Improving Extracorporeal Membrane Oxygenation Survival in COVID-19. Effect of a Bundle of Care

LEONARDO SALAZAR, ANDERSON BERMÚDEZ, RAUL VASQUEZ, MARIO CASTILLO, ALEJANDRA MENDOZA-MONSAVÉ, MARIA F. LANDINEZ, ANGELICA L. ORTIZ-CORDOBA, KARENH J. MENESES, WILFRAN J. FERRER, JULIANA BALLESTEROS, ANDRES ESPINOSA, MARIA P. PIZARRO, JORGE PINILLA-OJEDA, CINTHA P. MAYORGA-SUAREZ, ELKIN J. PARDO, IVAN H. MERCHEÑ, JAVIER ALVAREZ, RODRIGO DIAZ, CAMILO P. PIZARRO.

Veno-venous extracorporeal membrane oxygenation (ECMO) support surged during the COVID-19 pandemic. Our program changed the model of care pursuing to protect the multidisciplinary team from the risk of infection and to serve as many patients as possible. Patient–healthcare interactions were restricted, and the ECMO bed capacity was increased by reducing the ECMO specialist–patient ratio to 1:4 with non-ECMO trained nurses support. The outcomes worsened and we paused while we evaluated and modified our model of care. The ECMO bed capacity was reduced to allow a nurse ECMO–specialist nurse ratio 2:1 with an ECMO trained nurse assistant’s support. Intensivists, general practitioners, nurse assistants, and physical and respiratory therapists were trained on ECMO. Tracheostomy, bronchoscopy, and microbiological molecular diagnosis were done earlier, and family visits and rehabilitation were allowed in the first 48 hours of ECMO cannulation. There were 35 patients in the preintervention cohort and 66 in the postintervention cohort. Ninety days mortality was significantly lower after the intervention (62.9% vs. 31.8%, p = 0.003). Factors associated with increased risk of death were the need for cannulation or conversion to veno arterial or veno arterio venous ECMO, hemorrhagic stroke, and renal replacement therapy during ECMO. The interventions associated with a decrease in the risk of death were the following: early fiberoptic bronchoscopy and microbiological molecular diagnostic tests. Increasing the ECMO multidisciplinary team in relation to the number of patients and the earlier performance of diagnostic and therapeutic interventions, such as tracheostomy, fiberoptic bronchoscopy, molecular microbiological diagnosis of pneumonia, rehabilitation, and family support significantly decreased mortality of patients on ECMO due to COVID-19. ASAIO Journal 2022; 68;1233–1240

Key Words: extracorporeal membrane oxygenation, COVID-19, outcome and process assessment health care, survival analysis

Worldwide, until June 2021, there have been 3,531,000 deaths because of SARS COV-2 infection, and 10–20% of the patients required intensive care. SARS COV-2 has become the leading etiology of deaths within acute respiratory distress syndrome (ARDS). In a COVID-19 patients meta-analysis, the case fatality rate was estimated as 45% in the invasive mechanically ventilated population.

Extracorporeal membrane oxygenation (ECMO) can improve survival and is an alternative method to rescue patients with high mortality risk. In the last year, a significant increase in ECMO use has been reported, from 4,779 respiratory indications in adults in the extracorporeal life support organization registry during 2019 to 7161 in 2020.

Health centers have been rapidly transformed to address this pandemic, balancing the risk of contagion in health workers with the aim of better results for patients. Unfortunately, no studies have reported the impact of adjustment strategies for managing severe patients who have required management with ECMO.

During the first wave, our ECMO program changed the model of care. We experienced an increase morbidity and mortality. We stopped to cannulate patients for 2 weeks, asked for help, and made changes in our protocols before we start again. The study aims to evaluate the impact of a bundle of changes in the 90-day survival rate.

Methods

A quasi-experimental type, before and after, ambispective study was conducted of all confirmed COVID-19 patients who received support from ECMO support provided at the Fundación Cardiovascular de Colombia. A registry was created in RedCap (RM); the data captured included age, sex, history of immunocompromise, weight, conditions before ECMO admission (previous arrest, chronic renal failure requiring hemodialysis, and days of ventilation), and variables at the time of starting ECMO, such as initial configuration (veno venous or veno arterial), pH, positive end-expiratory pressure, plateau pressure, FiO2, PO2, PaCO2, P-peak, tidal volume, D dimer, creatinine, lymphocytes, and platelets. The primary outcome was actuarial mortality at 90 days. Secondary outcomes were ECMO complications and factors associated with survival between the two cohorts.

Patients with confirmed SARS-COV-2 infection who received ECMO in our institution from June 16, 2020, to March 14, 2021, were included.
During the first wave of the COVID-19 pandemic, the ECMO program of the Fundación Cardiovascular de Colombia faced an increase in patients with ECMO indication. It was decided to change the care model to respond to this contingency’s challenges.

The priority was to protect the multidisciplinary team from the risk of infection. Strategies were implemented to minimize contact between the multidisciplinary team and the patients. Aerosol-generating procedures were performed after 14 days of orotracheal intubation. A COVID-19 quantitative real-time polymerase chain reaction (RT-PCR) was requested in healthcare workers and patient relatives that developed COVID symptoms.

The second purpose was to serve as many patients as possible, even with the support of untrained personnel under the supervision of ECMO specialists. This led to the ratio between the ECMO specialist nurse and patients being 1:4 at the most critical moment.

After 3 months, there was a notable increase in the mortality of the program. It was decided to suspend the admission of new patients for 2 weeks and evaluate the care model with the support of the ECMO program of Clínica las Condes in Chile. It was decided to make changes in various aspects which are explained below.

Staff and Training

The maximum number of simultaneous patient runs on ECMO was decreased from 16 to 10 to have a maximum of two patients for each ECMO specialist nurse, with the support of a nursing assistant with basic training in ECMO. Two types of training were conducted. The ECMO specialist training course (40 hours of lectures, wet labs, high fidelity simulations plus 60 hours of supervised ECMO patient care) was provided to new ICU nurses, general practitioners, and intensivists. A basic ECMO patient care course (12 hours of lectures and 6 hours of high fidelity simulations) was provided to nursing assistants and respiratory, occupational, speech, and physical therapists. Changes in personnel and their training are given in Table 1.

Patient Care

Institutional guidelines

EOLIA trial ECMO indications were adopted in both cohorts. Percutaneous 25 femoral drainage and 21 jugular infusion cannulation was our initial approach. A centrifugal pump with a 5- or 7-L oxygenation membrane ECMO circuit was used according to the oxygen transfer patient needs. No continuous circuit pressures were measured. If the circuit flow/RMP relationship changed a perfusionist made a discrete circuit pressures measurement. As a result of ECMO medical devices shortage, many brands were used according with their availability (percutaneous cannulas: Medtronic, Livanova, Edwards. Centrifugal pumps: Medtronic, Maquet, Livanova, Abbot. Oxigenation Membranes: Livanova, Maquet, Eurosets). Patients were anticoagulated with unfractioned heparin drip to obtain a Partial Thromboplastin Time between 40 and 50 seconds. The heparin drip was stopped if the patient developed bleeding with increased transfusion needs and restarted once the bleeding was controlled.

Patient Management Changes

First cohort

An open tracheostomy was performed after 14 days of intubation. The patient was deeply sedated while was intubated with intravenous (iv) infusion of hypnotics, benzodiazepines, and opioids according with medication availability. After tracheostomy dexmedetomidine and new antipsychotics were started while sedatives drips were slowly weaned. Tracheal aspirates with aerobic and anaerobic cultures were used to diagnose ventilator pneumonia (VAP) and antibiotics were selected according with the antibiogram. Family visits were not allowed, and rehabilitation was restricted to passive mobilization.

Second cohort

A percutaneous tracheostomy was performed in the first 2 days after cannulation. Early weaning of iv sedatives and active prevention of delirium were attempted. Bronchoscopy with bronchoalveolar lavage (BAL) and multiplex PCR panel were used to diagnose VAP and select antimicrobial treatment. Family visits were allowed with contact and aerosols precautions. Early active mobilization and rehabilitation on ECMO were initiated in the first 72 hours after cannulation.

Data source and population

The data were collected during the hospitalization of the patients, and the review of the digital medical record was assigned with a double paired review methodology so that each record was evaluated by two general practitioners or intensivists; in cases of inconsistencies, the digital medical record was reviewed by a trained nursing professional to clarify the real value. The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the local medical ethics committee.

Statistical analysis

A descriptive analysis was carried out. To determine differences between the two cohorts before being put on ECMO,

| Health Workers Staff   | Cohort 1 (HW:Patient*) | Cohort 2 (HW:Patient*) |
|------------------------|------------------------|------------------------|
| ECMO specialist RN     | 1:4                    | 1:2                    |
| Resident Nurse, not ECMO specialist | 1:4                  | 0                      |
| Nurse technicians      | 1:3 without ECMO training | 1:2 with ECMO training |
| Respiratory and physical therapists | 1:8 without ECMO training | 1:3 with ECMO training |
| Intensivists with ECMO training | 1:16                  | 1:8                    |
| Staff intensivist specialist in ECMO | 1:16                  | 1:8                    |
| Nonspecialist physician | 1:16 without ECMO training | 1:8 with ECMO training |

*HW:Patient, Health worker-to-patient ratio.

ECMO, extracorporeal membrane oxygenation.
bivariate tests were carried out as appropriate. A 90-day survival table was made, considering the following outcomes: decannulation, ICU discharge, hospital discharge and death, presenting the probability of being in any of these stages in time discriminated by cohort. Then, a Kaplan–Meier analysis was performed, entering the significant variables into a multivariate model, using \( p < 0.2 \) as a reference. With the above, a COX analysis was carried out, confirming the model’s assumptions, evaluating interactions, residuals, and the model’s profiles.

As a secondary analyzes, the difference in the duration of hospitalization after cannulation was evaluated using survival analysis with Kaplan–Meier and ECMO complications with logistic regression.

**Results**

From June 16, 2020, to March 14, 2021, 101 patients with a confirmed diagnosis of COVID-19 and ECMO support were admitted and included in the study. The median duration of ECMO was 21 days (interquartile range 9–39) details of hospital stay can be seen in Appendix 1, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A827. Ninety-nine (98%) patients were cannulated and transferred with ECMO from other centers. Patient’s distribution is presented in Figure 1.

The demographic characteristics were well balanced between the two groups. Approximately 70% of the patients were men, only 11% were older than 60 years, and 37% were younger than 40 years old (Table 2).

The most frequent complication was major bleeding (55.5%), followed by the need for dialysis during ECMO (24.8%). When differentiating between the cohorts, there was a greater need for renal replacement therapy (RRT) in the first group (37.1% vs. 18.2%, \( p = 0.052 \)); other complications did not present significant differences (Table 3).

**Primary Outcome**

Mortality at 90 days is significantly lower after the intervention (62.9% vs. 31.8%, \( p = 0.003 \)). The probabilities for each outcome up to 90 days are shown in Figure 2 and in more detail in Appendix 1, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A827.

A univariate COX proportional hazard analysis was performed for mortality, defining the variables included in the multivariate model (Table 3). The performance of fiberoptic bronchoscopy with BAL, multiplex PCR panel, and tracheostomy in the first 2 days postcannulation was associated with a decrease in mortality (Table 4).

The variables potentially predictive of death were included in the multivariate model, taking a test statistic of \( p < 0.2 \) as a cutoff point. Belonging to the first cohort increases the risk of death 2.3 times. The need for cannulation or conversion to veno arterial or veno arterio venous ECMO increases the risk of dying four to seven times. Predictive complications of death were hemorrhagic stroke (HR 5.4) and RRT during ECMO (HR 2.7). The interventions associated with a decrease in the risk of death were fiberoptic bronchoscopy with BAL and multiplex PCR panel, with HR values of 0.34 and 0.36, respectively (Figure 3).

**Secondary Outcomes**

On day 7 postdecannulation, 25% of the patients in the first cohort had been discharged from the ICU, while on this same day in the second cohort, 70% had been discharged from the ICU (HR: 1.55, \( p = 0.19 \), 95% CI 0.80–2.98). In decannulated patients, at day 12 post-ECMO weaning: in the first group, 12% had been discharged, and in the second group, 61% had been discharged (HR: 1.63, \( p = 0.14 \), 95% CI 0.85–3.13) (Figure 4).

In the first cohort, the proportion of deceased patients was higher for each subgroup of complications. The analysis of subgroups by type of complication detected a significant difference in mortality for massive bleeding (15/20 vs. 14/36, \( p = 0.01 \)), pneumothorax (6/6 vs. 8/18, \( p = 0.02 \)), ventilator-associated pneumonia (17/27 vs. 17/51, \( p < 0.01 \)), and bacte remia (13/20 vs. 8/31, \( p < 0.01 \)) (Figure 5).
Discussion

This historical cohort study in patients diagnosed with COVID-19 who required ECMO shows that implementing a bundle of interventions related to the care model halved 90-day mortality (62.9% vs. 31.8% \( p = 0.004 \)). The ECMO outcomes in COVID-19 have been very heterogeneous, with mortalities varying between 90% and 36%.\(^7\)\(^-\)\(^10\) The registries with a large and diverse number of centers show mortalities between 50% and 40%.\(^11\)\(^-\)\(^12\) These registries show worse results in the second wave than the first, associated with the increase of new ECMO centers.\(^13\)

Our program faced abnormally high mortality in the first cohort associated with changes in the care model as a reaction to increased demand and the uncertainty and fear produced by the pandemic. Many decisions made at the beginning of the pandemic were ethically complicated. We think it is important to share the process of admitting a wrong choice and changing it. The decision to temporarily stop the admission of patients and analyze the situation with the support of a center of excellence in ECMO made it possible to design and implement a change in the model of care that positively impacted the results of the program.

The interventions carried out were focused on increasing the number of ECMO specialist nurses and intensivists to patient ratio, training nursing assistants, general practitioners, and rehabilitation professionals in ECMO to effectively integrate them into the multidisciplinary care team and increase the number and the quality of therapeutic interventions, even in patients in the infectious phase of the disease. These measures produced management changes that, in many cases, are intangible. Additionally, it is not possible to be sure of the specific weight of each intervention in the result. However, the application of all of them is likely to have a positive effect on ECMO survival in patients with severe ARDS due to COVID-19.

Table 2. Pre-ECMO Characteristics

|                         | Cohort 1 | Cohort 2 | \( p \) |
|-------------------------|----------|----------|--------|
| Number patients         | 101      | 35 (34.7)| 66 (65.3)| 0.242|
| Male gender             | 74 (73.3)| 23 (65.7)| 51 (77.3)| 0.952|
| Age                     |          |          |        |
| <40 years old           | 37 (36.6)| 14 (40)  | 23 (34.8)| 0.318|
| 40–50 years old         | 23 (22.8)| 7 (20)   | 16 (24.2)| 0.182|
| 51–60 years old         | 30 (29.7)| 10 (28.6)| 20 (30.3)| 0.779|
| 60–68 years old         | 11 (10.9)| 4 (11.4) | 7 (10.6) | 0.608|
| Patient background      |          |          |        |
| Immunocompromised*      | 4 (4)    | 0 (0)    | 4 (6.1) | 0.295|
| Chronic renal failure   | 0 (0%)   | 0 (0%)   | 0 (0%)  | -      |
| Anthropometric          |          |          |        |
| Normal BMI ≤ 25         | 12 (11.9)| 3 (8.6)  | 9 (13.6)| 0.212|
| Overweight              | 49 (48.5)| 19 (54.3)| 30 (45.5)| 0.764|
| Obesity                 | 11 (10.9)| 1 (2.9)  | 10 (15.2)| 0.903|
| Morbid obesity          | 29 (28.7)| 12 (34.3)| 17 (25.8)| 0.623|
| Previous to ECMO condition |        |          |        |
| Previous arrest         | 5 (5)    | 3 (8.6)  | 2 (3)   | 0.338|
| Renal replacement therapy | 6 (5.9) | 3 (8.6)  | 3 (4.5) | 0.415|
| Mechanical ventilation days before ECMO | 8 (3–8) | 6 (1–8) | 9 (4–8) | 0.058|
| Respiratory variables†‡ |          |          |        |
| pH‡                     | 7.35 (7.29–7.41) | 7.330 (7.26–7.44) | 7.355 (7.30–7.41) | 0.61|
| PaFiO\(_2\)‡           | 85 (68–106)| 92 (78–108)| 80 (67–103)| 0.300|
| PaCO\(_2\)‡            | 52.1 (42.9–64) | 52 (37–58.7) | 55.4 (43–64.8) | 0.363|
| Tidal volume‡           | 448.5 (405–500) | 445 (409–454) | 450 (405–520) | 0.146|
| D Dimet‡                | 2.2 (0.99–503) | 8.3 (1.24–555) | 2.1 (0.79–503) | 0.504|
| Creatinine‡             | 0.8 (0.61–1.0) | 0.84 (0.57–1.45) | 0.8 (0.61–0.94) | 0.521|
| Lymphocytes number‡     | 565 (12–940) | 773 (270–1,260) | 487 (6.8–830) | 0.104|
| Platelets number‡§      | 267 (171–334) | 246 (152–337) | 283 (183–321) | 0.653|
| Mobile ECMO             | 99 (98%) | 34 (97.1%) | 65 (98.5%) | 1.0|
| Transport               |          |          |        |
| Air                     | 31 (30.7%) | 16 (45.7%) | 15 (22.7%) | 0.178|
| Ambulance               | 68 (67.3%) | 18 (51.4%) | 50 (75.8%) | 1.0|
| Prone position          | 95 (94.1%) | 31 (88.6%) | 64 (97%)  | 0.178|

*Rheumatic disease, lupus, any type of transplant, cancer treatment, Gulver, and HIV.
†There was less sample due to data collection difficulties.
‡Median (interquartile range).
§1X1000.
BMI, body mass index; ECMO, extracorporeal membrane oxygenation.
ventilation through the culture of tracheal aspirates and antibiogram. These tests take several days to produce results and do not allow to define with certainty the best treatment when there is resistance to carbapenems. In the second cohort, more patients received fiberoptic bronchoscopy and multiplex PCR panel. Although the frequency of pneumonia

Table 3. In ECMO Run Variables

| Variable during ECMO | Cohort 1 | Cohort 2 | p   |
|----------------------|----------|----------|-----|
|                       | n (%)    | n (%)    |     |
| Initial ECMO cannulation configuration |          |          |     |
| VV                    | 97 (96%) | 31 (88.6%) | 66 (100%) | 0.013 |
| VA                    | 2 (2%)   | 2 (5.7%)  | 0 (0%)  |     |
| VAV                   | 2 (2%)   | 2 (5.7%)  | 0 (0%)  |     |
| Conversion to VA      | 13 (12.9%) | 6 (17.1%) | 7 (10.6%) | 0.365 |
| Conversion to VAV     | 19 (18.8%) | 7 (20%)   | 12 (18.2%) | 0.796 |
| Tracheostomy          | 83 (82.2%) | 23 (65.7%) | 60 (90.9%) | 0.002 |
| ECMO number of days until tracheostomy | 2 (1–3) | 6 (1–10) | 1 (1–2) | <0.001 |
| Infectious diseases studies |          |          |     |
| Molecular tests       | 34 (33.7%) | 8 (22.9%) | 26 (39.4%) | 0.094 |
| Alveolar bronchoscopic lavage | 52 (51.5%) | 13 (37.1%) | 39 (59.1%) | 0.036 |
| Any of the above      | 63 (62.4%) | 17 (48.6%) | 46 (69.7%) | 0.037 |
| Infectious during ECMO support |          |          |     |
| VAP                   | 78 (77.2%) | 27 (77.1%) | 51 (77.3%) | 1     |
| Bacteremia            | 51 (50.5%) | 20 (57.1%) | 31 (47%)  | 0.331 |
| Septic shock          | 45 (44.6%) | 20 (57.1%) | 25 (37.9%) | 0.064 |
| None of the previous  | 21 (20.8%) | 5 (14.3%) | 16 (24.2%) | 0.308 |
| Sputum culture        | 78 (77.2%) | 27 (77.1%) | 51 (77.3%) | 1     |
| Blood culture         | 54 (53.5%) | 22 (62.9%) | 32 (48.5%) | 0.168 |
| Resistant strains to carbapenems | 53 (52.5%) | 20 (57.1%) | 33 (50%)  | 0.535 |
| Organism              |          |          |     |
| Pseudomona aeruginosa | 42 (41.6%) | 16 (45.7%) | 26 (39.4%) | 0.540 |
| Klebsiella            | 21 (20.8%) | 8 (22.9%) | 13 (19.7%) | 0.798 |
| Others                | 9 (8.9%)  | 2 (5.7%)  | 7 (10.6%) | 0.491 |
| Antibiotic treatment  |          |          |     |
| Polymyxin             | 34 (33.7%) | 15 (42.9%) | 19 (28.8%) | 0.154 |
| Ceftazidime/avibactam | 26 (25.7%) | 2 (5.7%)  | 24 (36.4%) | 0.001 |
| Meropenem             | 81 (80.2%) | 31 (88.6%) | 50 (75.8%) | 0.189 |
| Complications         |          |          |     |
| Major bleeding        | 56 (55.5%) | 20 (57.1) | 36 (54.6) | 0.836 |
| RRT during ECMO       | 25 (24.8%) | 13 (37.1%) | 12 (18.2%) | 0.052 |
| Pneumothorax          | 24 (23.8%) | 6 (17.1)  | 18 (27.3) | 0.329 |
| Intracranial hemorrhage | 13 (12.9%) | 5 (14.3)  | 8 (12.1)  | 0.763 |
| Ischemic stoke        | 7 (5.7%)  | 2 (5.7)   | 5 (7.6)  | 1.0  |

Bold indicates statistically significant.
ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy; VA, veno arterial; VAV, veno arterio venous; VV, veno venous.

Figure 2. Percentage of survival in both groups.

Copyright © ASAIO 2022
frequency of septic shock and the need for RRT in this cohort.

The earlier and more frequent performance of the tracheostomy in the second cohort facilitated the removal of deep sedation and the awakening of the patients. Allowing the admission of family members and the early initiation of physical, respiratory, occupational, and speech therapy facilitate the management of delirium and help to stop and reverse the frailty of critical care patients. These interventions may facilitate a nearly 50% decrease in time to ICU discharge and hospitalization after ECMO decannulation.

An impact of the intervention is evidenced by reducing mortality in patients with complications, such as septic shock, pneumonia associated with mechanical ventilation, Table 4. Univariate Cox Proportional Hazard Analysis for Risk of Death

| Variables                        | Hazard Ratio | CI 95%    | p  |
|----------------------------------|--------------|-----------|----|
| Male gender                      | 2.49         | 1.05–5.91 | 0.04 |
| Age                              |              |           |    |
| <40 years old                    | 1            |           |    |
| 40–49 years old                  | 1.90         | 0.80–4.46 | 0.14 |
| 50–59 years old                  | 2.52         | 1.14–5.57 | 0.02 |
| 60–68 years old                  | 2.37         | 0.86–6.53 | 0.09 |
| RRT                              | 5.78         | 2.39–13.94| <0.01|
| Prone position                   | 0.33         | 0.11–0.92 | 0.04 |
| Initial configuration            |              |           |    |
| VV                               | 1            |           |    |
| VA                               | 6.28         | 1.46–27.09| 0.01 |
| VAV                              | 8.55         | 1.94–37.71| 0.01 |
| Conversion to VA                 | 2.81         | 1.41–5.60 | <0.01|
| Conversion to VAV                | 2.49         | 1.31–4.73 | <0.01|
| Tracheostomy                     | 0.57         | 0.27–1.19 | 0.14 |
| RRT during ECMO                  | 4.64         | 2.52–8.54 | <0.01|
| Infectious diseases              |              |           |    |
| studies                          |              |           |    |
| Molecular tests                  | 0.56         | 0.28–1.12 | 0.10 |
| Alveolar bronchoscopic lavage    | 0.40         | 0.22–0.75 | <0.01|
| Any of the above                 | 0.50         | 0.27–0.91 | 0.02 |
| Infections during ECMO support   |              |           |    |
| Ventilator-associated pneumonia  | 0.85         | 0.42–1.72 | 0.64 |
| Bacteremia                       | 0.77         | 0.42–1.40 | 0.38 |
| Septic shock                     | 2.08         | 1.13–3.84 | 0.02 |
| None of the previous             | 0.53         | 0.19–1.48 | 0.23 |
| Intracranial hemorrhage          |              |           |    |
| Ischemic stroke                  | 4.58         | 2.34–8.99 | <0.01|
| Major bleeding                   | 2.67         | 1.05–6.82 | 0.04 |
| Pneumothorax                     | 1.78         | 0.94–3.38 | 0.08 |

Bold indicates statistically significant.
ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy; VA, veno arterial; VAV, veno arterio venous; VV, veno venous.

**Figure 3.** Cox regression model.
pneumothorax, major bleeding, and the need for RRT. Perhaps, this result is a consequence of the greater availability of health personnel trained in ECMO.

This study has limitations. First, we had difficulty obtaining all the records of pre-ECMO hospital physiologic and ventilatory variables due to the high number of patients who came from outside the institution and the incomplete record of remission histories in both groups. It is possible that there are other variables with clinical relevance that can improve the survival model, but the design of our study meant that we were unable to recover these in their entirety. Another limitation was the low number of patients with complications, which does not allow statistical differences to be established with multivariate models. Finally, it is known that in quasi-experimental studies there is a temporary effect that cannot be fully controlled. As time passed, the approach to COVID patients changed in many aspects that cannot be objectively quantified in this study.

In conclusion, the implementation of a bundle that included an increase in the number of health personnel of the ECMO multidisciplinary team in relation to the number of patients and the earlier performance of diagnostic and therapeutic interventions, such as tracheostomy, fiberoptic bronchoscopy, molecular microbiological diagnosis of pneumonia, rehabilitation, and family support significantly decreased mortality and hospitalization time of patients on ECMO due to COVID-19.

References

1. World Health Organization: Weekly epidemiological update on COVID-19, 2021. Overview. Available at: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---1-june-2021
2. Immovilli P, Morelli N, Antonucci E, Radaelli G, Barbera M, Guidetti D: COVID-19 mortality and ICU admission: The Italian experience. Crit Care 24: 228, 2020.
3. Lim ZJ, Subramaniam A, Pomnapa Reddy M, et al: Case fatality rates for patients with COVID-19 requiring invasive mechanical ventilation. A meta-analysis. Am J Respir Crit Care Med 203: 54–66, 2021.
4. 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 396: 1071–1078, 2020.
5. Extracorporeal Life Support Organization (ELSO): ECLS Registry Report [Internet]. International Summary. 2021. Available at: https://www.elso.org/Portals/0/Files/Reports/2021_April/International%20Report%20April_page1.pdf
6. World Health Organization: Infection prevention and control during health care when coronavirus disease (COVID-19) is
suspected or confirmed [Internet]. Overview. 2021. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2021.1

7. Li X, Guo Z, Li B, et al: Extracorporeal membrane oxygenation for coronavirus disease 2019 in Shanghai, China. ASAIO J 66: 475–481, 2020.

8. Hu BS, Z Hu M, Jiang LX, et al: Extracorporeal membrane oxygenation (ECMO) in patients with COVID-19: A rapid systematic review of case studies. Eur Rev Med Pharmacol Sci 24: 11945–11952, 2020.

9. Fang J, Li R, Chen Y, et al: Extracorporeal membrane oxygenation therapy for critically ill coronavirus disease 2019 patients in Wuhan, China: A retrospective multicenter cohort study. Curr Med Sci 41: 1–13, 2021.

10. Osho AA, Moonsamy P, Hibbert KA, et al: Veno-venous extracorporeal membrane oxygenation for respiratory failure in COVID-19 patients: Early experience from a major academic medical center in North America. Ann Surg 272: e75–e78, 2020.

11. Lorusso R, Combes A, Lo Coco V, De Piero ME, Belohlavek J; EuroECMO COVID-19 WorkingGroup; Euro-ELSO Steering Committee: ECMO for COVID-19 patients in Europe and Israel. Intensive Care Med 47: 344–348, 2021.

12. Rabie AA, Azzam MH, Al-Fares AA, et al: Implementation of new ECMO centers during the COVID-19 pandemic: Experience and results from the Middle East and India. Intensive Care Med 47: 887–895, 2021.

13. Broman LM, Eksborg S, Lo Coco V, De Piero ME, Belohlavek J, Lorusso R; EuroECMO COVID-19 Working Group; Euro-ELSO Steering Committee: Extracorporeal membrane oxygenation for COVID-19 during first and second waves. Lancet Respir Med 9: e80–e81, 2021.

14. Simon M, Metschke M, Braune SA, Püschel K, Kluge S: Death after percutaneous dilatational tracheostomy: A systematic review and analysis of risk factors. Crit Care 17: R258, 2013.

15. Ergan B, Nava S: The use of bronchoscopy in critically ill patients: Considerations and complications. Expert Rev Respir Med 12: 651–663, 2018.

16. Peiffer-Smadja N, Bouadma L, Mathy V, et al: Performance and impact of a multiplex PCR in ICU patients with ventilator-associated pneumonia or ventilated hospital-acquired pneumonia. Crit Care 24: 366, 2020.

17. Kwak PE, Connors JR, Benedict PA, et al: Early outcomes from early tracheostomy for patients with COVID-19. JAMA Otolaryngol Head Neck Surg 147: 239–244, 2021.

18. Abrams D, Javidfar J, Farrand E, et al: Early mobilization of patients receiving extracorporeal membrane oxygenation: A retrospective cohort study. Crit Care 18: R38, 2014.