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ORIGINAL ARTICLE

Experience with ECMO therapy for acute respiratory distress syndrome treatment throughout the COVID-19 pandemic

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KEYWORDS
COVID-19;
Adult respiratory distress syndrome;
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Mortality

Abstract
Objective: To analyze our experience with extracorporeal membrane oxygenation (ECMO) therapy for acute respiratory distress syndrome (ARDS) treatment during the COVID-19 pandemic.
Design: Retrospective, observational, single center study.
Setting: Third-level hospital in Spain.
Patients: Adult patients with COVID-19 ARDS treated with an ECMO system in our center between March 2020 and March 2023.
Interventions: Retrospective collection of variables during hospital admission and follow-up.
Main Variables of Interest: Demographic variables, clinical history, variables related to ECMO therapy, COVID-19 wave number, in-hospital mortality, adverse events, ICU and hospital length of stay, and functional status at follow-up were collected.
Results: Eighty-one patients were included. Of these, 61 patients (75%) died during hospitalization. Patients who died were older and had more comorbidities. During the second, third, and sixth waves, mortality was higher. In the multivariate analysis, the only independent predictor

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of mortality was age (OR 1.24 95% CI (1.027−1.5, *P* = 0.025). After discharge, 40% of patients had difficulties returning to normal life due to respiratory failure requiring oxygen and arthropathies.
Conclusion: In-hospital mortality increased during the pandemic. Older age was the only independent predictor of mortality. After discharge, no deaths were recorded during the first 18 months of follow-up, although 40% of surviving patients had respiratory and motor sequelae making it difficult for them to return to a normal life.

PALABRAS CLAVE
COVID-19;
Síndrome de distrés respiratorio agudo;
Oxigenación de membrana extracorpórea;
Mortalidad

Experiencia con terapia ECMO para el tratamiento del síndrome de distrés respiratorio agudo durante la pandemia de COVID-19

Resumen
Objetivo: Analizar nuestra experiencia con la terapia de soporte con membrana de oxigenación extracorpórea (ECMO) para tratar el síndrome de distrés respiratorio agudo (SDRA) durante la pandemia de COVID-19.
Diseño: Estudio retrospectivo y observacional de un único centro.
Ámbito: Hospital de tercer nivel en España.
Pacientes: Pacientes adultos con COVID-19 tratados con sistema ECMO por SDRA en nuestro centro entre Marzo 2020 y Marzo 2023.
Intervenciones: Recogida retrospectiva de variables durante el ingreso y el seguimiento.
Variables de interés principales: Se recogieron variables demográficas, antecedentes clínicos, variables relacionadas con la terapia ECMO, numero de ola de COVID-19, mortalidad hospitalaria, eventos adversos, duración de estancia en UCI y en hospital y estado funcional en el seguimiento.
Resultados: Se incluyeron 81 pacientes. De ellos 61 pacientes (75%) fallecieron durante la hospitalización. Los pacientes que fallecieron tenían más edad y más comorbilidad. Durante la segunda, tercera y sexta olas la mortalidad fue mayor. En el análisis multivariante, el único predictor independiente de mortalidad fue la edad (OR 1.24 IC 95% (1.027−1.5, P = 0.025). Después del alta, el 40% de los pacientes presentaban dificultades para retornar a una vida normal por insuficiencia respiratoria que precisaba de oxígeno y artropatías.
Conclusión: La mortalidad hospitalaria aumentó durante la pandemia. Tener mayor edad fue el único predictor independiente de mortalidad. Tras el alta, ningún paciente falleció durante los primeros 18 meses de seguimiento, aunque el 40% de los pacientes supervivientes presentan secuelas respiratorias y motoras que dificultan su regreso a una vida normal.

Introduction

Coronavirus disease 2019 (COVID-19), declared as pandemic on March 11, 2020[1] by the World Health Organization (WHO), results from human infection with the SARS-CoV-2 virus. Until March 10, 2023, there were 676,609,955 confirmed cases of COVID-19 worldwide with a mortality of 6,881,955 patients (1.01%).[2] In Spain, on that same date, there were 13,770,429 confirmed cases of COVID-19 with 115,239 deaths (0.86% mortality),[2] whereas in the Region of Murcia (Spain) to March 13, 2023, there were 465,270 declared cases with 2531 deaths (0.54% mortality).[3]

Although most patients with COVID-19 have mild symptoms or are asymptomatic, between 5% and 12% of hospitalized patients for COVID-19 may develop acute respiratory distress syndrome (ARDS) requiring even intubation and mechanical ventilation. In these cases, mortality can exceed 80%,[4] mainly due to respiratory failure, with a small number dying from combined respiratory and cardiac failure.[5]

The WHO and the CDC[6] accept ECMO (Extracorporeal membrane Oxygenation) therapy as a treatment for the most severe ARDS, with good results in other ARDS caused by viruses such as the H1N1 Influenza.[7] However, the role of ECMO systems in treating COVID-19 remains to be defined. Initial studies on the experience with ECMO in patients with COVID-19 who developed severe ARDS indicated high mortality even with ECMO therapy.[8]

This study aimed to analyze ECMO therapy for severe ARDS due to COVID-19 in a tertiary hospital. We sought to determine hospital mortality, reasons for mortality, complications, and post-discharge outcomes. Additionally, we explored the influence of pandemic infection waves on patients receiving ECMO.

Methods

A retrospective, observational, and single-center study was performed in a tertiary referral hospital for ECMO therapy between March 2020 and March 2023.

Patients ≥18 years with ARDS (according to the Berlin criteria[9]) secondary to COVID-19 and treated with ECMO therapy were included. COVID-19 was diagnosed by PCR or a positive antigen test for SARS-CoV-2, and all patients were treated in our institution's Intensive Care Unit (ICU). Both venovenous and veno-arterial ECMO systems were included. Patients treated with ECMO therapy for ARDS for reasons other than COVID-19 were excluded.

At inclusion, we recorded demographic variables, medical history, chronic treatment, baseline laboratory values, gasometric and ventilatory variables, therapies for COVID-19, and ECMO-related variables. The COVID-19 waves and the predominant SARS-CoV-2 variant in each wave were documented. During hospitalization, we monitored in-hospital mortality along with its causes, in addition to other complications and adverse events, including infection (suspected on clinical signs, along with the administration of systemic antibiotics) (respiratory, bacteriemia, sepsis, and urinary infection), renal failure, major bleeding (if intervention is needed to control it or if a significant amount of blood products is required), neurological complications (ischemic stroke, intracranial bleeding), respiratory complications (pneumothorax, embolism), and heparin-induced thrombocytopenia. We also recorded the length of stay in ICU, length of stay in hospital, and the functional status of patients after hospital discharge using the New York Heart Association (NYHA) classification and the Barthel Index to measure performance in basic activities of daily living. Health assessments were conducted 1-month after discharge and every 6-months thereafter through face-to-face contacts and/or telephone calls. Additionally, we checked medical records for potential contacts in other hospitals or primary care centers.

The ELSO and SEMICYUC guidelines for managing anticoagulation and the ECMO system were followed during therapy.[10–12] The goal was to maintain a hemoglobin level of 10 g/dL, and COVID-19 patients were treated with standard lung-protective mechanical ventilation settings (tidal volume 6 mL/kg and plateau pressure <30 cmH_2O).[11,12]

According to data from the Ministry of Health, the different waves of COVID-19 suffered in Spain throughout 2020–2022[13] were listed (first wave: from March 13, 2020, to June 21, 2020; second wave: from June 22, 2020, to December 6, 2020; third wave: from December 7, 2020, to March 14, 2020; fourth wave: from March 15, 2021 to June 19, 2021; fifth wave: from June 20, 2021 to October 14, 2021; and sixth wave: from October 15, 2021, to December 31, 2022).

The Ethics Committee from our center approved the study (Internal Code 2022-11-2-HCUVA), which exempted the researchers from the need for informed consent.

Statistical analysis

Categorical variables were expressed as frequencies and percentages and compared with the Pearson χ^2 test or Fisher's test. In quantitative variables, the normality of the distribution was verified using the Kolmogorov-Smirnov test. Variables were expressed as the mean ± standard deviation or using the median (interquartile range, IQR), as appropriate. Analyses were run with the Student's *t*-test or the Mann-Whitney *U* test

Variables were analyzed using univariate logistic regression models for in-hospital mortality. Subsequently, all the variables with significant p-values (≤0.05) in the univariate analyses were included in multivariate logistic regression models, stepwise forward method. The results were reported as odds ratio (OR) with corresponding 95% confidence interval (CI). Receiver Operating Characteristics (ROC) curve analysis was used to determine the predictive ability of the quantitative variables significantly related to mortality, and the cut-off values that provided the maximum sensitivity and specificity were determined.

All statistical analyses were performed using the SPSS software package (IBM SPSS Statistics, Version 24, Armonk, NY, USA). A p-value ≤0.05 was considered statistically significant.

Results

Until March 2023, 327 patients were admitted to our ICU for severe SARS-COV-2 infection. Of these, 81 patients (25% of patients treated in the ICU for COVID-19) required ECMO supportive therapy for ARDS due to COVID-19 that did not respond to conventional therapy and were therefore included in the study (58 [72%] males, mean age of 50.9 ± 10.3 years) (Table 1). Hypertension and obesity were the most prevalent comorbidities (40% and 38%, respectively), followed by dyslipidemia (27%). In our study population, 85% received corticosteroids, 39% monoclonal antibodies, and 24% antiviral medications as treatment for COVID-19 before ECMO support.

Regarding the presentation of COVID-19, the most common symptoms were dyspnea (82%), fever (77%), and cough (64%). All patients had severe ARDS according to the Berlin criteria[9] with a median PaO2/FiO2 (PF ratio) of 82 (IQR 65—90) mmHg, a median pre-ECMO preimplantation pH of 7.37 (IQR 7.25—7.43), a median pre-implantation PO2 of 65.7 (IQR 52.3–78.4) mmHg, and a median PCO2 of 52 (IQR 37.6–71.4) mmHg. The use of the prone position as a preimplantation therapeutic measure was very frequent in our study cohort (94%). Seventy-seven (95%) patients required veno-venous ECMO, while 4 (5%) patients required veno-arterial ECMO. Of these last 4 patients, 3 were switched from veno-venous ECMO to veno-arterial ECMO due to poor hemodynamic progress. Only 1 patient required veno-arterial ECMO support from the beginning. No patients transitioned from veno-arterial ECMO to veno-venous ECMO.

The mean number of days between the onset of the COVID-19 symptoms and orotracheal intubation was 12 ± 6 days. The median time for mechanical ventilation was 24 (IQR 14—42) days. The mean PEEP of ECMO therapy was 12.3 ± 2.6 cm H_2O. The median time between the onset of clinical COVID-19 and the start of ECMO therapy was 17.5 (IQR 13–26) days. The median time between orotracheal intubation and ECMO cannulation was 6 (IQR 3—12) days. Patients remained at a median of 12.5 on ECMO (IQR

Table 1 Baseline characteristics of the patients.

	N = 81
Demographics	
Age (years), mean ± standard deviation	50.9 ± 10.3
Male	58 (73%)
Body mass index (kg/m^2)	34.3 ± 6.9
Comorbidities	
Hypertension	32 (39%)
Diabetes Mellitus	16 (20%)
Ischemic heart disease	1 (1%)
Peripheral artery disease	3 (4%)
Obesity (BMI > 30 kg/m^2)	31 (38%)
Dyslipidemia	22 (27%)
Chronic kidney disease	6 (7%)
Asthma/COPD	12 (15%)
Immunosuppression	7 (9%)
Smoking	4 (5%)
Baseline lab test results	
Creatinine (mg/dl)	0.68 (0.52—0.99)
Lactate (mmol/L)	1.3 (1—2.1)
Total bilirrubine (mg/dl)	0.45 (0.29—0.7)
CRP (mg/dl)	7.9 (1.27—19)
Procalcitonin (ng/mL)	0.21 (0.13—0.46)
Fibrinogen (mg/dl)	600 ± 231
D-dimer (mg/L)	902 (534—2812)
Leukocytes (n X mcL)	12,325 (9137—19,447)
Platelets (n X mcL)	278,000 (207,750—380,750)
Arterial blood gases	
PaO_2/FiO_2 (mm Hg)	82 (65—90)
pH	7.37 (7.25—7.43)
PO_2 (mm Hg)	66 (52—78)
PCO_2 (mm Hg)	52 (38—71)
Ventilatory Parameters	
PEEP (cm H_2O)	12 (810—14.2)
Peak Inspiratory Pressure (cm H_2O)	36 (30—44)
Mean Airway Pressure (cm H_2O)	30 (25—40)
Clinical manifestation of COVID-19	
Dyspnoea	66 (82%)
Fever	62 (77%)
Cough	52 (64%)
Chest pain	9 (11%)
Myalgias	21 (26%)
General malaise	37 (46%)

BMI: body mass index; COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein; PaO_2/FiO_2: The ratio of partial pressure of oxygen in arterial blood (PaO_2) to the fraction of inspiratory oxygen concentration (FiO_2); PO_2: partial pressure of oxygen; PCO_2: partial pressure of carbon dioxide; PEEP: positive end-expiratory pressure.

5.5—25.7) days. The median stay in the ICU was 27 (IQR 20—46) days, whereas for hospitalization it was 28.5 (IQR 21—56) days (Table 2).

During the pandemic, the number of patients assisted with ECMO therapy varied across different waves. In the first wave, 5 patients received ECMO support, accounting for

Table 2 Times (median IQR) (*n* = 81).

Mechanical ventilation time (days)	24 (14—42)
Time on ECMO (days)	12.5 (5.5—25.7)
Time in ICU (days)	27 (20—46)
Time in Hospital (days)	28.5 (21—56)
Long ECMO (>30 days)	13 (16%)
Pre-ECMO prone position	75 (94%)
Days between mechanical ventilation and ECMO	6 (3—12)

ECMO: extracorporeal membrane oxygenator; ICU: intensive care unit.

20% of the COVID-19 patients treated in the ICU during that period. This figure increased to 25 in the second wave, representing 22.5% of ICU COVID-19 patients. During the third wave, the absolute number decreased to 16 patients, constituting 26% of all COVID-19 patients treated in the ICU. In the fourth wave, only 3 patients received ECMO therapy, making up 25% of ICU patients. The fifth wave, with 8 patients, represented 32% of ICU patients with COVID-19. Finally, 24 patients were assisted with ECMO therapy in the sixth wave, which accounted for 26% of those treated in the ICU (Fig. 1).

Patients with COVID-19 assisted with ECMO therapy presented a high morbidity rate. Seventy-three (90%) patients had an infection at some level during admission (respiratory infection, bacteremia and sepsis, and urinary infection). Due to the anticoagulant therapy required to maintain the ECMO systems, 42 (52%) patients experienced major bleeding during ECMO treatment. Twenty-four (30%) patients had pneumothorax, and 22 (27%) had heparin-induced thrombocytopenia. Thrombosis or pulmonary thromboembolism episodes were presented in 13 (16%) and 8 (10%) patients, respectively.

Concerning mortality, 61 patients died during hospitalization, representing a 75% mortality rate. When we analyzed mortality according to the successive waves of COVID-19, we found significant differences between waves ($p = 0.012$). During the second, third, and sixth waves, the mortality rate exceeded 80%. In the fourth wave, it was 67%, while the fifth wave recorded 50%. The first wave had a mortality rate of 20% (Table 3, Fig. 2). Concerning the predominant variants of the SARS-CoV-2 virus in each wave in our study population, the predominant strain was B1, originating in Wuhan, in the first three waves, and the alpha variant predominated in the fourth wave. However, in the fifth and sixth waves, the delta variant was predominant followed by a low percentage of omicron in the sixth wave.

The leading causes of mortality among patients on ECMO therapy were multi-organ failure (36%), respiratory failure (26%), sepsis (22%), and cardiorespiratory arrest (14%). Seven (8.6%) patients had their life support adjusted due to the irreversibility of their multiorgan failure, with an average of 14.7 ± 7.4 days of ECMO support in this group. Of note, patients who died were older (53.7 ± 8 *vs*. 41.8 ± 11.4, $p < 0.001$), and more frequently had hypertension (49% *vs*. 5%, $p = 0.001$), dyslipidemia (33% vs. 5%, $p = 0.017$), a higher creatinine (0.8 [IQR 0.58—1] mg/dL *vs*. 0.55 [IQR 0.47—0.72] mg/dL, $p = 0.008$), and experienced a longer interval between COVID-19 symptoms and mechanical ven-

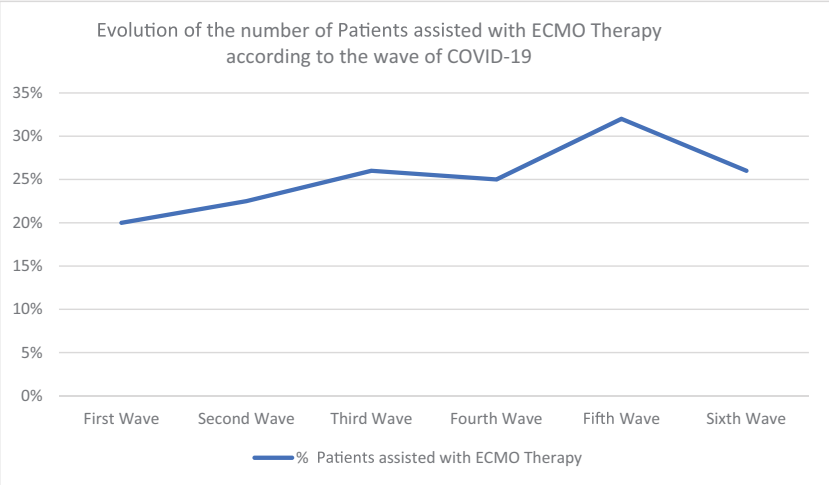


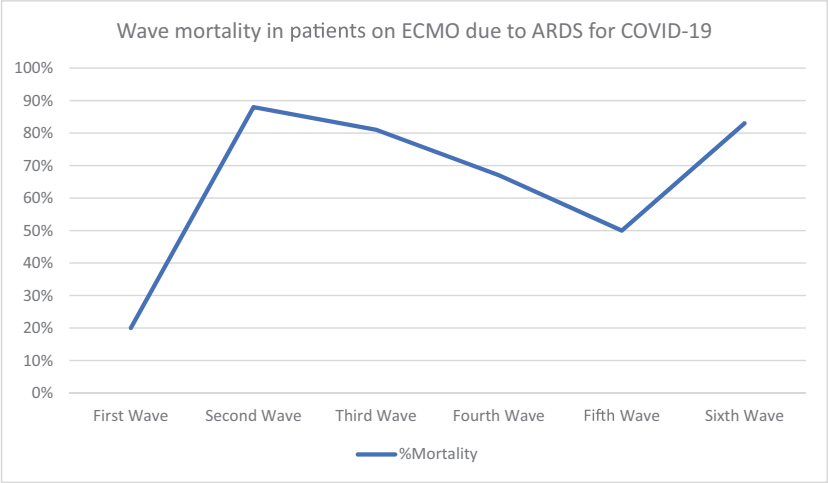
Figure 1 Evolution of the number of Patients assisted with ECMO Therapy according to the wave of COVID-19. ECMO: Extracorporeal Membrane Oxygenation; ARDS: Acute Respiratory Distress Syndrome.

Table 3 Comparison of living and dead patients on ECMO due to ARDS for COVID-19.

	Patients who die (*N* = 61)	Patients who survived (*N* = 20)	p-value
Age (years)	53.7 ± 8	41.8 ± 11.4	<0.001
Male	47 (77%)	12 (60%)	0.229
BMI (kg/m^2)	34.2 ± 7	34.7 ± 7	0.881
Obesity (BMI ≥ 30 kg/m^2)	24 (39%)	6 (30%)	0.542
Hypertension	30 (49%)	1 (5%)	0.001
Diabetes Mellitus	15 (24.6%)	1 (5%)	0.066
Dyslipidemia	20 (33%)	1 (5%)	0.017
Pre ECMO tracheo	16 (26.2%)	9 (45%)	0.083
Hemofilter	28 (46%)	2 (10%)	0.005
Any major bleeding	27 (44%)	15 (75%)	0.008
Wave number			
1[a]	1 (20%)	4 (80%)	0.012
2[a]	22 (88%)	3 (12%)	
3[a]	13 (81%)	3 (19%)	
4[a]	2 (67%)	1 (33%)	
5[a]	4 (50%)	4 (50%)	
6[a]	19 (83%)	5 (17%)	
Pre-ECMO creatinine	0.8 (0.58—1)	0.55 (0.47—0.72)	0.008
Pre-ECMO CRP	10.59 (1.8—20.8)	1.77 (0.75—8.69)	0.065
Days on mechanical ventilation	20 (13—30)	49 (28—63)	<0.001
Days on ECMO	11 (3.5—21-5)	24 (12—31)	0.006
Length of stay in ICU (days)	24 (18.5—33.5)	57 (36—72)	<0.001
Length of stay in hospital (days)	26 (20—34)	72 (64—79)	<0.001
Long ECMO (>30 days)	8 (13%)	5 (25%)	0.863
Days from COVID-19 clinic to mechanical ventilation	13.3 ± 6.3	8.8 ± 5.7	0.014
Days of COVID-19 clinic to ECMO	18 (14.5—27)	17 (10—23)	0.244
Days from mechanical ventilation to ECMO	3 (5—12)	8 (5—14)	0.133
Days from tracheostomy to ECMO	4 (2—9)	5 (3—9)	0.619

BMI: Body Mass Index; ECMO: extracorporeal membrane oxygenation; CRP: C-reactive protein; ICU: intensive care unit.

tilation (13.3 ± 6.3 *vs*. 8.8 ± 5.7 days, $p = 0.014$) compared to patients who survived. There were no significant differences between the two groups regarding obesity (39% *vs*. 30%, $p = 0.542$) (Table 3). After ECMO implantation, patients who died required hemofiltration therapy more frequently (46% *vs*. 11%, $p = 0.005$). These patients also had a shorter time on mechanical ventilation (20 [IQR 13—30] days *vs*. 49 [IQR 28—63] days, $p < 0.001$), shorter time on ECMO (11 [IQR 3.5—21.5] days *vs*. 24 [IQR 12—31] days, $p = 0.006$), spent less time in the ICU (24 [IQR 18.5—33.5] days *vs*. 57 [IQR 36—72] days, $p < 0.001$), and less time hospitalized (26 [IQR 20—34] days *vs*. 72 [IQR 64—79] days, $p < 0.001$), than the survivor patients (Table 3).



p-value = 0.012

ECMO: Extracorporeal Membrane Oxygenation; ARDS: Acute Respiratory Distress Syndrome

Figure 2 Wave mortality in patients on ECMO Therapy due to ARDS for COVID-19.

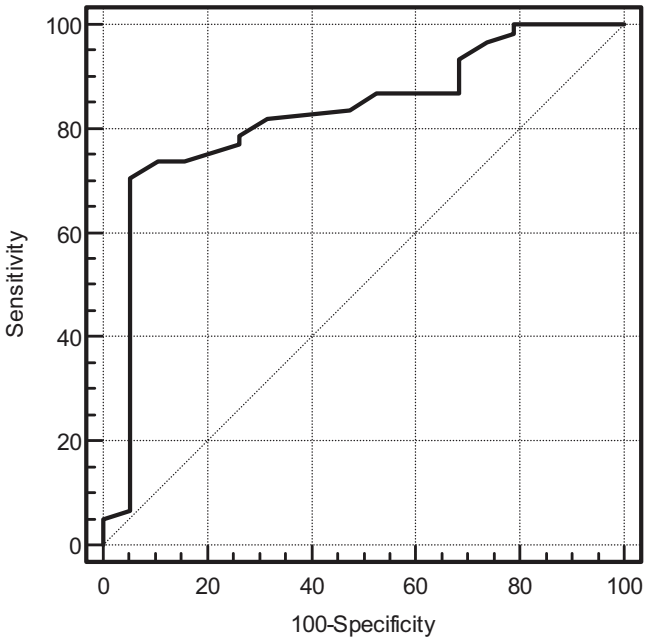


Figure 3 ROC curve for mortality and age in COVID-19 patients assisted with ECMO.

In the multivariate logistic regression analysis, only age was an independent predictor of mortality in these patients with ARDS due to COVID-19 requiring ECMO therapy (OR 1.24, 95% CI 1.027–1.50; $p = 0.025$). After ROC analysis, age achieved a predictive ability (according to the c-index) of 0.826 (95% CI 0.75—0.90) (Fig. 3). The best cut-off point was an age >51 years with a sensitivity of 70.5% and a specificity of 95%.

Later, a clinical follow-up during a mean of 18 ± 10 months of the 20 patients discharged from the hospital showed that 12 (60%) patients were in NYHA functional class I, 5 (25%) were in functional class II, and 3 (15%) were in NYHA functional class III. According to the Barthel Index, 5 (25%) patients were discharged with moderate dependency, another 5 (25%) patients had slight dependency, and the remaining 10 (50%) patients exhibited minimal dependency or independence. Eight (40%) patients recognized difficulties in returning to a normal working life due to secondary sequelae of ARDS that required ECMO assistance and a long stay in the ICU and hospital, mainly respiratory failure requiring oxygen and arthropathies.

Discussion

Our work reflects our experience with the ECMO therapy of ARDS caused by the SARS-CoV-2 throughout the COVID-19 pandemic.

The first interesting result from our cohort of 81 patients with COVID-19-related ARDS who received ECMO therapy was the incidence of pneumothorax, which was somewhat higher than the rate reported by other authors for COVID-19 patients requiring mechanical ventilation.[14] This suggests that our patients had severe lung involvement with significant lung damage and stiffness, despite the use of lung-protective ventilation settings.

Regarding mortality, the in-hospital mortality rate found in our patients was high (75%). Initial studies reported a 94% mortality of patients treated with ECMO for ARDS caused by COVID-19,[8] which raised concerns among some clinicians about the usefulness of ECMO in ARDS caused by COVID-19. However, meta-analyses and subsequent systematic reviews showed lower mortality (between 37% and 49%).[15] These mortality rates were supported by various observational multicenter studies.[16–23] Nonetheless, many of these studies were cross-sectional, with the pandemic still ongoing and

some of the patients analyzed still on ECMO or in-hospital, or they were studies focused only on the first wave of the pandemic, such as the EuroECMO-COVID.[20] On the contrary, other studies from Germany and Poland reported mortality of patients on ECMO due to ARDS due to COVID-19 close to 70%.[16,24–27]

Notably, there was an increase in mortality from the second wave of the COVID-19 pandemic in our cohort. Other researchers have described this fact throughout the pandemic.[16–20,28–31] This paradoxical situation has been explained by various reasons.[18,29–31] One of them is the increase in non-invasive respiratory support before ECMO, which could cause a more fibrotic lung at the time of mechanical ventilation, and subsequent connection to ECMO therapy and therefore more difficult to recover. Another potential reason is the use of dexamethasone in all patients with COVID-19 since the publication of the Recovery trial,[32] which could cause a selection of patients for more invasive therapies who do not respond to steroids. Moreover, the increase in bacterial infections added to the increase in treatments with corticosteroids or monoclonal antibodies that modulate the inflammatory and immunological response of the patient, and finally the liberalization of the indication of ECMO systems for the treatment of ARDS caused by COVID-19, given the good initial results. The fact is that this increase in the mortality of patients on ECMO during the evolution of the pandemic differentiates it from other indications of ECMO due to ARDS of non-COVID-19 origin.[31]

On the other hand, like Shih et al.[33] we did not find differences in mortality among the different variants of the SARS-CoV-2 virus predominant throughout the pandemic, unlike Schmidt et al.,[17] who did find higher mortality associated with the delta variant of SARS-CoV-2.

Interestingly, patients in our study who survived were placed on mechanical ventilation earlier than those who died. This aligns with other research showing that early intubation in COVID-19 patients correlates with lower mortality rates.[34] Consequently, delaying the transition from non-invasive ventilation to mechanical ventilation beyond 48 h may increase mortality.[34]

The main cause of hospital death among our patients was a multi-organ failure, followed by respiratory failure and sepsis. Such figures were very similar to those published by Lorusso et al. in a study of the EuroECMO-COVID study group.[20]

In our study, the only independent predictor of in-hospital mortality was age. This predictor also appears in other works as the main predictor of mortality in general COVID-19 infection[24,35] and in patients with ARDS caused by SARS-CoV-2, assisted with ECMO therapy.[16–23,36–38] In our analysis, the best cut-off point for age was >51 years. This data could guide us in future pandemics on the use of ECMO therapies in patients with ARDS, although it must be taken with great caution since it is much lower than the cut-off point applied by other studies of >65 years.[38] However, it seems to underline that ECMO therapy in patients with ARDS due to COVID-19 is more effective under 50 years of age, as pointed out by Karagiannidis et al.[39]

Finally, we achieved a follow-up of 100% for the patients discharged from our hospital, and no patient died during the follow-up. Unlike, the series by Lorusso et al.[20] report a mortality of 5% at 6 months after discharge. In our series, 60% of the discharged patients had an active working life 18 months after hospital discharge, a percentage higher than that found in other works showing that only 24% of the discharged patients had resumed their regular work 6 months after discharge[20] or 38% of the discharged patients who returned to work in the Chommeloux et al. series,[40] 1-year after hospital discharge, although our average follow-up was higher than these studies. This fact may be attributed to the early intervention of rehabilitation and physiotherapy services with these patients even while they were supported with ECMO devices in the ICU.

Limitations

Our study has certain limitations. First, it is a retrospective, single-center study with few patients; hence our results may not apply to other centers. Association does not imply causality; therefore, our results should be considered a hypothesis generator. In the analysis of ventilatory variables, tidal volume and plateau pressure were not included. We did not analyze patients in whom it was decided not to implant ECMO support. We did not know the viral variants that infected each case studied. We analyzed the predominant variant of the virus during the pandemic in our region. In clinical follow-up, we lack a more objective and standardized evaluation of lung function and a psychological evaluation of these patients.

Anyway, this work reflects our center's experience in treating ARDS from SARS-CoV-2 using ECMO during the COVID-19 pandemic, including a complete 18-month follow-up for survivors. This knowledge can guide future pandemic responses. It is crucial to avoid the futile use of ECMO in patients with low survival chances and to maintain strict indication criteria. A model from the Greater Paris area[19] involved a centralized evaluation of ECMO requests, which is worth noting. Regular reviews of ECMO outcomes and indications will help enhance protocols for future ARDS patients.

Conclusion

In our experience, patients with ARDS due to SARS-CoV-2 who underwent ECMO therapy experienced high mortality and morbidity. In-hospital mortality increased during the pandemic, with older age as the sole independent predictor. However, once discharged, no patients died within the first 18 months of follow-up, though 40% faced respiratory and motor sequelae, affecting their ability to return to normal work and social life.

CRediT authorship contribution statement

JMAL: gathered data, coordinated the conceptualization and design of the study, writing and edition of the manuscript, and performed the statistical analysis.

JMRC: participated in the conceptualization and design of the study, writing, and edition of the manuscript, and performed the statistical analysis.

CVA: participated in the revision and edition of the manuscript.

AVV: participated in the revision and edition of the manuscript.

AS: participated in the revision and edition of the manuscript.

DPM: participated in the revision and edition of the manuscript.

JBM: participated in the revision and edition of the manuscript.

FG: participated in the revision and edition of the manuscript.

MSP: gathered data and participated in the revision and edition of the manuscript.

RJ: participated in the revision and edition of the manuscript.

SJCL: participated in the revision and edition of the manuscript.

CAM: gathered data, participated in the conceptualization and design of the study, and writing and edition of the manuscript.

All the authors approved the final version.

Declaration of Generative AI and AI-assisted technologies in the writing process

While writing this manuscript, the authors used no generative artificial intelligence tools.

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Declaration of competing interest

None.

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