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Extracorporeal Membrane Oxygenation in the Treatment of Severe Pulmonary and Cardiac Compromise in COVID-19: Experience with 32 patients

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Abstract

As COVID-19 cases surge worldwide, an urgent need exists to enhance our understanding of the role of extracorporeal membrane oxygenation (ECMO) in the management of severely ill patients with COVID-19 who develop acute respiratory and cardiac compromise refractory to conventional therapy. The purpose of this manuscript is to review our initial clinical experience in 32 patients with confirmed COVID-19 treated with ECMO.

A multi-institutional registry and database was created and utilized to assess all patients who were supported with ECMO provided by SpecialtyCare. 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 all of our patients with COVID-19 supported with ECMO, with an analytic window starting March 17, 2020 when our first COVID-19 patient was placed on ECMO, and ending April 9, 2020.

During the 24 days of this study, 32 consecutive patients with COVID-19 were placed on ECMO at 9 different hospitals. As of the time of analysis, 17 remain on ECMO, 10 died prior to or shortly after decannulation, and 5 are alive and extubated after removal from ECMO, with one of these 5 discharged from the hospital. Adjunctive medication in the surviving patients while on ECMO was as follows: 4 of 5 survivors received intravenous steroids, 3 of 5 survivors received antiviral medications (Remdesivir), 2 of 5 survivors were treated with anti-interleukin-6-receptor monoclonal antibodies (Tocilizumab or Sarilumab), and 1 of 5 survivors received hydroxychloroquine.

An analysis of 32 COVID-19 patients with severe pulmonary compromise supported with ECMO suggests 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 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.

I. Introduction

As of April 9, 2020, 1,579,690 patients around the world have been diagnosed with confirmed Coronavirus Disease 2019 (COVID-19), with 94,807 associated deaths (6.0% mortality worldwide) [1]. Meanwhile, in the United States of America, as of April 9, 2020, 452,582 patients have been diagnosed with confirmed COVID-19, with 16,129 associated deaths to date (3.6% mortality in the USA) [1]. Most deaths in patients with COVID-19 are due to severe respiratory failure, with a small group succumbing to combined pulmonary and cardiac failure [2, 3].

Extracorporeal membrane oxygenation (ECMO) is an advanced life support modality that was initially used to treat severe neonatal respiratory failure [4, 5]. Over time, the use of ECMO has expanded, with ECMO presently utilized widely to treat multiple forms of severe acute respiratory and/or cardiac failure in neonates, infants, children, and adults [5, 6]. In the 2009 CESAR trial, adults with severe acute respiratory failure were randomized to treatment with ECMO versus maximal conventional ventilatory support and management (e.g. steroids, prone positioning, bronchoscopy, and inhaled nitric oxide). In that study, 63% (57/90) of patients allocated to consideration for treatment using ECMO survived to 6 months without disability compared to 47% (41/87) of those allocated to conventional management.

In 2009 and 2010, the "swine-flu" H1N1 pandemic caused thousands of deaths in the United States. According to the Centers for Disease Control and Prevention (CDC) of the United States, from April 12, 2009 to April 10, 2010, there were "60.8 million cases (range: 43.3-89.3 million), 274,304 hospitalizations (range: 195,086-402,719), and 12,469 deaths (range: 8868-18,306) in the United States due to the (H1N1)pdm09 virus" [7]. During the H1N1 pandemic, ECMO was used successfully to salvage patients with severe respiratory failure, with an associated 79% survival [8].

As COVID-19 cases surge worldwide, an urgent need exists to enhance our understanding of the role of ECMO in the management of severely ill patients with COVID-19. The purpose of this report is to review our early clinical experience with the use of ECMO in 32 patients with confirmed COVID-19 and severe pulmonary compromise, some of whom also developed severe cardiac compromise.

II. Material and methods

A real time cohort study was conducted of all patients with confirmed COVID-19 who were supported with ECMO therapy provided by SpecialtyCare; a multi-institutional registry and database was created and utilized to assess these patients. (SpecialtyCare is a United States provider of allied health services: predominantly perfusion services and intraoperative neuromonitoring, based in Brentwood, Tennessee, USA. [https://specialtycareus.com/]) 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 database is prospectively maintained on all patients and has been used for data collection and analysis. The database used is a component of the SCOPE™ registry, SpecialtyCare, Nashville, Tennessee [https://specialtycareus.com/].

This analysis includes all of our patients with documented COVID-19 infection who were supported with ECMO, with an analytic window starting March 17, 2020, when our first COVID-19 patient was placed on ECMO, and ending April 9, 2020. Entry criteria for placement on ECMO was determined by the individual patient care team at the each of the 9 hospitals submitting data; all patients were placed on ECMO with severe respiratory failure felt to be refractory to conventional management. The decision to initiate ECMO, the mode of therapy (i.e. veno-veno, veno-arterial, etc.), and the cannulation strategy were all determined by the individual ECMO-Teams, as determined by their individual institutional protocols and guidelines.

Descriptive analysis of the entire cohort was performed using mean, standard deviation, median, and interquartile range, as appropriate. The primary outcome of interest was mortality during the index hospitalization. Potential differences in categorical variables by mortality group were assessed using chi-square and Fisher's exact tests, while possible differences in continuous variables by mortality group were assessed using Kruskal-Wallis rank sum tests and Welch's ANOVA.

Institutional Review Board approval and waiver of the need for consent were obtained. The human subjects' research protocol for this study was reviewed and approved by an independent Institutional Review Board. Institutional ethics review board approval was obtained for the use of data from the SCOPE^{TM} registry (Protocol #012017, ADVARRA Center for IRB Intelligence, 6940 Columbia Gateway Drive, Suite 110, Columbia, Maryland, 21046, USA).

III. RESULTS

During the 24 days of this study, 32 consecutive patients with COVID-19 were placed on ECMO at 9 different hospitals. Table 1 depicts the number of patients with COVID-19 placed on ECMO at each hospital and the geographic location of each hospital, as well as data about the number of patients in each State diagnosed with COVID-19, hospitalized for COVID-19 and dead. These regional data contextualize the data from each hospital,

As of the time of analysis, 17 out of 32 patients remain on ECMO, 10 died prior to or shortly after decannulation, and 5 are alive following discontinuation of ECMO. All of the 5 survivors have been separated from mechanical ventilation, with one having been discharged from the hospital to date. Table 2 provides detailed data about all 32 patients with COVID-19 treated with ECMO. Of note, 14 of 32 patients (43.8%) had obesity, 11 of 32 patients (34.4%) had diabetes, 4 of 32 patients (12.5%) had heart disease, 3 of 32 patients (9.4%) had cancer, and 3 of 32 patients (9.4%) had asthma.

Table 3 provides detailed data about 15 patients with COVID-19 treated with ECMO and no longer on ECMO and compares the characteristics of the 5 survivors to the 10 non-survivors. Adjunctive medication in the surviving patients while on ECMO was as follows: 4 of 5 survivors received intravenous steroids, 3 of 5 survivors received antiviral medications (Remdesivir), 2 of 5 survivors were treated with anti-interleukin-6 receptor monoclonal antibodies (Tocilizumab or Sarilumab), and 1 of 5 survivors received hydroxychloroquine. In the 10 patients who died, documented causes of death were: respiratory failure (6/10), disseminated intravascular coagulation (DIC, 2/10), multisystem organ failure (MSOF) including acute kidney injury (1/10), and cerebral bleeding while on ECMO (1/10).

None of these 32 patients were placed on ECMO during cardiopulmonary resuscitation (i.e. extracorporeal CPR [or ECPR]) was not utilized in this cohort). All 5 survivors were supported only with veno-venous ECMO. Furthermore, no patients receiving partial or complete veno-arterial ECMO have survived decannulation (Five patients were supported with partial or complete veno-arterial ECMO: three have died and 2 remain on ECMO). Zero patients were converted from veno-venous ECMO to veno-arterial ECMO. Zero patients were converted from veno-venous ECMO to V-AV ECMO (ECMO with systemic venous inflow with dual systemic venous and systemic arterial outflow [combined veno-venous and veno-arterial ECMO]).

Figure 1 depicts the current status of all 32 Covid-19 ECMO patients. Figure 2 depicts the number of patients cannulated each week. Figure 3 depicts the distribution of hours on ECMO, comparing the Survivors with the Non-survivors. Figure 4 depicts the distribution of the age of the patients, comparing the Survivors with the Non-survivors.

A brief case history of one of these patients is enlightening: A 51 white female with no past medical history sustained an orthopedic injury while on vacation in Vail, Colorado. On March 7, 2020, she underwent elective repair of her ankle injury. During extubation from the orthopedic

procedure, frothy pink sputum was noted. The patient was isolated, tested for COVID-19, and found to be positive. She was soon reintubated and was transferred to a tertiary care center near Denver, Colorado on March 13, 2020. She developed acute respiratory distress syndrome (ARDS) and was proned. On March 19, 2020, she was placed on veno-venous ECMO. On March 22, 2020, she received her first of 9 doses of compassionate use Remdesivir. On March 27, 2020, her respiratory status improved and her ECMO flow and ventilatory settings were weaned. Two days later, on March 29, 2020, after 10 days on ECMO, she was successfully decannulated and separated from ECMO. On April 1, 2020, she was extubated. On April 8, 2020, she was discharged from the hospital on room air and went to a rehabilitation facility for her orthopedic injury.

IV. Discussion

Clinical guidelines for the management of patients with COVID-19 have been released by the World Health Organization (WHO) [9] and the CDC [10]. The Extracorporeal Life Support Organization (ELSO) [11] and The American Society for Artificial Internal Organs (ASAIO) [12] both recently published guidelines about the role of ECMO in treating patients with COVID-19. Nevertheless, the role of ECMO in the management of these challenging patients remains unclear. Here, we report on our recent initial experience in 32 severely ill COVID-19 patients with severe pulmonary compromise, some of whom also developed severe cardiac compromise. While readily deployed, our initial experience demonstrated that 22/32 patients are alive (68%), with 17/32 (53.1%) alive on ECMO, though with only 5/15 (33.3%) surviving to date post ECMO removal. While our early limited experience does not allow for subgroup analysis, it is important to note that all 5 survivors were supported with only veno-veno ECMO. Thus, survival of patients treated with only veno-venous ECMO and separated from veno-venous ECMO is 5 out of 12 (41.7%) – outcomes that are reasonable in the context of contemporary use of ECMO for ARDS in adults [6]. Our hope is that this early experience will provide information about the real-world results of ECMO in patients with

COVID-19 pneumonia and facilitate decision-making at the bedside. Further, this analysis will inform and drive future research to improve outcomes. Out of this analysis and subsequent experience with ECMO, insight will arise as to the appropriate role, timing, and utility of ECMO in patients with severe COVID-19.

A recently published retrospective, single-center study included all 99 patients with confirmed COVID-19 pneumonia in Wuhan Jinyintan Hospital between January 1, 2020 and January 20, 2020 [13]. Patients had clinical manifestations of fever (82 [83%] patients), cough (81 [82%] patients), shortness of breath (31 [31%] patients), muscle ache (11 [11%] patients), confusion (nine [9%] patients), headache (eight [8%] patients), sore throat (five [5%] patients), rhinorrhea (four [4%] patients), chest pain (two [2%] patients), diarrhea (two [2%] patients), and nausea and vomiting (one [1%] patient). Radiographic evaluation documented that 74 (75%) patients showed bilateral pneumonia, 14 (14%) patients showed multiple mottling and ground-glass opacity, and one (1%) patient had pneumothorax. 17 (17%) patients developed acute respiratory distress syndrome. Oxygen therapy was used in 75 (76%), non-invasive (i.e. face mask) mechanical ventilation was used in 13 (13%), invasive mechanical ventilation was used in 4 (4%), continuous renal replacement therapy (CRRT) was used in 9 (9%), and ECMO was used in 3 (3%). Eleven patients (11%) patients died of multiple organ failure.

An additional publication from Wuhan describes 52 critically ill adult patients with COVD-19 pneumonia who were admitted to the intensive care unit (ICU) of Wuhan Jin Yin-tan hospital (Wuhan, China) between late December, 2019, and Jan 26, 2020. Six of these patients were supported with ECMO with an alarmingly high mortality of 83% (5 out of 6) [14, 15]. Clearly, very limited published information exists about the role of ECMO in patients with COVID-19.

Our analysis of 32 patients from 9 hospitals reveals that ECMO may play a meaningful role in salvaging select critically ill patients with COVID-19. Out of 32 consecutive patients with COVID-19 were placed on ECMO at 9 different hospitals: 17 remain on ECMO, 10 died prior to or shortly after decannulation, 5 are alive after separation from ECMO. All 5 of the survivors are extubated, and one has been discharged from the hospital on room air. Thus, 5 out of 15 patients (33.33%) who have been decannulated so far have survived. Our early experience seems to indicate that patients who require veno-arterial support have a poor prognosis in comparison to patients who require only veno-venous support. From our experience to date, further study will be necessary to tease out predictors of those COVID patients most likely to benefit from this therapy. Hopefully as centers gain experience with this challenging and complex clinical problem, patient selection and outcomes will improve.

The Extracorporeal Life Support Organization (ELSO) maintains an on-line worldwide registry of COVID-19 patients treated with ECMO [16]. As of April 9, 2020, in the ELSO registry, the entire global experience of COVID-19 patients supported with ECMO is 216 suspected or confirmed COVID-19 patients and 212 confirmed COVID-19 patients, with 9 out of 30 (30%) discharged alive. The North American experience of COVID-19 patients supported with ECMO is 150 confirmed COVID-19 patients, with 108 patients still on ECMO and 42 patients listed as completed ECMO. These data from ELSO provide an overall snapshot of the scope of ECMO use in patients with COVID-19, both worldwide and in in North America. Our multi-institutional analysis of 32 patients with COVID-19 treated at 9 hospitals provides more detailed information about the early challenges and results.

To provide guidance about the use of ECMO in severely ill COVID-19 patients, the American Society for Artificial Internal Organs (ASAIO) has recently developed and published a recommendations statement as to emerging and best practices for ECMO in COVID-19, as a living document that will be updated periodically to help fine tune ECMO selection and best practices [12].

To compliment this recent publication, ASAIO has developed a database specific to ECMO use in severe COVID-19 to aid in this effort. Merging and synergizing data between databases such as those obtained by SpecialtyCare, ELSO, and ASAIO, as well as other sources, will begin to provide insight about the relevant exposure, demographics, comorbidities, and clinical and laboratory variables that may be predictive of outcome, inform selection of patients, guide timing of initiation of ECMO, or even suggest futility.

Of note, it is also interesting that 4 of the 5 ECMO survivors received intravenous steroids. While the decision to use steroids was determined by the individual providers, the use of steroids was discouraged in the early Chinese reports, as well as in some of the current COVID-19 management guidelines [17]. This observation clearly illustrates that there is still much to be understood about the potential therapeutic options in this extremely heterogenous population.

The concerning poor outcomes associated with veno-arterial ECMO in patients with COVID-19 suggest that the combined COVID-19 respiratory and cardiac failure might convey an inherently poor prognosis, regardless or treatment, or that alternative support therapies might be better suited for this complex pathophysiologic scenario. For example, anecdotal unpublished experiences suggest that veno-veno ECMO might be used to support isolated respiratory failure and if the patient has concomitant cardiac failure, then targeted right or left ventricular temporary percutaneous support might be considered (i.e. right ventricular or left ventricular Impella [Abiomed, Inc., Danvers, Massachusetts]).

Our initial findings also illustrate the need for further data regarding the optimal cannulation strategy in these patients. Ultimately, the situation of each patient will need to be individualized by the local Team with consideration of the physiologic needs, comfort in cannulation and cannula management (especially since some of these patients might be considered for prone positioning), as well as available resources. There may be some debate regarding cannula types and locations of

vascular access in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is important to remember that the causative pathogen of COVID-19 is highly contagious and transmitted typically via respiratory droplets/fomites (although there are some concerns for other modes of viral transmission) [7]. Therefore, it is critical that at the time of cannulation, strict sterile technique along with respiratory droplet isolation precautions, including negative airflow isolation, be adhered to by the cannulating and management Team. Cannulation in the context of COVID-19 is performed with full airborne and droplet precautions. The cannulation team is restricted to the surgeon, one assistant and the perfusionist, and is performed in a negative pressure room. All Team members must wear appropriate personal protective equipment, beyond the sterile gowns, gloves, and hats used in the operating room, including appropriate N-95 masks and full protective eye-wear [18]. Ultrasound-guided access of the right internal jugular vein and right femoral vein can minimize the duration of cannulation. Avoiding the use of dual lumen bicaval cannulas will decrease the need for either TEE or fluoroscopy, each of which may unnecessarily increase exposure and time. Another potential strategy is to position the isolated patient with the ECMO console facing towards a window so that the ECMO Specialist is able to view the control panel and parameters without having to stay in the room, thereby minimizing patient contact and potential pathogen exposure.

As experience matures, a better understanding of contraindications to ECMO in COVID-19 patients is necessary and will emerge. While there are few absolute contraindications, given the concerns for limited resources, as protocols are developing, there are concerns that advanced relative age (i.e. >65 years/old), multiple comorbidities, acute or chronic end-organ failure, and recent cardiopulmonary arrest are inherently associated with a poor prognosis in COVID-19 patients placed on ECMO. Some have advocated restricting mechanical support to veno-venous rather than veno-arterial ECMO. Each patient must be considered on a case-by-case basis, with great hesitation regarding candidacy in the context of advanced age, and those comorbidities that portend a poor

prognosis, including diabetes, heart disease, obesity, and especially patients with underlying terminal disease, central nervous system hemorrhage, and evidence of MSOF. Finally, many centers have adopted a policy that COVID-19 patients are not candidates for ECPR, a policy related to both poor prognosis and protection of the healthcare team.

Our multi-center experiences suggest that there is some potential role for ECMO in appropriately selected patients with COIVID-19. While the risk factors and variables that contribute to optimal outcomes are inherently complex and probably reflect individual center experiences and available resources, it can be argued that it would be unethical to withhold ECMO , – or consideration for referral to an experienced ECMO center – in patients who might potentially benefit from this therapy [19].

Future Directions

Much remains to be learned about the role of ECMO in these patients. From our analysis to date, no specific demographic, clinical, or laboratory data, to date, is predictive of outcome with ECMO in patients with COVID-19. Similarly, the role of multiple medications in the treatment of COVID-19 remains unclear, including intravenous steroids while on ECMO, antiviral medications (Remdesivir), anti-interleukin-6 receptor monoclonal antibodies (Tocilizumab, Siltuximab, or Sarilumab), and hydroxychloroquine.

Accumulating evidence suggests that a subgroup of patients with severe COVID-19 have a cytokine storm syndrome in which a cascade of activated cytokines leads to harmful auto-amplifying inflammatory cytokine production [20. 21. 22]. Termed the “cytokine storm”, this response often leads to organ damage and increases the risk of death. Among COVID-19 patients which have received ECMO, a strong positive correlation exists between mortality and high cytokine levels, most notably IL-6 [15, 22, 23, 24]. Ruan and colleagues documented that that IL-6 concentrations differed significantly between survivors and non-survivors of COVID-19, with non-survivors having up to 1.7-

times higher values [22, 24]. Multiple therapeutic strategies might mitigate "cytokine storm", including antibody therapies (e.g. Tocilizumab, Sarilumab, Siltuximab), therapeutic plasma exchange (TPE), and even direct removal of cytokines. TPE can reduce cytokine levels by separating and removing plasma from blood and replacing the removed plasma with fresh frozen plasma [25]. CytoSorb® [https://cytosorbents.com/products/cyto-sorb/] is an extracorporeal cytokine adsorber that has been approved in the European Union to reduce toxic levels of cytokines; this technology might be combined with ECMO to treat cytokine storm associated with sever COVID-19 pneumonia. Initial experience with this approach has recently been reported [26, 27]. It is a fact that each of these theoretical treatment options merit additional investigation.

Limitations

This analysis reports very preliminary data. Additional follow-up is required on all surviving patients. Further patient accrual will enhance continued analysis of outcomes. Although our experience is the largest published analysis of COVID-19 patients treated with ECMO to date, we recognize that our dataset is relatively small, and we plan to continue gathering data to provide additional insight as to guideposts for patient selection and predictors of outcomes. It is our hope that by sharing our experience, other centers and patients may benefit.

V. Conclusion

Our early experience and analysis of 32 patients from 9 hospitals reveals that ECMO plays a role in the stabilization and survival of select critically ill patients with COVID-19. During 24 days, 32 consecutive patients with COVID-19 placed on ECMO at 9 different hospitals: 17 remain on ECMO, 10 died prior to or shortly after decannulation, 5 are alive and extubated after separation from ECMO, and one of these 5 has been discharged from the hospital. 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. A

tremendous amount of information still needs to be learned about the role of ECMO in treating patients these sickest of patients with COVID-19.

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Legends for Figures:

Figure 1 depicts the current status of all 32 covid-19 ECMO patients.

Figure 2 depicts the number of patients cannulated each week.

Figure 3 depicts the distribution of hours on ECMO, comparing the Survivors with the Non-survivors.

Figure 4 depicts the distribution the age of the patients, comparing the Survivors with the Non-survivors.

Table 1. Number of patients with COVID-19 placed on ECMO at each hospital and the geographic location of each hospital, along with data about the number of patients in each State diagnosed with COVID-19, hospitalized for COVID-19 and dead.

Hospital	Number of Patients with COVID-19 placed on ECMO	State	Patients in State Diagnosed with COVID-19 as of April 13, 2020	Patients in State Hospitalized as of April 13, 2020	Patients in State in Intensive Care Unit as of April 13, 2020	Deaths in State as of April 13, 2020
A	10	California	23338[a]	3124[a]	1177[a]	758[a]
B	7	Texas	15492[b]	1538[b]		364[b]
C	3	Colorado	8280[c]	1636[c]		357[c]
D	3	Washington, D.C.	2197[d]			72[d]
E	3	Pennsylvania	26490[e]	2440[e]		647[e]
F	2	Florida	21865[f]	3249[f]		614[f]
G	2	Pennsylvania	26490[e]	2440[e]		647[e]
H	1	Hawaii	530[g]			9[g]
I	1	Indiana	8955[h]	737[h]		436[h]
Total: 32 Patients, 9 Centers						

a https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/Immunization/ncov2019.aspx
b https://txdshs.maps.arcgis.com/apps/opsdashboard/index.html#/ed483ecd702b4298ab01e8b9cafc8b83
c https://covid19.colorado.gov/case-data
d https://coronavirus.dc.gov/release/coronavirus-data-april-14-2020
e https://www.health.pa.gov/topics/disease/coronavirus/Pages/Cases.aspx
f https://floridahealthcovid19.gov/
g https://health.hawaii.gov/coronavirusdisease2019/what-you-should-know/current-situation-in-hawaii/
h https://www.coronavirus.in.gov/

Table 2. Overview of Patients with COVID-19 treated with ECMO

	Level	Overall
N		32
Days from COVID Diagnosis to Intubation (mean (SD))		2.47 (3.52)
Days from COVID Diagnosis to Intubation (median [IQR])		1.00 [1.00, 3.00]
Days from Intubation to Cannulation (mean (SD))		4.26 (2.35)
Days from Intubation to Cannulation (median [IQR])		4.00 [2.00, 6.50]
Days on ECMO (mean (SD))		7.33 (3.31)
Days on ECMO (median [IQR])		6.00 [5.00, 10.00]
Hours on ECMO (mean (SD))		166.53 (81.31)
Hours on ECMO (median [IQR])		143.00 [105.00, 233.00]
Age (mean (SD))		52.41 (12.49)
Age (median [IQR])		52.41 (12.49)
Gender (Count (%))	Female	10 (31.2)
	Male	22 (68.8)
Cancer (Count (%))	No	28 (87.5)
	Unknown	1 (3.1)
	Yes	3 (9.4)
Diabetes (Count (%))	No	20 (62.5)
	Unknown	1 (3.1)
	Yes	11 (34.4)
Heart Disease (Count (%))	No	27 (84.4)
	Unknown	1 (3.1)
	Yes	4 (12.5)
Obesity (Count (%))	No	17 (53.1)
	Unknown	1 (3.1)
	Yes	14 (43.8)
Asthma (Count (%))	No	27 (84.4)
	Unknown	2 (6.2)
	Yes	3 (9.4)
Proned Before ECMO (Count (%))	No	7 (21.9)
	Unknown	5 (15.6)
	Yes	20 (62.5)
CVVH or CRRT Used (Count (%))	No	10 (31.2)
	Unknown	10 (31.2)
	Yes	12 (37.5)
ECMO Type (Count (%))	Unknown	1 (3.1)
	V-A	3 (9.4)
	V-AV to V-V	1 (3.1)
	V-V	25 (78.1)
	V-V, VV-A	1 (3.1)
	V-V, VV-V	1 (3.1)
Anticoagulation Type (Count (%))	Argatroban	2 (6.2)
	Heparin	28 (87.5)
	Unknown	2 (6.2)
Anti-Interleukin-6 receptor monoclonal antibodies (Count (%))	No	26 (81.2)
	Yes	6 (18.8)
Anti-Viral Medication (Count (%))	No	26 (81.2)
	Yes	6 (18.8)
Hydroxychloroquine (Count (%))	No	31 (96.9)
	Yes	1 (3.1)
Intravenous Steroids (Count (%))	Unknown	27 (84.4)
	Yes	5 (15.6)

Legend:
V-A = veno-arterial ECMO
V-AV = ECMO with systemic venous inflow with dual systemic venous and systemic arterial outflow (i.e., V-V and V-A combined)
V-V = veno-venous ECMO
VV-A = V-A ECMO with dual systemic venous cannulation for inflow (typically bicaval systemic venous drainage)
VV-V = V-V ECMO with dual systemic venous cannulation for inflow (typically bicaval systemic venous drainage)

Table 3. Overview of Patients with COVID-19 treated with ECMO and no longer on ECMO

	Level	Mortality on ECMO	Successful Wean from ECMO	p
N		10	5	
Days from COVID Diagnosis to Intubation (mean (SD))		0.00 (1.41)	3.00 (3.46)	0.308
Days from COVID Diagnosis to Intubation (median [IQR])		0.00 [-0.50, 0.50]	1.00 [1.00, 3.00]	0.135
Days from Intubation to Cannulation (mean (SD))		4.67 (2.08)	3.80 (2.39)	0.623
Days from Intubation to Cannulation (median [IQR])		4.00 [3.50, 5.50]	4.00 [2.00, 5.00]	0.651
Days on ECMO (mean (SD))		6.80 (3.08)	8.40 (3.85)	0.397
Days on ECMO (median [IQR])		6.00 [5.00, 9.50]	8.00 [6.00, 10.00]	0.497
Hours on ECMO (mean (SD))		153.40 (76.54)	192.80 (93.08)	0.396
Hours on ECMO (median [IQR])		135.50 [103.50, 223.50]	170.00 [133.00, 232.00]	0.54
Age (mean (SD))		56.70 (12.81)	52.80 (10.47)	0.567
Age (median [IQR])		56.70 (12.81)	52.80 (10.47)	0.567
Gender (Count (%))	Female	2 (20.0)	3 (60.0)	0.333
	Male	8 (80.0)	2 (40.0)	
Cancer (Count (%))	No	9 (90.0)	4 (80.0)	1
	Yes	1 (10.0)	1 (20.0)	
Diabetes (Count (%))	No	5 (50.0)	3 (60.0)	1
	Yes	5 (50.0)	2 (40.0)	
Heart Disease (Count (%))	No	9 (90.0)	5 (100.0)	1
	Yes	1 (10.0)	0 (0.0)	
Obesity (Count (%))	No	5 (50.0)	2 (40.0)	1
	Yes	5 (50.0)	3 (60.0)	
Asthma (Count (%))	No	10 (100.0)	4 (80.0)	0.714
	Yes	0 (0.0)	1 (20.0)	
Proned Before ECMO (Count (%))	No	3 (30.0)	1 (20.0)	0.962
	Unknown	2 (20.0)	0 (0.0)	
	Yes	5 (50.0)	4 (80.0)	
CVVH or CRRT Used (Count (%))	No	2 (20.0)	3 (60.0)	0.782
	Unknown	4 (40.0)	0 (0.0)	
	Yes	4 (40.0)	2 (40.0)	
ECMO Type (Count (%))	V-A	1 (10.0)	0 (0.0)	0.604
	V-AV to V-V	1 (10.0)	0 (0.0)	
	V-V	6 (60.0)	5 (100.0)	
	V-V, VV-A	1 (10.0)	0 (0.0)	
	V-V, VV-V	1 (10.0)	0 (0.0)	
Anticoagulation Type (Count (%))	Argatroban	2 (20.0)	0 (0.0)	0.788
	Heparin	8 (80.0)	5 (100.0)	
Anti-Interleukin-6 receptor monoclonal antibodies (Count (%))	No	9 (90.0)	3 (60.0)	0.494
	Yes	1 (10.0)	2 (40.0)	
Anti-Viral Medication (Count (%))	No	9 (90.0)	2 (40.0)	0.494
	Yes	1 (10.0)	3 (60.0)	
Hydroxychloroquine (Count (%))	No	10 (100.0)	4 (80.0)	0.714
	Yes	0 (0.0)	1 (20.0)	
Intravenous Steroids (Count (%))	Unknown	9 (90.0)	1 (20.0)	N/A
	Yes	1 (10.0)	4 (80.0)	

Legend:
V-A = veno-arterial ECMO
V-AV = ECMO with systemic venous inflow with dual systemic venous and systemic arterial outflow (i.e., V-V and V-A combined)
V-V = veno-venous ECMO
VV-A = V-A ECMO with dual systemic venous cannulation for inflow (typically bicaval systemic venous drainage)
VV-V = V-V ECMO with dual systemic venous cannulation for inflow (typically bicaval systemic venous drainage

Figure 1

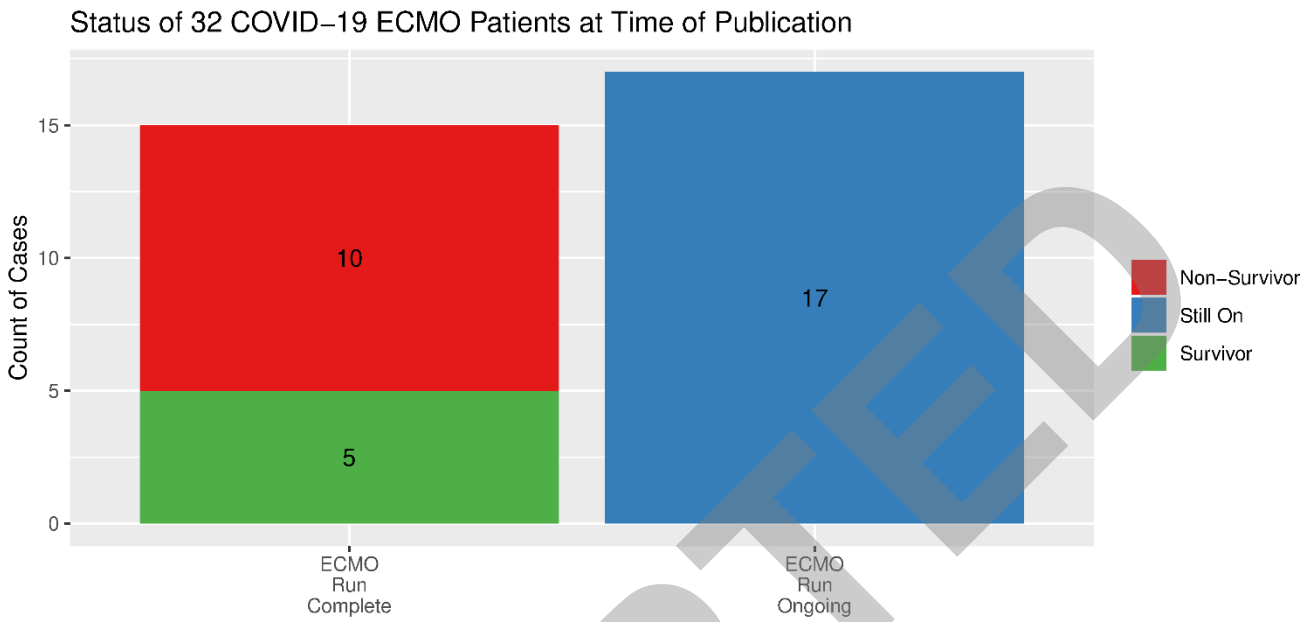

Figure 2

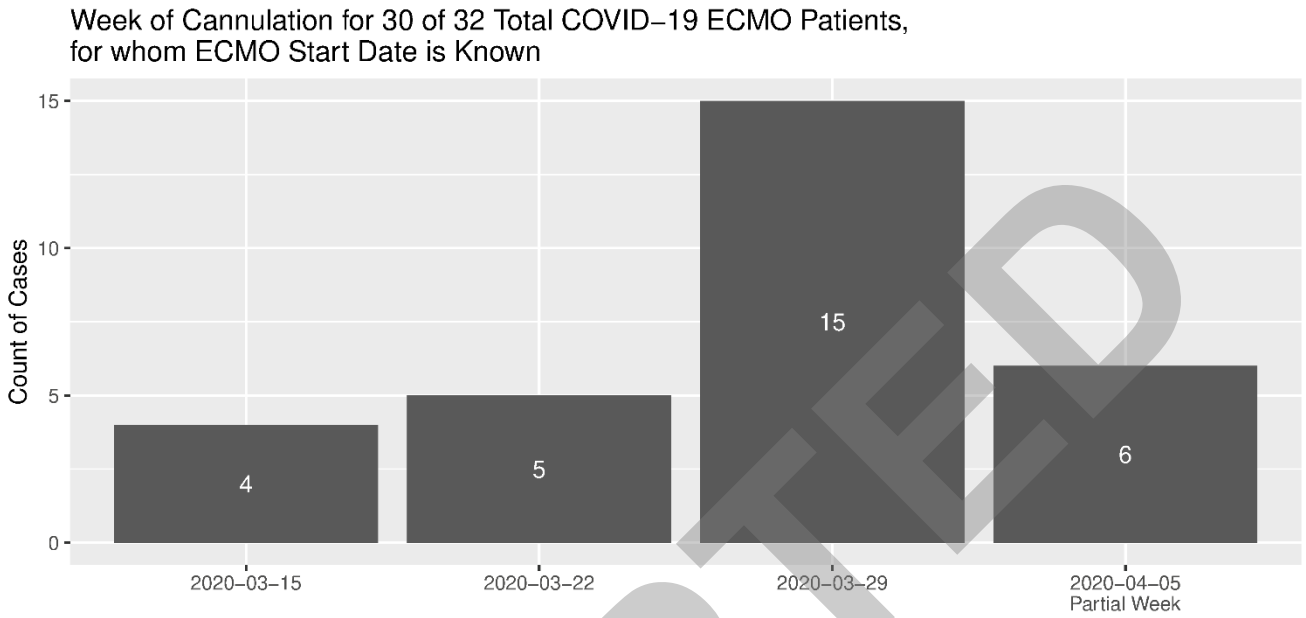

Figure 3

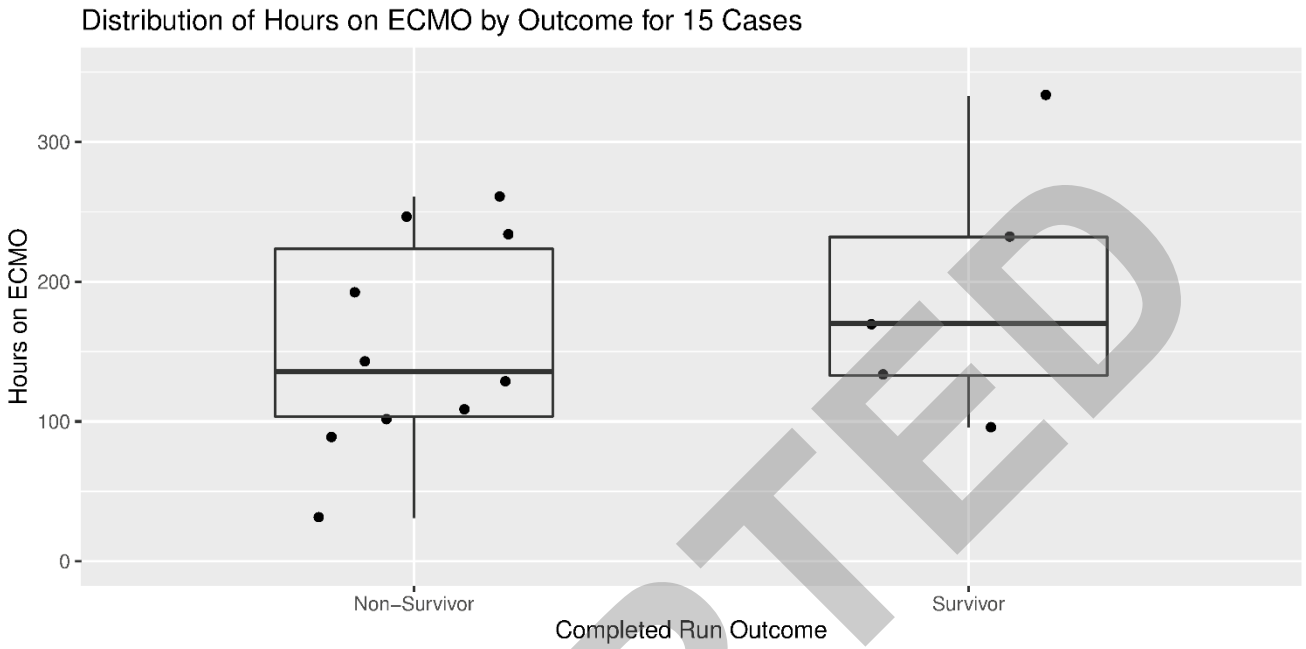

Figure 4