6–42)

IQR = interquartile range.

liberation from mechanical ventilation, and one other patient required long-term supplemental oxygen, only with unusual exertion. Also, 83% of previously independent survivors were independent in all activities of daily living, while 92% were independent within the home. Only one patient, with multifocal ischemic strokes, demonstrated evidence of cognitive impairment. Other findings, however, confirm the long-term burden of disease expected in this most severe stratum of illness. Only 50% of previously employed patients had returned to work, with the rest attributing their inability to work directly to impairments caused by COVID-19. While 40% screened positive for likely depression, 60% either screened positive or were borderline for likely anxiety, and 40% screened positive for likely PTSD. These findings suggest that meaningful long-term outcomes can be achieved with the use of ECMO in COVID-19 but also that survivors require substantial support from rehabilitation and mental health services. This study is the first to prospectively report functional, cognitive, and psychologic outcomes 1 year following the use of ECMO in the first wave of the pandemic. An additional strength of our study is the availability of prospective outcome data on all survivors, obtained across multiple domains using validated assessment tools.

It is possible that patients selected for ECMO (i.e., “survived” a selection process) had greater fitness for good long-term outcomes, it is therefore important to understand if our cohort differed markedly in baseline characteristics from the broad population of COVID-19 patients likely to be managed with ECMO. Institutional criteria for use of ECMO in COVID-19 were broad by design and prioritized the use of conventional treatment strategies prior to initiation of ECMO. The median age of our population was slightly, but not markedly, lower than the median age of the ELSO global cohort of COVID-19 patients managed with ECMO (47 vs 50 yr) (35). Other baseline parameters were comparable, including comorbidities, body mass index, and P/F ratio prior to initiation of ECMO. Median PEEP prior to ECMO was higher in our cohort (18 cm H₂O vs 14 cm H₂O) and days of intubation prior to initiation of ECMO were longer (7 vs 3.2 d). Of note, 100% of patients in our cohort required vasopressors (60% in ELSO) and 100% of ARDS patients underwent prone ventilation (57% in ELSO) and neuromuscular blockade (71% in ELSO) prior to initiation of ECMO.

Our cohort therefore may have been slightly younger but more severely ill at the time of ECMO initiation.

Our findings are comparable to those of studies of ARDS patients managed with ECMO prior to the pandemic. Interviews of 67 ARDS survivors treated with ECMO in France a median of 17 months from discharge revealed that physical impairment was common, with anxiety, depression, or PTSD present in 34%, 25%, and 16%, respectively (36). A study of 33 ARDS survivors in Italy interviewed greater than 2 years after management with venovenous ECMO revealed increased physical and psychologic impairment compared with normative data, with 42% screening positive on HADS for anxiety and depression, and 47% screening positive for PTSD (37). A more recent systematic review with 6 months to 3 years follow-up revealed health-related quality of life scores below normative data for the healthy population (38); however, scores in ECMO patients were equivalent or superior to those treated with conventional measures (38, 39). Early data are available in survivors of COVID-19–related critical illness. In a study from New York City, 87% of 45 COVID-19 critical illness survivors demonstrated physical impairment 1 month after discharge with psychologic impairment in 48% (40). In an Italian study, 73% of 45 previously employed COVID-19 critical illness survivors had returned to work at 6-months (41). There are as-yet limited long-term outcome data in COVID-19 patients managed with ECMO. Consistent with our study, a multicenter study from Europe demonstrated that the 47% in-hospital survival following the use of ECMO in COVID-19 was sustained at 6 months (11). An as yet unpublished study presented at the American Association for Thoracic Surgery 101st annual meeting described approximately 70% short-term survival in 46 COVID-19 patients managed with ECMO as well as 262 COVID-19 patients managed with conventional mechanical ventilation (42). Retrospective 3-month follow-up data, available for 67% of survivors, revealed that half reported cognitive impairment, ICU-acquired weakness and depression, anxiety, or PTSD. At 3 months, over a quarter required supplemental oxygen and one in six were back to work. However, these outcomes were similar in patients treated with ECMO compared with more conventional measures.

The source of the anxiety, depression, and PTSD in these patients is unclear. Several studies suggest

that the use of sedatives, opiates, and neuromuscular blockade (43–45), as well as delusional memories (46), are important risk factors for PTSD and psychiatric disease following critical illness. Delirium, and the extended use of all these medications, were universal among survivors in our study. In addition, free-response answers from some subjects suggest particular anxiety in the presence of groups and crowds, with concern for reinfection, in survivors. Of note, long-term cognitive impairment was uncommon in our study. Despite literature reports of significant cognitive dysfunction after critical illness (47), studies in non-COVID ECMO ICU survivors report more variable results (48–52). A multicenter study to track the long-term cognitive, physical, and emotional recovery of COVID-19 ECMO survivors has recently been initiated by the Outcomes and Recovery After COVID-19 Leading to ECMO Group and will provide important data in the future (53). The younger median age of survivors in our study (41 yr), as well as the higher level of education (median 16 yr), likely conferred a greater degree of cognitive reserve (47). Age is likely a significant contributing factor to cognitive impairment after critical illness (54–57), both due to the general decline in cognitive reserve with age and an increase in neurologic disease in older patients (58, 59). Another factor that may impact the occurrence of cognitive dysfunction is the time point of assessment—patients are more likely to demonstrate cognitive difficulties in the first 2 months after a hospital stay than they are after a year (59). In contrast to studies that perform long-term assessment of cognitive function, an Italian study reported cognitive impairment in 80% of COVID-19 patients admitted to an inpatient rehabilitation unit shortly after their acute illness (54). The method of determination of cognitive impairment following COVID-19 has also varied—studies that rely on self-reported cognitive dysfunction may be more likely to report a high rate of impairment compared those that use well-validated measures, while screening out patients with confounding psychiatric comorbidities. In a recent study of patients without COVID-19 managed with ECMO and assessed with both self-reported cognitive symptoms and formal neuropsychologic testing at 18–24 months, 70% self-reported cognitive symptoms; however, neuropsychologic test scores did not significantly differ from healthy controls after controlling for depression (49). Similarly, an early post-COVID study that screened

out patients with mental health history and assessed attention, executive functioning, working memory, and reaction time with full neuropsychologic assessments detected only mild dysfunction in sustained attention at 2 to 3 weeks posthospitalization (60). All other cognitive domains were consistent with the performance of the control group. In the New York study of COVID-19 critical illness survivors, which used the telephone MoCA to screen patients, only 8% demonstrated cognitive impairment, similar to our study (40).

Our study has several limitations. The sample size is small, and meaningful multivariate analysis could not be performed to evaluate hypotheses. Our study was purely descriptive to provide an early estimate of the long-term burden of disease in a population with limited long-term data. A survivorship selection bias may be present in our study despite our institution's broad ECMO selection criteria. Overall, our cohort was slightly younger but more severely ill compared with the ELSO global cohort (35). All interviews were conducted over telephone; however, all instruments used were either developed to be appropriate for, or have versions validated for, telephone use (20, 24, 30, 32, 61, 62). We had data on only three patients managed with venoarterial ECMO. Outcome data from the first wave may not reflect outcome data with the use of ECMO later in the pandemic. Current inhospital mortality reported by the ELSO from 7,135 COVID-19 ECMO patients is higher (48%) compared with the original ELSO report (39%) in the first wave of the pandemic (35). Only 35% of the patients in our group received glucocorticoids since most were managed prior to publication of data from clinical trials demonstrating a survival benefit (63). We do not as yet have 1-year functional, cognitive, and psychologic outcome information from critically ill COVID-19 patients managed without ECMO for comparison; however, prospective data collection is currently underway.

In conclusion, functional impairment, anxiety, depression, and PTSD symptoms were common a year following the use of ECMO in COVID-19; however, the majority were independent in activities of daily living, and half had returned to work. Cognitive impairment was uncommon.

1 Department of Neurosurgery, University of Michigan, Ann Arbor, MI.

2 Department of Neurology, University of Michigan, Ann Arbor, MI.

- 3 Department of Emergency Medicine, Division of Emergency Critical Care, University of Michigan, Ann Arbor, MI.
- 4 Department of Physical Medicine and Rehabilitation, Division of Rehabilitation Psychology and Neuropsychology, University of Michigan, Ann Arbor, MI.
- 5 Department of Surgery, University of Michigan, Ann Arbor, MI.
- 6 Department of Cardiac Surgery, University of Michigan, Ann Arbor, MI.
- 7 Department of Internal Medicine, Division of Pulmonary Critical Care Medicine, University of Michigan, Ann Arbor, MI.
- 8 Department of Anesthesiology, University of Michigan, Ann Arbor, MI.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (<http://journals.lww.com/ccejjournal>).

The authors have disclosed that they do not have any potential conflicts of interest.

This study was performed at the University of Michigan, Ann Arbor, MI.

For information regarding this article, E-mail: vrabajee@yahoo.com

REFERENCES

1. Johns Hopkins University: COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). 2021. Available at: <https://coronavirus.jhu.edu/map.html>. Accessed June 17, 2021
2. Badulak J, Antonini MV, Stead CM, et al; ELSO COVID-19 Working Group Members: Extracorporeal membrane oxygenation for COVID-19: Updated 2021 guidelines from the Extracorporeal Life Support Organization. *ASAIO J* 2021; 67:485–495
3. Munshi L, Walkey A, Goligher E, et al: Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: A systematic review and meta-analysis. *Lancet Respir Med* 2019; 7:163–172
4. Barrett KA, Hawkins N, Fan E: Economic evaluation of venovenous extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *Crit Care Med* 2019; 47:186–193
5. Yang X, Yu Y, Xu J, et al: Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. *Lancet Respir Med* 2020; 8:475–481
6. Barbaro RP, MacLaren G, Boonstra PS, et al; Extracorporeal Life Support Organization: Extracorporeal membrane oxygenation support in COVID-19: An international cohort study of the Extracorporeal Life Support Organization registry. *Lancet* 2020; 396:1071–1078
7. Kon ZN, Smith DE, Chang SH, et al: Extracorporeal membrane oxygenation support in severe COVID-19. *Ann Thorac Surg* 2021; 111:537–543
8. Jacobs JP, Stammers AH, Louis JS, et al: Multi-institutional analysis of 100 consecutive patients with COVID-19 and severe pulmonary compromise treated with extracorporeal membrane oxygenation: Outcomes and trends over time. *ASAIO J* 2021; 67:496–502
9. Jacobs JP, Stammers AH, St Louis J, et al: Extracorporeal membrane oxygenation in the treatment of severe pulmonary and cardiac compromise in coronavirus disease 2019: Experience with 32 patients. *ASAIO J* 2020; 66:722–730
10. Shaefi S, Brenner SK, Gupta S, et al; STOP-COVID Investigators: Extracorporeal membrane oxygenation in patients with severe respiratory failure from COVID-19. *Intensive Care Med* 2021; 47:208–221
11. Biancari F, Mariscalco G, Dalén M, et al: Six-month survival after extracorporeal membrane oxygenation for severe COVID-19. *J Cardiothorac Vasc Anesth* 2021; 35:1999–2006
12. Mo X, Jian W, Su Z, et al: Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J* 2020; 55:2001217
13. Chou SH, Beghi E, Helbok R, et al; GCS-NeuroCOVID Consortium and ENERGY Consortium: Global incidence of neurological manifestations among patients hospitalized with COVID-19—a report for the GCS-NeuroCOVID Consortium and the ENERGY Consortium. *JAMA Netw Open* 2021; 4:e2112131
14. Needham DM, Davidson J, Cohen H, et al: Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. *Crit Care Med* 2012; 40:502–509
15. Mikkelsen ME, Still M, Anderson BJ, et al: Society of Critical Care Medicine's international consensus conference on prediction and identification of long-term impairments after critical illness. *Crit Care Med* 2020; 48:1670–1679
16. Hodgson CL, Udy AA, Bailey M, et al: The impact of disability in survivors of critical illness. *Intensive Care Med* 2017; 43:992–1001
17. Li R, Zhou Y, Liu X, et al: Functional disability and post-traumatic stress disorder in survivors of mechanical ventilation: A cross-sectional study in Guangzhou, China. *J Thorac Dis* 2021; 13:1564–1575
18. Ranieri VM, Rubenfeld GD, Thompson BT, et al; ARDS Definition Task Force: Acute respiratory distress syndrome: The Berlin definition. *JAMA* 2012; 307:2526–2533
19. Centers for Disease Control and Prevention: Symptoms of COVID-19. 2021. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>. Accessed May 26, 2021
20. Ustün TB, Chatterji S, Kostanjsek N, et al; WHO/NIH Joint Project: Developing the World Health Organization Disability Assessment Schedule 2.0. *Bull World Health Organ* 2010; 88:815–823
21. van Swieten JC, Koudstaal PJ, Visser MC, et al: Interobserver agreement for the assessment of handicap in stroke patients. *Stroke* 1988; 19:604–607
22. Patel N, Rao VA, Heilman-Espinoza ER, et al: Simple and reliable determination of the modified Rankin Scale score in neurosurgical and neurological patients: The mRS-9Q. *Neurosurgery* 2012; 71:971–975
23. World Health Organization: Global COVID-19 Clinical Platform Case Report Form (CRF) for Post COVID condition (Post COVID-19 CRF). 2021. Available at: [https://www.who.int/publications/i/item/global-covid-19-clinical-platform-case-report-form-\(crf\)-for-post-covid-condition-\(post-covid-19-crf\)](https://www.who.int/publications/i/item/global-covid-19-clinical-platform-case-report-form-(crf)-for-post-covid-condition-(post-covid-19-crf)). Accessed August 7, 2021

24. Ustun TB, Kostanjsek N, Chatterji S, et al: Measuring Health and Disability: Manual for WHO Disability Assessment Schedule (WHODAS 2.0). 2010. Available at: <https://apps.who.int/iris/handle/10665/43974>. Accessed July 30, 2021
25. Federici S, Bracalenti M, Meloni F, et al: World Health Organization disability assessment schedule 2.0: An international systematic review. *Disabil Rehabil* 2017; 39:2347–2380
26. Cheung MK, Hung AT, Poon PK, et al: Validation of the World Health Organization Assessment Schedule II Chinese Traditional Version (WHODAS II CT) in persons with disabilities and chronic illnesses for Chinese population. *Disabil Rehabil* 2015; 37:1902–1907
27. Schlote A, Richter M, Wunderlich MT, et al: WHODAS II with people after stroke and their relatives. *Disabil Rehabil* 2009; 31:855–864
28. Soberg HL, Finset A, Roise O, et al: The trajectory of physical and mental health from injury to 5 years after multiple trauma: A prospective, longitudinal cohort study. *Arch Phys Med Rehabil* 2012; 93:765–774
29. Hodgson CL, Fulcher B, Mariajoseph FP, et al; SCOPE Study Investigators on behalf of the International ECMO Network: A core outcome set for research in patients on extracorporeal membrane oxygenation. *Crit Care Med* 2021 Jun 2. [online ahead of print]
30. Wong A, Nyenhuis D, Black SE, et al: Montreal Cognitive Assessment 5-minute protocol is a brief, valid, reliable, and feasible cognitive screen for telephone administration. *Stroke* 2015; 46:1059–1064
31. Zigmond AS, Snaith RP: The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67:361–370
32. Bovin MJ, Marx BP, Weathers FW, et al: Psychometric properties of the PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (PCL-5) in veterans. *Psychol Assess* 2016; 28:1379–1391
33. Rosendahl J, Kisyova H, Gawlytta R, et al: Comparative validation of three screening instruments for posttraumatic stress disorder after intensive care. *J Crit Care* 2019; 53:149–154
34. Gagnon G, Hansen KT, Woolmore-Goodwin S, et al: Correcting the MoCA for education: Effect on sensitivity. *Can J Neurol Sci* 2013; 40:678–683
35. Extracorporeal Life Support Organization (ELSO): COVID-19 Cases on ECMO in the Extracorporeal Life Support Organization (ELSO) Registry. 2021. Available at: <https://www.elseo.org/default.aspx>. Accessed July 30, 2021
36. Schmidt M, Zogheib E, Rozé H, et al: The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *Intensive Care Med* 2013; 39:1704–1713
37. Sanfilippo F, Ippolito M, Santonocito C, et al: Long-term functional and psychological recovery in a population of acute respiratory distress syndrome patients treated with VV-ECMO and in their caregivers. *Minerva Anestesiol* 2019; 85:971–980
38. Kurniawati ER, Rutjens VGH, Vranken NPA, et al: Quality of life following adult veno-venous extracorporeal membrane oxygenation for acute respiratory distress syndrome: A systematic review. *Qual Life Res* 2021; 30:2123–2135
39. Wilcox ME, Jaramillo-Rocha V, Hodgson C, et al: Long-term quality of life after extracorporeal membrane oxygenation in ARDS survivors: Systematic review and meta-analysis. *J Intensive Care Med* 2020; 35:233–243
40. Martillo M, Dangayach N, Tabacof L, et al: Postintensive care syndrome in survivors of critical illness related to coronavirus disease 2019: Cohort study from a New York City Critical Care Recovery Clinic. *Crit Care Med* 2021; 49:1427–1438
41. Careno L, Dalla Corte F, Haines RW, et al: Return to work after coronavirus disease 2019 acute respiratory distress syndrome and intensive care admission: Prospective, case series at 6 months from hospital discharge. *Crit Care Med* 2021 May 26. [online ahead of print]
42. Taylor LJ, Ramani C, Fakhri S, et al: Long-term recovery of COVID-19 survivors is not negatively impacted by ECMO: A multicenter study from the ORACLE Group. American Association for Thoracic Surgery (AATS) 101st Annual Meeting. Virtual. April 30–May 2, 2021
43. Wade DM, Howell DC, Weinman JA, et al: Investigating risk factors for psychological morbidity three months after intensive care: A prospective cohort study. *Crit Care* 2012; 16:R192
44. Girard TD, Shintani AK, Jackson JC, et al: Risk factors for post-traumatic stress disorder symptoms following critical illness requiring mechanical ventilation: A prospective cohort study. *Crit Care* 2007; 11:R28
45. Nelson BJ, Weinert CR, Bury CL, et al: Intensive care unit drug use and subsequent quality of life in acute lung injury patients. *Crit Care Med* 2000; 28:3626–3630
46. Jones C, Griffiths RD, Humphris G, et al: Memory, delusions, and the development of acute posttraumatic stress disorder-related symptoms after intensive care. *Crit Care Med* 2001; 29:573–580
47. Marra A, Pandharipande PP, Girard TD, et al: Co-occurrence of post-intensive care syndrome problems among 406 survivors of critical illness. *Crit Care Med* 2018; 46:1393–1401
48. Daou M, Lauzon C, Bullen EC, et al: Long-term cognitive outcomes and sleep in adults after extracorporeal life support. *Crit Care Explor* 2021; 3:e0390
49. Marsh LC, Leach RM, Blane J, et al: Long-term cognitive and psychiatric outcomes of acute respiratory distress syndrome managed with extracorporeal membrane oxygenation. *Respir Med* 2021; 183:106419
50. Sylvestre A, Adda M, Maltese F, et al: Long-term neurocognitive outcome is not worsened by the use of venovenous ECMO in severe ARDS patients. *Ann Intensive Care* 2019; 9:82
51. Tramm R, Ilic D, Sheldrake J, et al: Recovery, risks, and adverse health outcomes in year 1 after extracorporeal membrane oxygenation. *Am J Crit Care* 2017; 26:311–319
52. von Bahr V, Kalzén H, Hultman J, et al: Long-term cognitive outcome and brain imaging in adults after extracorporeal membrane oxygenation. *Crit Care Med* 2018; 46:e351–e358
53. Mayer KP, Jolley SE, Etchill EW, et al; Outcomes and Recovery After COVID-19 Leading to ECMO (ORACLE) Group: Long-term recovery of survivors of coronavirus disease (COVID-19) treated with extracorporeal membrane oxygenation: The next imperative. *JTCVS Open* 2021; 5:163–168
54. Alemanno F, Houdayer E, Parma A, et al: COVID-19 cognitive deficits after respiratory assistance in the subacute phase: A COVID-rehabilitation unit experience. *PLoS One* 2021; 16:e0246590

55. Hopkins RO: The brain after critical illness: Effect of illness and aging on cognitive function. *Crit Care* 2013; 17:116
56. Guerra C, Linde-Zwirble WT, Wunsch H: Risk factors for dementia after critical illness in elderly Medicare beneficiaries. *Crit Care* 2012; 16:R233
57. Guerra C, Hua M, Wunsch H: Risk of a diagnosis of dementia for elderly medicare beneficiaries after intensive care. *Anesthesiology* 2015; 123:1105–1112
58. Sasannejad C, Ely EW, Lahiri S: Long-term cognitive impairment after acute respiratory distress syndrome: A review of clinical impact and pathophysiological mechanisms. *Crit Care* 2019; 23:352
59. Inouye SK, Marcantonio ER, Kosar CM, et al: The short-term and long-term relationship between delirium and cognitive trajectory in older surgical patients. *Alzheimers Dement* 2016; 12:766–775
60. Zhou H, Lu S, Chen J, et al: The landscape of cognitive function in recovered COVID-19 patients. *J Psychiatr Res* 2020; 129:98–102
61. Janssen PM, Visser NA, Dorhout Mees SM, et al: Comparison of telephone and face-to-face assessment of the modified Rankin Scale. *Cerebrovasc Dis* 2010; 29:137–139
62. National Center for PTSD: Using the PTSD Checklist for DSM-V (PCL-5). 2021. Available at: <https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp>. Accessed July 30, 2021
63. Sterne JAC, Murthy S, Diaz JV, et al; WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group: Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: A meta-analysis. *JAMA* 2020; 324:1330–1341