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Extracorporeal Membrane Oxygenation Retrieval in Coronavirus Disease 2019: A Case-Series of 19 Patients Supported at a High-Volume Extracorporeal Membrane Oxygenation Center

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Objective: To evaluate the performance of the extracorporeal membrane oxygenation retrieval team at a high-volume extracorporeal membrane oxygenation center during the coronavirus disease 2019 pandemic.

Design: Observational study including all adult patients with confirmed infection due to severe acute respiratory syndrome coronavirus-2 cannulated at other centers and transported on extracorporeal membrane oxygenation to the ICU of the Vall d'Hebron University Hospital between 15 March and 10 June 2020.

Setting: The ICU (capacity expanded to 200 during the pandemic) of the Vall d'Hebron University Hospital (a 1,100-bed public university hospital in Barcelona), the referral center for extracorporeal respiratory support in Catalonia (7.5 million inhabitants).

Patients: Extracorporeal membrane oxygenation was considered if the Pao_2/Fio_2 ratio less than 80 mm Hg (refractory to prone position) and/or $Paco_2$ greater than 80 mm Hg and pH less than 7.25 for more than 6 hours, and no contraindications for extracorporeal support were present.

Interventions: Venovenous extracorporeal membrane oxygenation was initiated in the primary center. Then, patients were transferred to the ICU of the Vall d'Hebron University Hospital where they received support until respiratory improvement. After decannulation, patients were discharged for rehabilitation at the primary center.

Measurements and Main Results: Nineteen patients with severe acute respiratory syndrome coronavirus-2 infection and with a mean Pao_2/Fio_2 ratio of 71 mm Hg (57–118 mm Hg) despite prone positioning and a mean $Paco_2$ of 70 mm Hg (47–110 mm Hg) were transferred to our center from their primary hospital after cannulation and received venovenous extracorporeal membrane oxygenation support. Prior to cannulation, six patients (31.5%) presented vascular thrombosis, and nine (47.4%) were already receiving anticoagulant therapy. Eighteen transfers were carried out with no significant complications. While on extracorporeal membrane oxygenation, thrombotic events were recorded in nine patients (47.4%) and hemorrhagic events in 13 (68.4%). Thirteen patients (68.4%) were successfully weaned, and 12 (63.1%) were discharged home.

Conclusions: Extracorporeal membrane oxygenation retrieval can rescue young, previously healthy patients with severe coronavirus disease 2019 in whom all the conventional respiratory measures have failed. Thrombotic and hemorrhagic complications are frequent in this cohort.

Key Words: coronavirus; coronavirus disease 2019; extracorporeal membrane oxygenation; extracorporeal membrane oxygenation retrieval; extracorporeal membrane oxygenation transport; severe acute respiratory syndrome coronavirus 2

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A significant percentage of critically ill patients with the coronavirus disease 2019 (COVID-19) may develop hypoxemia and/or respiratory acidosis that are refractory to conventional measures including prone positioning. Extracorporeal membrane oxygenation (ECMO) in its venovenous configuration has been shown to be effective in improving gas exchange while allowing a reduction in the mechanical power delivered by mechanical ventilation (MV) in the most severe cases of respiratory failure (1). The results of the first published reports of the use of ECMO in COVID-19 were discouraging (2–8); however, in those studies, key specific data about patient selection and specific management directly related with outcomes after ECMO are lacking. Further, although the concentration of patients at high-volume ECMO centers has been associated with better outcomes (9), there are no published data available regarding the feasibility of ECMO retrieval of patients with COVID-19.

In the present case series, we describe the activity of the ECMO retrieval team at a regional high-volume ECMO reference center during this pandemic period, focusing on the clinical characteristics of the patients, ECMO management, and outcomes. We also provide details of the activations that were requested but finally rejected.

MATERIALS AND METHODS

A retrospective analysis was performed of the prospectively recorded data of all the adult patients with confirmed infection due to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) cannulated at other centers and transported on ECMO to the Vall d'Hebron University Hospital (VHUH) between 15 March and 15 June. Data from all the other activations of the ECMO retrieval team in this period were also recorded and analyzed.

The VHUH is a 1,100-bed public university hospital in Barcelona with a 54-bed ICU. The ICU capacity was expanded to 200 during the pandemic, and in all, more than 300 critically ill COVID-19 patients were admitted. Criteria for ECMO team activation were a ratio of Pao_2 to the FIo_2 less than 80 mm Hg, refractory to prone positioning (defined by a ratio increase of < 20% after at least 12 hr), and/or a $Paco_2$ greater than 80 mm Hg and pH less than 7.25 for more than 6 hours. The contraindications for extracorporeal support, together with a brief description of the VHUH ECMO program and its modification during COVID-19 pandemic, are detailed in **Appendix 1** (Supplemental Digital Content, http://links.lww.com/CCX/A357). A radiological evaluation of the presence of thrombosis was done if clinically apparent, no routine screening was performed. Hemorrhagic complications were recorded as so if the patient required more than 20 mL/Kg/d of packed RBC or needed other intervention such as surgery or embolization.

The VHUH institutional review board issued a waiver for informed consent since only deidentified patient data were used. Data were collected prospectively by investigators and stored in the ECMO database. Continuous variables are expressed as mean and range and categorical as percentages. No analysis for statistical significance was performed.

RESULTS

Population

Nineteen patients with COVID-19 were transferred from their primary hospital after cannulation and received respiratory extracorporeal support at the VHUH, all with a venovenous configuration. The characteristics of the population and the respiratory condition prior to ECMO are detailed in **Table 1**. The main indication was refractory hypoxemia, with a mean Pao_2/FIo_2 ratio of 71 mm Hg (57–118 mm Hg) despite prone positioning. Respiratory acidosis was also common ($Paco_2$ of 70 mm Hg [47–110 mm Hg]), and the mechanical power delivered to the respiratory system was high. In 11 cases (57.9%), the team had no information about vessel diameter prior VHUH departure due to the impossibility of placing the proned patient in the supine position because of life-threatening respiratory deterioration when mobilized to this position.

Cannulation, Transport, and ECMO Management

Significant information on cannulation, transport, and ECMO management is summarized in **Table 2**. Prior to cannulation,

TABLE 1. Characteristics of the Population and Respiratory Condition Pre Extracorporeal Membrane Oxygenation

Variables	Mean (Range) or *n* (%)
Age, yr	50.5 (31–64)
Gender, male	16 (84.2)
Hypertension	7 (36.8)
Body mass index, kg/m^2	31.9 (22.2–40.8)
Days since intubation	8.6 (0–17)
Indication	Refractory hypoxemia: 17 (89.5); refractory respiratory acidosis: 2 (10.5)
Pao_2/FIo_2 at cannulation, mm Hg	70.8 (57–118)
pH at cannulation	7.2 (6.9–7.4)
$Paco_2$ at cannulation, mm Hg	70.4 (47–110)
Positive end-expiratory pressure at cannulation, cm H_2O	11.2 (6–17)
Tidal volume at cannulation, mL	410 (280–500)
Driving pressure, cm H_2O	24.4 (20–30)
Respiratory rate at cannulation, beats/min	28 (22–38)
Prone before ECMO	19 (100)
Inhaled nitric oxide before ECMO	1 (5.2)
Neuromuscular blockade before ECMO	19 (100)
Impossibility to place the patient supine before arrival of the ECMO team	11 (57.9)

ECMO = extracorporeal membrane oxygenation.

Continuous variables are expressed as means (ranges) and categorical variables as *n* (%).

TABLE 2. Cannulation, Transport, and Extracorporeal Membrane Oxygenation Management

Variables	Mean (Range) or *n* (%)
Vascular thrombosis prior to cannulation	6 (31.5)
Patient anticoagulated prior to cannulation	9 (47.4)
ECMO configuration	Venovenous: 19 (100)
Cannulation strategy	LFV to RFV: 14 (73.7); LFV to RJV: 3 (15.7); RFV to RJV: 1 (5.3); RFV to LFV: 1 (5.3)
Distance between primary center and Vall d'Hebron University Hospital, km	33.8 (5–160)
Duration of service, hr	5.6 (3.5–8.5)
Life-threatening complications during transport	1 (5.2)
Minor complications during transport	Flow fluctuations: 4 (21); peripheral oxygen saturation < 85%: 2 (10.5)
ECMO flow during transport, L/min	4 (3.5–4.8)
ECMO flow at ICU, L/min	3.9 (3.4–4.8)
Inspiratory pressure during ECMO, cm H_2O	12.1 (10–14.5)
Respiratory rate during ECMO, breaths/min	11.6 (10–14)
Fiberbronchoscopy performed while on ECMO	2.5 (0–7)
CT performed while on ECMO	0.6 (0–3)
Patients with thrombotic complications while on ECMO	9 (47.4)
Patients with hemorrhagic complications while on ECMO	13 (68.4)
Patients with renal failure requiring continuous renal replacement therapy	4 (21)
Patients with cytokine hemoadsorption	3 (15.7)

ECMO = extracorporeal membrane oxygenation, LFV = left femoral vein, RFV = right femoral vein, RJV = right jugular vein.

Continuous variables are expressed as means (ranges) and categorical variables as *n* (%).

vascular thrombosis was present in six patients (31.5%), and almost half of the cohort (47.4%) received anticoagulation. The femorofemoral approach was the most common cannulation strategy (78.9%), and a mean drainage diameter of 24.5F (23–25F) allowed a mean ECMO flow of 4 L/min despite daily negative fluid balance. Ground transport (ambulance) was used in all the services. There were no (or only minor) complications during transport, except in one case in which pulseless electrical activity (PEA) was evidenced, resulting in death despite conversion to extracorporeal cardiopulmonary resuscitation. The cardiac rhythm, the stability of hemoglobin and electrolytes the absence of pericardial occupation, and presence of dilated right ventricle in the echocardiography made us hypothesize that the cardiac arrest was secondary to a massive pulmonary thromboembolism.

As soon as extracorporeal support was initiated, the mechanical power delivered to the respiratory system was notably decreased (mean inspiratory pressure of 12.1 cm H_2O [10–14.5 cm H_2O] and respiratory rate of 11.6 breaths/min [10–14 breaths/min]). During ECMO support, a mean of 2.5 (0–7) fiberbronchoscopies and 0.6 (0–3) CT per patient were performed. Four patients (21%) needed continuous renal replacement therapy and three (15.7%) extracorporeal cytokine hemoadsorption.

All the patients received heparin infusion, with a daily mean of activated clotting time of 156.4 seconds (128–181.3 s). Despite this, thrombotic events were detected in nine patients (47.4%), with six (31.5%) being diagnosed of deep venous thrombosis and five (26.3%) needing circuit change. Hemorrhagic events were identified in 13 patients (68.4%), five of them needing surgery or embolization. Regarding the site of bleeding, seven patients (36.8%) suffered airways and/or lung hemorrhage, three (15.7%) cannula-related bleeding, two (10.5%) gastrointestinal blood loss, and one (5.2%) hematuria. No thrombotic or hemorrhagic complications were directly associated with patient death.

TABLE 3. Outcomes After Extracorporeal Membrane Oxygenation Support Evaluated on 15 June

Variables	Mean (Range) or *n* (%)
ECMO status	Weaned: 13 (68.4); ongoing: 2 (10.5); deceased: 4 (21.1)[a]
Respiratory status of weaned patients	No support: 12 (92.3); mechanical ventilation weaning process: 1 (7.7)
Alive patients needing percutaneous tracheostomy	15 (100)
ECMO days of weaned patients	10.7 (2–33)
Patients discharged from Vall d'Hebron University Hospital for rehabilitation	13 (68.4)
Patients discharged home	12 (63.1)

ECMO = extracorporeal membrane oxygenation.

[a]Cause of death: suspected massive pulmonary thromboembolism, refractory thoracic bleeding, and two cases of ventilator-associated pneumonia with sepsis.

Continuous variables are expressed as means (ranges) and categorical variables as *n* (%).

Outcomes

By 15 June, 68.4% of the patients had been successfully weaned and discharged to their primary center, 10.5% were still on ECMO, and 21.1% had died despite the support (**Table 3**). At that time, 92.3% of weaned patients were breathing spontaneously, with no respiratory support, and only one patient was still in the

process of MV weaning. In all, 63.1% of the patients were discharged home.

Other VHUH ECMO Retrieval Team Activations

In the same period, the team received 41 other calls from 18 centers. More hours of prone positioning were suggested in 41.4% of cases and changes in MV variables in 12.2%. ECMO contraindications were found in 46.3%, advanced age being the most common (68.4%). Other frequent contraindications were long time on MV (19.5%), immunosuppression (7.3%), and morbid obesity (7.3%).

DISCUSSION

This is the largest published report of ECMO retrieval of patients with severe COVID-19 disease. More than two thirds of the patients were successfully weaned, and 63.1% could be discharged home.

Life-threatening complications may occur during ECMO transport. Furthermore, transporting patients with SARS-CoV-2 infection is particularly difficult due to the characteristics of the disease and also due to the requirement of operator protection for contagion (9). In our series, 18 of 19 ECMO transports occurred with no significant incidents. One patient developed PEA during transport, probably due to pulmonary embolism and subsequently died. Other difficulties that we encountered included anticoagulation prior to cannulation, previous venous thrombosis, and lack of information on vein diameter due to the impossibility of placing the patient in the supine position, but, in our series, they did not complicate the performance of the technique.

Only four of 19 patients died on ECMO, a low rate compared with most of the reports in the literature of its use in patients with COVID-19 (2–8). However, those publications report very short series or compilations of small numbers of cases at many different centers. It has been shown that concentrating ECMO cases in high-volume centers markedly improves outcomes (10). A recently published experience of 17 patients supported with ECMO in a French high-volume ECMO center reported a 58.9% ICU survival at 60 days, similar to our figures (11). They also report frequent thrombotic and hemorrhagic events. There are other circumstances that may explain our positive results. First, ECMO allowed a significant decrease in the mechanical power applied to the lungs, which has been shown to be associated with better outcomes in patients with acute respiratory distress syndrome (ARDS) (12). In our series, it was possible to substantially reduce the inspiratory pressure, together with the respiratory rate, after the initiation of extracorporeal support. Further, certain diagnostic and therapeutic maneuvers that are life-threatening with MV support alone could be safely performed with ECMO. We performed fiberbronchoscopy with secretion clearance and microbiological surveillance in most patients, in many cases on a daily basis, which helped to improve respiratory evolution and antibiotic therapy titration. ECMO also allowed the in-hospital transport of patients to the CT scan. Images helped clinicians to adjust treatment and better evaluate the evolution of the lung disease.

Thrombotic and hemorrhagic complications in our cohort were frequent. In fact, the circuit had to be changed in five patients. This is to be expected, since COVID-19 has been associated with coagulation disorders that might be exacerbated by the extracorporeal system (13). Interestingly, these complications did not have a direct impact on mortality: possible reasons for this include the careful VHUH ECMO team training, the centralization of patients in the same unit, the adequate nurse-patient ratio, and the use of updated anticoagulation management protocols.

The uncertainties surrounding the evolution of COVID-19 disease and prognosis of these very severe ARDS patients, together with the association of ECMO with high resource consumption, mean that the decision to indicate the technique is particularly difficult. In fact, we ruled out 41 activations proposed by the ECMO retrieval team during the study period, either on the grounds that the respiratory condition was not sufficiently severe to benefit from the technique or due to the presence of contraindications that made the indication of ECMO futile. The most common reason for ruling out ECMO was advanced age. The exact cut-off point for age is a matter of debate, but sufficient evidence is available to show that mortality in ECMO increases in the older population.

The single-center design of this report may be considered as a limitation. However, ECMO management and protocols vary widely between centers. This variability may alter the conclusions obtained regarding the usefulness of the technique in patients with COVID-19, and in fact, we see this as a weakness of previously published articles which include small numbers of cases from many different centers (4–6, 14, 15). Although the sample in this observational study is one of the largest published to date (19 patients), it is not large enough to allow any definitive conclusions to be drawn.

CONCLUSIONS

In spite of this limitation, this study shows that ECMO retrieval by an experienced team can rescue young, previously healthy patients with severe COVID-19 in whom all conventional respiratory measures have failed. Thrombotic and hemorrhagic complications are frequent in this cohort.

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REFERENCES

1. Peek GJ, Mugford M, Tiruvoipati R, et al; CESAR trial collaboration: Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): A multicentre randomised controlled trial. *Lancet* 2009; 374:1351–1363
2. Henry BM, Lippi G: Poor survival with extracorporeal membrane oxygenation in acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19): Pooled analysis of early reports. *J Crit Care* 2020; 58:27–28
3. Zeng Y, Cai Z, Xianyu Y, et al: Prognosis when using extracorporeal membrane oxygenation (ECMO) for critically ill COVID-19 patients in China: A retrospective case series. *Crit Care* 2020; 24:148
4. Li X, Guo Z, Li B, et al: Extracorporeal membrane oxygenation for Coronavirus disease 2019 in Shanghai, China. *ASAIO J* 2020; 66:475–481
5. Ruan Q, Yang K, Wang W, et al: Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* 2020; 46:846–848
6. Yang X, Yu Y, Xu J, et al: Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. *Lancet Respir Med* 2020; 8:475–481
7. Zhou F, Yu T, Du R, et al: Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet* 2020; 395:1054–1062
8. Wu C, Chen X, Cai Y, et al: Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020; 180:934–943
9. Lassen C, Alois P, Derya A, et al: Out-of-center initiation of venovenous extracorporeal membrane oxygenation in COVID-19 patients. *ASAIO J* 2020; In Press
10. Barbaro RP, Odetola FO, Kidwell KM, et al: Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. *Am J Respir Crit Care Med* 2015; 191:894–901
11. Falcoz PE, Monnier A, Puyraveau M, et al: Extracorporeal membrane oxygenation for critically ill patients with COVID-19-related acute respiratory distress syndrome: Worth the effort? *Am J Respir Crit Care Med* 2020; 202:460–463
12. Serpa Neto A, Deliberato RO, Johnson AEW, et al; PROVE Network Investigators: Mechanical power of ventilation is associated with mortality in critically ill patients: An analysis of patients in two observational cohorts. *Intensive Care Med* 2018; 44:1914–1922
13. Kowalewski M, Fina D, Słomka A, et al: COVID-19 and ECMO: The interplay between coagulation and inflammation-a narrative review. *Crit Care* 2020; 24:205
14. Jacobs JP, Stammers AH, St Louis J, et al: Extracorporeal membrane oxygenation in the treatment of severe pulmonary and cardiac compromise in Coronavirus disease 2019: Experience with 32 patients. *ASAIO J* 2020; 66:722–730
15. Yang X, Cai S, Luo Y, et al: Extracorporeal membrane oxygenation for Coronavirus disease 2019-induced acute respiratory distress syndrome: A multicenter descriptive study. *Crit Care Med* 2020; 48:1289–1295