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Multi-institutional Analysis of 200 COVID-19 Patients Treated With Extracorporeal Membrane Oxygenation: Outcomes and Trends

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ABSTRACT

BACKGROUND The role of extracorporeal membrane oxygenation (ECMO) in the management of patients with COVID-19 continues to evolve. The purpose of this analysis is to review our multi-institutional clinical experience involving 200 consecutive patients at 29 hospitals with confirmed COVID-19 supported with ECMO.

METHODS This analysis includes our first 200 COVID-19 patients with complete data who were supported with and separated from ECMO. These patients were cannulated between March 17 and December 1, 2020. Differences by mortality group were assessed using χ^2 tests for categoric variables and Kruskal-Wallis rank sum tests and Welch's analysis of variance for continuous variables.

RESULTS Median ECMO time was 15 days (interquartile range, 9 to 28). All 200 patients have separated from ECMO: 90 patients (45%) survived and 110 patients (55%) died. Survival with venovenous ECMO was 87 of 188 patients (46.3%), whereas survival with venoarterial ECMO was 3 of 12 patients (25%). Of 90 survivors, 77 have been discharged from the hospital and 13 remain hospitalized at the ECMO-providing hospital. Survivors had lower median age (47 versus 56 years, $P < .001$) and shorter median time from diagnosis to ECMO cannulation (8 versus 12 days, $P = .003$). For the 90 survivors, adjunctive therapies on ECMO included intravenous steroids (64), remdesivir (49), convalescent plasma (43), anti-interleukin-6 receptor blockers (39), prostaglandin (33), and hydroxychloroquine (22).

CONCLUSIONS Extracorporeal membrane oxygenation facilitates survival of select critically ill patients with COVID-19. Survivors tend to be younger and have a shorter duration from diagnosis to cannulation. Substantial variation exists in drug treatment of COVID-19, but ECMO offers a reasonable rescue strategy.

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As of January 28, 2021, 100,986,160 patients around the world have been diagnosed with Coronavirus Disease 2019 (COVID-19), with 2,177,611 associated deaths (2.16% mortality worldwide).[1] Meanwhile, in the United States, as of January 28, 2021, 25,599,961 patients have been diagnosed with confirmed COVID-19, with 429,214 associated deaths

Drs Sestokas and Stammers disclose a financial relationship with SpecialtyCare.

The Supplemental Table can be viewed in the online version of this article (10.1016/j.athoracsur.2021.06.026) on http://www.annalsthoracicsurgery.org.

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(1.68% mortality in the US).[1] Most deaths of patients with COVID-19 are due to severe respiratory failure, with a small group succumbing to combined pulmonary and cardiac failure.[2,3]

We previously published an analysis of our initial 32 COVID-19 patients with severe pulmonary compromise supported with extracorporeal membrane oxygenation (ECMO)[4] and concluded that "ECMO may play a useful role in salvaging select critically ill patients with COVID-19. Additional patient experience and associated clinical and laboratory data must be obtained to further define the optimal role of ECMO in patients with COVID-19 and acute respiratory distress syndrome (ARDS). These initial data may provide useful information to help define the best strategies to care for these challenging patients, and may also provide a framework for much-needed future research about the use of ECMO to treat patients with COVID-19."

Several recently published analyses describe cohorts of COVID-19 patients supported with ECMO.[4-8] Early data from Wuhan, China, reported an alarmingly high rate of mortality of 83% (5 of 6) among COVID-19 patients supported with ECMO.[5,6] More recent data, however, reveal improved survival of COVID-19 ECMO patients.[4,7,8] Both recent individual institutional reports,[7] as well as recent reports from multi-institutional registries.[8] present detailed analyses with promising results. Our previous report from our multi-institutional database[4] corroborates these findings from individual institutions[7] and multi-institutional registries,[8] and in addition, provides more granular, detailed information than a large-scale registry and more generalizable information than can be garnered from analysis of a single institution. Clearly, the role of ECMO in the management of severely ill patients with COVID-19 continues to evolve. The purposes of this manuscript are (1) to review our multi-institutional clinical experience based on 200 consecutive patients with confirmed COVID-19 with severe pulmonary compromise who were supported with and separated from ECMO at 29 hospitals; and (2) to document outcomes and trends in management over time.

MATERIAL AND METHODS

A prospective, multi-institutional cohort study was conducted of all patients with confirmed COVID-19 who were supported with ECMO at 29 different hospitals. Supplemental Table 1 documents the regional distribution of these 200 patients at 29 hospitals in 18 states in the United States. A multi-institutional database was created and utilized to assess these patients. This database is prospectively maintained on all patients and has been used for data collection and analysis. The database used is a component of the SpecialtyCare Operative Procedural Registry (SCOPE [https://specialtycareus.com/]). (SpecialtyCare is a US provider of Allied Health services, and the SCOPE registry contains data from more than 1 million perfusion procedures at more than 300 hospitals in more than 40 states. This manuscript describes the experience with ECMO to support a subset of these patients with COVID-19.) Data captured included patient characteristics, pre-COVID-19 risk factors and comorbidities, confirmation of COVID-19 diagnosis, features of ECMO support, specific medications utilized to treat COVID-19, and short-term outcomes through hospital discharge.

This analysis includes our first 200 patients with complete data who had confirmed COVID-19 and were supported with ECMO, starting with our first COVID-19 patient who was placed on ECMO on March 17, 2020, and ending with a patient placed on ECMO on December 1, 2020. These 200 patients include 188 patients supported with venovenous ECMO and 12 patients supported with venoarterial ECMO. The initial cohort included our first 206 patients who had confirmed COVID-19 and were supported with and decannulated from ECMO; 6 patients (1 survivor and 5 nonsurvivors) were excluded from this analysis because of incomplete data. Inclusion in the analysis required complete data in the following fields: ECMO start date; ECMO end date; outcome (alive or dead); no more than one missing pre-COVID comorbidities (asthma, cancer, chronic renal failure, diabetes mellitus, heart disease, hypertension, obesity); and no more than one missing adjunctive therapeutic interventions (antiviral medications, antimalarial medications, convalescent plasma, interleukin-6 blockers, prostaglandin, steroids).

Criteria for placement on ECMO were determined by the individual patient care teams at each of the contributing 29 hospitals; all patients who were supported with ECMO had the diagnosis of COVID-19 with severe respiratory failure deemed to be refractory to conventional management. The decision to initiate ECMO, the mode of therapy (ie, venovenous, venoarterial, and so forth), and the cannulation strategy were each determined by the individual ECMO teams, in keeping with their respective individual institutional protocols and guidelines. Tables 1 and 2 provide P/F ratio, which is defined as the arterial partial pressure of oxygen (Pa_{O_2}) of the patient divided by the fraction of inspired oxygen (FIO_2, expressed as a decimal) that the patient is receiving.

Descriptive analysis of the entire cohort was performed using mean and standard deviation or median and interquartile range (IQR), as appropriate. The primary outcome of interest was mortality during the index hospitalization. Potential differences in categoric variables by mortality group were assessed using χ^2 tests, and potential differences in continuous variables by mortality group were assessed using Kruskal-Wallis rank sum tests and Welch's analysis of variance, as appropriate.

Institutional Review Board approval and waiver of the need for consent were obtained. The human subjects research protocol for this study was reviewed and

TABLE 1 Overview of 200 Patients With COVID-19 Supported by Extracorporeal Membrane Oxygenation

COVID Patient Variables	Overall (n = 200)
Nonsurvivors	110 (55)
Survivors	90 (45)
Diagnosis to intubation, d, mean (SD)	7.45 (6.82)
Diagnosis to intubation, d	6.50 (2-12)
Intubation to cannulation, d, mean (SD)	4.81 (4.72)
Intubation to cannulation, d	4 (1-6)
Diagnosis to cannulation, d, mean (SD)	11.1 (8.22)
Diagnosis to cannulation, d	10 (5-16)
ECMO, d, mean (SD)	20.3 (16.1)
ECMO, d	15 (9-28)
ECMO, h, mean (SD)	475 (386)
ECMO, h	339 (200-670)
Age, y, mean (SD)	49.8 (12.1)
Age, y	51 (40-59)
Sex	
Female	62 (31)
Male	138 (69)
Asthma	
No	167 (83.5)
Yes	33 (16.5)
Cancer	
No	194 (97)
Yes	6 (3)
Chronic renal failure	
No	187 (94)
Yes	12 (6.0)
Diabetes mellitus	
No	124 (62)
Yes	76 (38)
Heart disease	
No	178 (89)
Yes	22 (11)
Hypertension	
No	106 (53)
Yes	94 (47)
Obesity	
No	72 (36)
Yes	128 (64)
One or more comorbid conditions	
No	32 (16)
Yes	168 (84)
Prone position before ECMO	
No	73 (36.7)
Yes	126 (63.3)
P/F ratio[a] before ECMO, mean (SD)	69.5 (27)
Tracheostomy performed	
No	130 (65)
Yes	70 (35)
Number of circuit changes	0 (0-1)
One of more circuit changes	
No	130 (67.4)
Yes	63 (32.6)
CVVH or CRRT used	
No	135 (68.9)
Yes	61 (31.1)

(*Continued in the next page*)

TABLE 2 Comparison of the 110 Survivors to 90 Nonsurvivors

COVID Patient Variables	Nonsurvivors (n = 110)	Survivors (n = 90)	*P* Value
Diagnosis to intubation, d, mean (SD)	9.18 (7.42)	5.21 (5.24)	.001
Diagnosis to intubation, d	9.00 (2.25-13.8)	3.50 (1-9.25)	.005
Intubation to cannulation, d, mean (SD)	5.30 (5.30)	4.18 (3.80)	.196
Intubation to cannulation, d	4 (1-8)	3 (1-5)	.314
Diagnosis to cannulation, d, mean (SD)	12.8 (8.96)	9.10 (6.76)	.001
Diagnosis to cannulation, d	12 (6-17)	8 (4-14)	.003
ECMO, d, mean (SD)	21 (15.9)	19.3 (16.4)	.472
ECMO, d	18 (9.25-28)	12.5 (8-27.2)	.25
ECMO, h, mean (SD)	493 (381)	454 (393)	.488
ECMO, h	412 (217-668)	292 (192-648)	.251
Age, y, mean (SD)	52.5 (11.8)	46.4 (11.7)	<.001
Age, y	56 (45.2-61)	47 (36-56.8)	<.001
Sex			
Female	29 (26.4)	33 (36.7)	.157
Male	81 (73.6)	57 (63.3)	
Asthma			
No	91 (82.7)	76 (84.4)	.893
Yes	19 (17.3)	14 (15.6)	
Cancer			
No	106 (96.4)	88 (97.8)	.692
Yes	4 (3.6)	2 (2.2)	
Chronic renal failure			
No	102 (93.6)	85 (94.4)	1
Yes	7 (6.4)	5 (5.6)	
Diabetes mellitus			
No	64 (58.2)	60 (66.7)	.279
Yes	46 (41.8)	30 (33.3)	
Heart disease			
No	96 (87.3)	82 (91.1)	.525
Yes	14 (12.7)	8 (8.9)	
Hypertension			
No	59 (53.6)	47 (52.2)	.955
Yes	51 (46.4)	43 (47.8)	
Obesity			
No	37 (33.6)	35 (38.9)	.534
Yes	73 (66.4)	55 (61.1)	
One or more comorbid conditions			
No	15 (13.6)	17 (18.9)	.416
Yes	95 (86.4)	73 (81.1)	
Prone position before ECMO			
No	38 (34.9)	35 (38.9)	.661
Yes	71 (65.1)	55 (61.1)	
P/F ratio[a] pre-ECMO, mean (SD)	73.1 (31.9)	64.9 (18.1)	.08
Tracheostomy performed			
No	76 (69.1)	54 (60)	.233
Yes	34 (30.9)	36 (40)	
Number of circuit changes	0 (0-1)	0 (0-1)	.914
One or more circuit changes			
No	71 (67.6)	59 (67)	1
Yes	34 (32.4)	29 (33)	
CVVH or CRRT used			

(*Continued in the next page*)

TABLE 1 Continued

COVID Patient Variables	Overall (n = 200)
ECMO type	
Venoarterial	12 (6)
Venovenous	188 (94)
Anticoagulation type	
Argatroban	11 (5.5)
Bivalirudin	28 (14.1)
Heparin	160 (80.4)
Antiviral medication	
No	91 (45.5)
Yes	109 (54.5)
Convalescent plasma	
No	90 (47.6)
Yes	99 (52.4)
Hydroxychloroquine	
No	154 (77)
Yes	46 (23)
Interleukin-6 blocker	
No	122 (61.6)
Yes	76 (38.4)
Prostaglandin	
No	116 (58.3)
Yes	83 (41.7)
Steroids	
No	56 (28)
Yes	144 (72)

[a]The P/F ratio is the arterial partial pressure of oxygen (Pa_{O_2}) divided by the fraction of inspired oxygen (F_{IO_2}) expressed as a decimal. Values are median (interquartile range) or n (%) unless otherwise indicated. CRRT, continuous renal replacement therapy; CVVH, continuous venovenous hemofiltration; ECMO, extracorporeal membrane oxygenation.

TABLE 2 Continued

COVID Patient Variables	Nonsurvivors (n = 110)	Survivors (n = 90)	*P* Value
No	72 (67.3)	63 (70.8)	.71
Yes	35 (32.7)	26 (29.2)	
ECMO type			
Venoarterial	9 (8.2)	3 (3.3)	.255
Venovenous	101 (91.8)	87 (96.7)	
Anticoagulation type			
Argatroban	6 (5.5)	5 (5.6)	.961
Bivalirudin	16 (14.7)	12 (13.3)	
Heparin	87 (79.8)	73 (81.1)	
Antiviral medication			
No	50 (45.5)	41 (45.6)	1
Yes	60 (54.5)	49 (54.4)	
Convalescent plasma			
No	47 (45.6)	43 (50)	.651
Yes	56 (54.4)	43 (50)	
Hydroxychloroquine			
No	86 (78.2)	68 (75.6)	.787
Yes	24 (21.8)	22 (24.4)	
Interleukin-6 blocker			
No	71 (65.7)	51 (56.7)	.246
Yes	37 (34.3)	39 (43.3)	
Prostaglandin			
No	59 (54.1)	57 (63.3)	.243
Yes	50 (45.9)	33 (36.7)	
Steroids			
No	30 (27.3)	26 (28.9)	.924
Yes	80 (72.7)	64 (71.1)	

[a]The P/F ratio is the arterial partial pressure of oxygen (Pa_{O_2}) divided by the fraction of inspired oxygen (F_{IO_2}) expressed as a decimal. Values are median (interquartile range) or n (%) unless otherwise indicated. CRRT, continuous renal replacement therapy; CVVH, continuous venovenous hemofiltration; ECMO, extracorporeal membrane oxygenation.

approved by an independent Institutional Review Board. Institutional Ethics Review Board approval was obtained for the use of data from the SCOPE database (Protocol #012017, ADVARRA Center for IRB Intelligence, Columbia, Maryland).

RESULTS

Two hundred consecutive patients with COVID-19 were supported with ECMO at 29 different hospitals. All 200 patients have since been separated from ECMO: 90 patients survived (45%) and 110 patients died (55%). Of the 90 survivors, 77 patients have been discharged from the hospital to date. Table 1 provides detailed data about all 200 patients with COVID-19 treated with ECMO. Of note, of 200 patients, 128 (64%) were obese, 94 (47%) had hypertension, 76 (38%) had diabetes, 33 (16.5%) had asthma, 22 (11%) had heart disease, 12 (6%) had chronic renal failure, and 6 (3%) had cancer. The median time on ECMO was 15 days (IQR, 9 to 28).

Table 2 provides detailed data comparing the characteristics of 90 survivors with 110 nonsurvivors. Survivors were generally younger, with a lower median age (47 versus 56 years, $P < .001$). Survivors also had a shorter median interval from the diagnosis of COVID-19 to cannulation for ECMO (8 versus 12 days, $P = .003$). Although duration on ECMO was shorter among survivors than nonsurvivors, this trend was not statistically significant: median time on ECMO for survivors was 12.5 days (IQR, 8 to 27), and median time on ECMO for nonsurvivors was 18 days (IQR, 9 to 28).

For the 90 surviving patients, adjunctive therapies received while on ECMO were intravenous steroids (64 of 90), antiviral medications (remdesivir [49 of 90]), convalescent plasma (43 of 90), anti-interleukin-6 receptor monoclonal antibodies (tocilizumab or sarilumab [39 of 90]), prostaglandin (33 of 90), and hydroxychloroquine (22 of 90).

This analysis includes all patients with COVID-19 supported with ECMO at the 29 hospitals participating in this study during the period of this analysis. None of these 200 patients was placed on ECMO during cardiopulmonary resuscitation. Extracorporeal cardiopulmonary resuscitation was not utilized for COVID-19 patients at these 29

hospitals. Of 90 survivors, 87 (97%) were supported only with venovenous ECMO. Furthermore, only 3 of 12 patients (25%) supported with venoarterial ECMO survived. Of the 110 patients who died, documented causes of death were respiratory failure (63), multisystem organ failure including acute kidney injury (12), disseminated intravascular coagulation (8), sepsis (7), cardiac arrest (6), cerebral bleeding while on ECMO (5), central nervous system injury (2), air embolism (1), pulmonary embolism (1), pneumothorax (1), and unknown (4).

Figure 1 is a Consolidated Standards of Reporting Trials (CONSORT) flow diagram that depicts the distribution of all 200 patients by category of outcome. Of 90 survivors, 77 have been discharged from the hospital and 13 remain hospitalized at the ECMO-providing hospital. Figure 2 depicts the distribution of the age of the patients, comparing the survivors with the nonsurvivors. Figure 3 depicts the distribution of hours on ECMO, comparing the survivors with the nonsurvivors. Figure 4 depicts the monthly trends over time in the utilization of adjunctive therapies in patients with COVID-19 while supported with ECMO during the 9 months of this analysis.

COMMENT

Our multi-institutional analysis of 200 consecutive COVID-19 patients who were supported with ECMO and subsequently decannulated provides clear evidence that ECMO facilitates salvage and survival of select critically ill patients with COVID-19. Survivors had lower median age (47 versus 56 years, $P < .001$) and shorter median interval from diagnosis to ECMO cannulation (8 versus 12 days, $P = .003$). Survival with venovenous ECMO was 87 of 188 patients (46.3%), whereas survival with venoarterial ECMO was 3 of 12 patients (25%). Substantial variation exists in the use of adjunctive drugs and therapies in the treatment of COVID-19, but these findings support the selective use of venovenous ECMO as a reasonable rescue strategy.

Clinical guidelines for the management of patients with COVID-19 have been released by the World Health Organization[9] and the Centers for Disease Control and Prevention of the United States.[10] The Extracorporeal Life Support Organization[11] and the American Society for Artificial Internal Organs[12] have also both published guidelines regarding the role of ECMO in treating patients with COVID-19. Nevertheless, the role of ECMO in the management of these challenging patients remains unclear.

Kon and colleagues[7] reported a retrospective analysis of all patients with COVID-19 admitted to New York University Langone Health Manhattan campus from March 10, 2020, to April 24, 2020, who were evaluated for ECMO support. Among 321 patients intubated for COVID-19, 77 (24%) were evaluated for ECMO support, and 27 (8.4%) were supported with venovenous ECMO. No patients were supported with venoarterial ECMO. At the time of publication of their manuscript, survival was 96.3%, with only 1 death to date in more than 350 days of total ECMO support. Thirteen patients (48.1%) remained on ECMO support, and 13 patients (48.1%) were successfully decannulated. Of the 13 decannulated patients, 7 (25.9%) were discharged from the hospital and 6 (22.2%) remained in hospital, with 4 on room air. The researchers concluded, "The early outcomes presented here suggest that the judicious use of ECMO support in severe COVID-19 may be clinically beneficial."[7]

In contrast, the use of venoarterial ECMO in patients with COVID-19 has been associated with poor survival. Indeed, in patients with COVID-19, if the extent of end organ damage necessitates venoarterial ECMO, then the prognosis is poor in comparison with patients having isolated respiratory dysfunction requiring only venovenous ECMO. Furthermore, if the disease is so severe that the patient has a cardiac arrest refractory to cardiopulmonary resuscitation without ECMO, the patient is unlikely to survive and the use of venoarterial ECMO is likely to be futile.

Barbaro and colleagues[8] reported a cohort study of 1035 patients aged 16 years or more with confirmed COVID-19 who had ECMO support initiated between January 16 and May 1, 2020, at 213 hospitals in 36 countries, using data from the Extracorporeal Life Support Organization registry. At the time of publication, of these 1035 patients, 67 (6%) remained hospitalized, 311 (30%) were discharged home or to an acute rehabilitation center, 101 (10%) were discharged to a long-term acute care center or unspecified location, 176 (17%) were discharged to another hospital, and 380 (37%) died. The estimated cumulative incidence of inhospital mortality 90 days after the initiation of ECMO was 37.4% (95% confidence interval, 34.4% to 40.4%). Mortality was 39% (380 of 968) in patients with a final disposition of death or hospital discharge. In the subset of patients receiving venovenous ECMO and characterized as having acute respiratory distress syndrome, estimated inhospital mortality 90 days after the initiation of ECMO was 38% (95% confidence interval, 34.6% to 41.5%). Extracorporeal membrane oxygenation for circulatory support was independently associated with higher inhospital mortality (hazard ratio 1.89; 95% confidence interval, 1.20 to 2.97).

Shih and colleagues[13] recently reported an analysis of 37 patients with severe COVID-19 acute respiratory distress syndrome who "were initiated on venovenous ECMO support at one of four ECMO referral hospitals within a large health care system. Initiation of ECMO occurred on median day 11.5 following admission, and, of the successfully decannulated patients, median time on ECMO was 17 days. Survival to discharge from ECMO center has occurred in 21/37 patients (56.8%)." These findings are also consistent with our analysis. Recently, successful

transition from the initial intent of bridge to recovery to subsequent bridge to lung transplantation has been described in a small number of patients with COVID-19.[14]

VALUE OF THIS ANALYSIS. Our study adds to the body of knowledge and the literature by providing more granular multi-institutional data about our cohort of 200 patients with COVID-19 supported with ECMO at 29 hospitals. As previously described, several published analyses have studied the outcomes of ECMO in patients with COVID-19, and these outcomes have been quite heterogenous.[4-8] Our analysis of the SpecialtyCare SCOPE registry adds another dataset of multi-institutional data to the growing body of literature about the use of ECMO in patients with COVID-19 and demonstrates that support with ECMO facilitates salvage and survival of select critically ill patients with COVID-19.

In our analysis, survival of patients supported with only venovenous ECMO was 46.3% (87 of 188). Survival of patients requiring venoarterial ECMO was poor (3 of 12; 25%). Our finding of higher survival with venovenous ECMO in comparison with venoarterial ECMO in patients with COVID-19 is consistent with the published literature, but is not statistically significant ($P = .255$). It is likely that if the extent of end organ damage necessitates venoarterial ECMO in patients with COVID-19, then the prognosis is poor in comparison with patients having isolated respiratory dysfunction requiring only

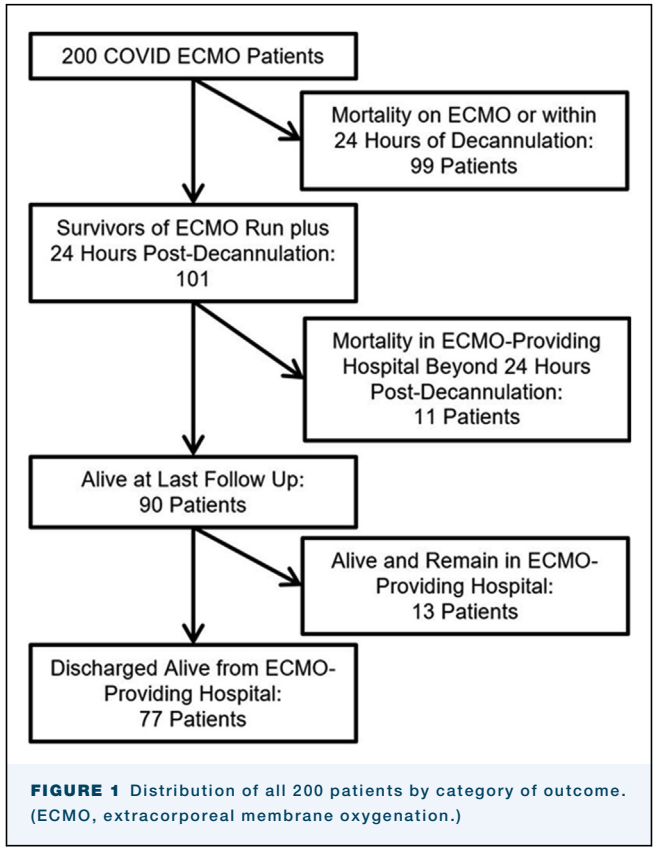

FIGURE 1 Distribution of all 200 patients by category of outcome. (ECMO, extracorporeal membrane oxygenation.)

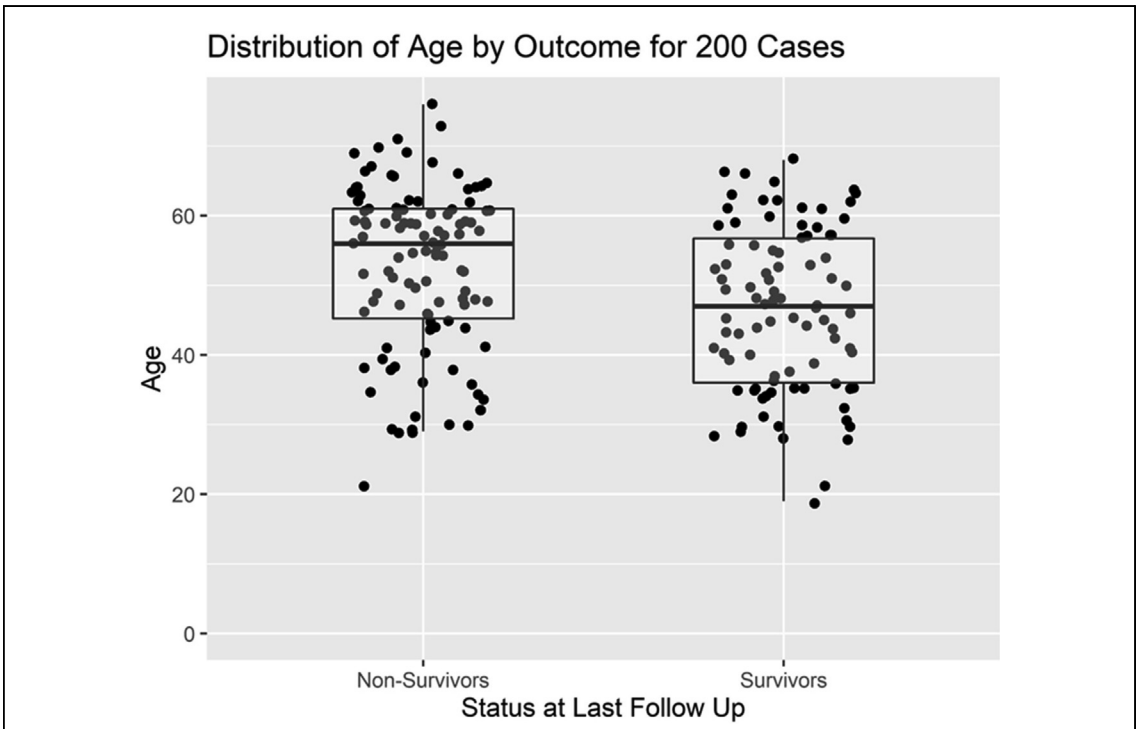

FIGURE 2 Distribution of age of patients, comparing survivors with nonsurvivors.

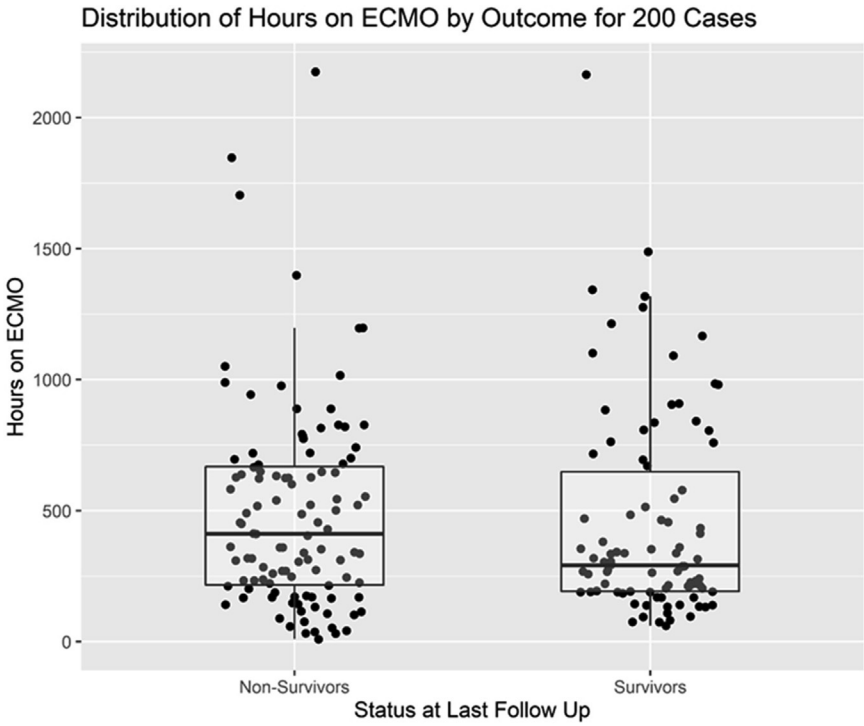

FIGURE 3 Distribution of hours on extracorporeal membrane oxygenation (ECMO), comparing survivors with nonsurvivors.

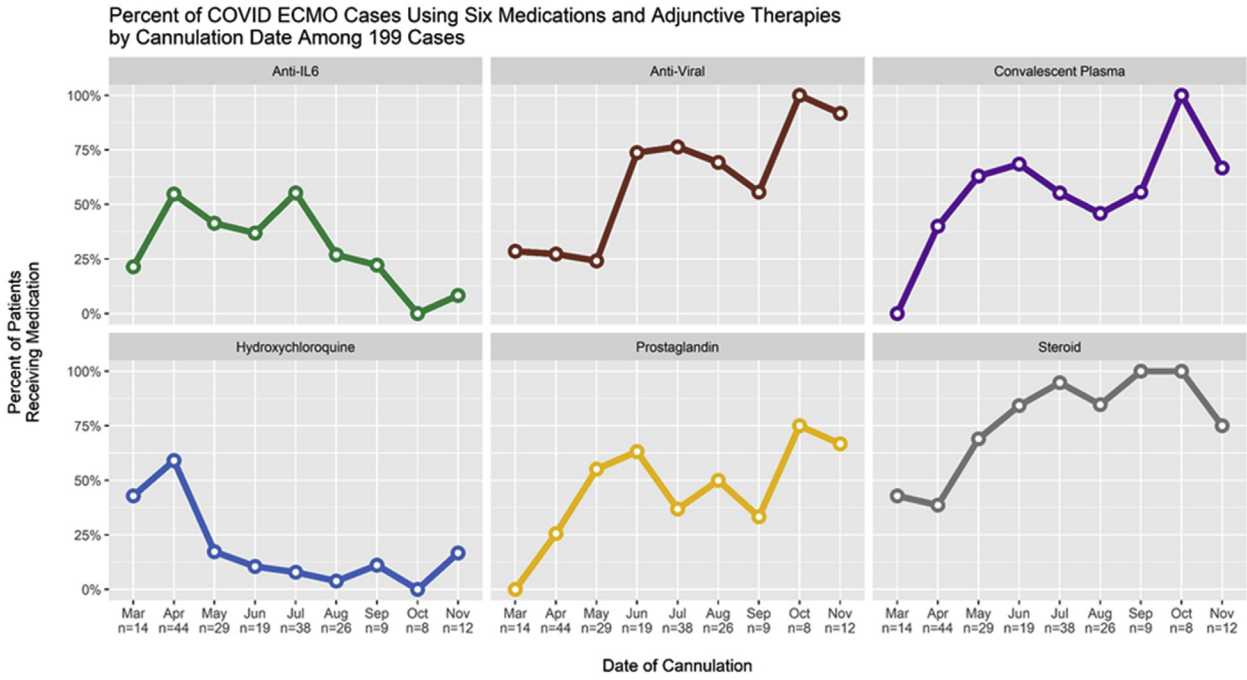

FIGURE 4 Monthly trends over time in the utilization of six adjunctive therapies in patients with COVID-19 while supported with extracorporeal membrane oxygenation (ECMO) during the 9 months of analysis: anti-interleukin-6–receptor monoclonal antibodies (tocilizumab or sarilumab [green line]); antiviral medications (remdesivir [brown line]); convalescent plasma (purple line); hydroxychloroquine (blue line); Flolan (prostaglandin [yellow line]); and intravenous steroids (gray line).

venovenous ECMO. Our study also reveals that, not surprisingly, survivors were younger than nonsurvivors (median age 47 for survivors versus 56 years for nonsurvivors, $P < .001$). This finding is consistent with the study from Barbaro and colleagues,[8] in which patients more than 40 years of age had an increasing risk of mortality compared with patients aged 16 to 39 years. Our study also reveals that survivors had a shorter median interval from the diagnosis of COVID-19 to cannulation for ECMO (8 versus 12 days, $P = .003$). This finding supports earlier consideration for use of ECMO in patients with COVID-19 and severe respiratory failure.

Finally, our study also documents that substantial variation exists in the use of adjunctive therapies in the treatment of COVID-19. The use of these various adjunctive medications and treatments has changed over time as more information has been obtained regarding the role and potential success of these medications.

FUTURE DIRECTIONS. Much remains to be learned about the role of ECMO in these patients. From our analysis, no specific demographic, clinical, or laboratory data, to date, is predictive of outcome with ECMO in patients with COVID-19, with the exception of younger age. Survivors tend to be younger and have a shorter duration from diagnosis to cannulation. Meanwhile, the role of multiple medications in the treatment of COVID-19 remains unclear: none of the adjunct therapies appeared to be associated with survival.

It is known that COVID-19 patients have faced challenges with thrombosis, and one third of the patients in this series required at least one circuit change. In the more recent era of our series bivalirudin has been used more commonly; however, the impact of the use of bivalirudin versus heparin needs additional investigation.

Several factors provide evidence that COVID-19 is different than other causes of respiratory failure, such as the flu; (1) no cause of respiratory failure has ever generated such a large utilization of ECMO in the history of medicine; (2) no cause of respiratory failure has ever generated this level of concern about the risks to health care providers caring for patients supported with ECMO; and (3) no cause of respiratory failure has ever placed this level of stress and this amount of resource consumption on the health care system.

Nevertheless, we believe that many of the lessons that have been learned by caring for COVID-19 patients supported with ECMO will likely be applicable to a variety of other etiologies of respiratory failure, now and in the future, as exemplified by the following lessons: (1) Earlier initiation of ECMO for patients with COVID-19 and respiratory failure appears to be associated with better outcomes, and this finding is likely true for other forms of respiratory failure as well. (2) Prolonged venovenous ECMO runs allow for the recovery of the native lungs in some patients with COVID-19 and facilitate bridge to lung transplantation in others. The use of such prolonged venovenous ECMO runs to support adults with respiratory failure is likely to become more common secondary to these valuable lessons learned during the COVID-19 pandemic.

STUDY LIMITATIONS. This analysis is based on the available data in our database. Potential limitations include patient selection bias, institutional bias, confounding bias, and potential underpowering of the analysis. Additional follow-up is required on all surviving patients. Further patient accrual will enhance continued analysis of outcomes. We plan to continue gathering data to provide additional insight into guideposts for patient selection and predictors of outcomes. It is our hope that by sharing our experience, other centers and patients may benefit.

CONCLUSION. Our experience and analysis of 200 consecutive patients at 29 hospitals reveal that ECMO facilitates salvage and survival of select critically ill patients with COVID-19. Survivors tend to be younger. Survival of patients supported with only venovenous ECMO is 46.3% in our cohort. Survivors had a shorter median interval from the diagnosis of COVID-19 to cannulation for ECMO, supporting earlier consideration for use of ECMO in patients with COVID-19 and severe respiratory failure. Substantial variation exists in drug treatment of COVID-19, but ECMO offers a reasonable rescue strategy. Additional gathering and analysis of data will inform appropriate selection of patients and provide guidance as to best use of ECMO in terms of timing, implementation, duration of support, and best criteria for discontinuation. Expansion of studies such as the current analysis presented here will provide a means to further define the role of ECMO in the management of severely compromised patients with COVID-19 and will serve to refine the optimal use of ECMO in these patients, with the goal of continuing to enhance survival.

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