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RESEARCH ARTICLE

Retrospective Evaluation of Covid-19 Patients Treated with Extracorporeal Membrane Oxygenation and Cannulation Types Applied

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ABSTRACT

Objective: Pneumonia associated with the novel coronavirus disease 2019 (COVID-19) can lead to respiratory failure with deep hypoxemia requiring endotracheal intubation and mechanical ventilation. Patients who do not respond to optimal conventional mechanical ventilation may be candidates for administration by extracorporeal membrane oxygenation (ECMO) in institutions with appropriate resources (equipment and personnel). This study aimed to compare the effects of cannulation types on mortality.

Materials and Methods: Patients followed up at the intensive care unit between April 2020 and May 2021 with the diagnosis of COVID-19 and who received ECMO support were screened. Demographic data of the patients, initiation of ECMO, ECMO type, type of inserted cannula, duration of intubation, intensive care unit and hospital stays, P/F levels were collected from the Hospital Information Management System and retrospectively analyzed.

Results: Among the patients with ARDS who underwent ECMO, 4 were females and 24 were males. When hemodynamic parameters were compared, no statistically significant difference was found between the groups. All patients needed high doses of inotropic agents. Of the 28 Covid-19 patients who underwent ECMO, 25 (89.3%) died. Eight patients left ECMO, but only 3 of the patients who left ECMO were discharged. No statistically significant difference was found in terms of the onset of ECMO after intubation (p=0.62). Mean ECMO time applied to the patients was determined as 10.6±9.6 days.

Conclusion: ECMO is a rescue treatment requiring the participation of a multidisciplinary team of experienced medical professionals with training and expertise in initiating, maintaining and discontinuing ECMO in critical patients.

Keywords: ARDS, cannulation, COVID-19, ECMO, hypoxia, mortality, pandemic

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INTRODUCTION

The novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection and its clinical manifestation as Coronavirus Disease 2019 (COVID-19) have become a worldwide public health problem since the first diagnosis of the disease in Wuhan in December 2019.[1] Globally, as of April 17, 2021, there have been 139.501.934 confirmed cases of COVID-19, including 2.992.193 deaths, reported by WHO (mortality of 2.1%).[2]

Although most patients with COVID-19 have mild symptoms, some patients have severe respiratory failure requiring intensive care unit (ICU) and mechanical ventilation.[3] Mortality is high in patients with COVID-19 who develop severe respiratory failure and require mechanical ventilation.[4] While little is still known about the true effectiveness of extracorporeal membrane oxygenation (ECMO) in COVID-19, it can serve as a life-saving salvage therapy.

The indication for ECMO in COVID-19 patients is severe pneumonia with acute respiratory compromise refractory to optimal conventional management including standard lung-protective ventilation strategy, prone positioning, and neuromuscular blockade.[5] The criteria to follow for ECMO

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are PaO_2/FiO_2 <100 mmHg and/or arterial blood PH <7.2 and PaCO2 >60 mmHg.[6] Other parameters are mechanical ventilation <7 days, age < 65 years, ventilator frequency <35 breath per minute (bpm), and plateau pressure >30 cm H_2O. [7] VV ECMO requires that deoxygenated venous blood be removed from the patient, circulated through an oxygenator, and then returned to the venous system of the oxygenated and decarboxylated blood.[8]

The most common cannulation configuration is percutaneous insertion of two cannulas, one placed in the right internal jugular vein (IJ) and the other in the femoral vein.[8] Alternatively, a single double-lumen ECMO cannula can be placed in the right IJ vein. This cannula is inserted percutaneously into the right IJ vein, with the most distal part of the cannula rests the inferior vena cava.[8]

Cannulation should be done under visual fluoroscopic control for the wire. When the cannula crosses the right atrium, it is associated with risks of cannula misplacement and right ventricular perforation.[9] Another option for cannulation may be under transthoracic echocardiography, transesophageal echocardiography, or a combination of transesophageal echocardiography and fluoroscopic guidance.[10]

We aimed to compare the effects of cannulation types on mortality, patient survival and clinical progress by retrospectively examining COVID-19 patients who received ECMO treatment in our clinic.

MATERIALS and METHODS

Ethics approval for this study was provided by the Ethical Committee of İstanbul Medipol University Hospitals, on 18 February 2021 (Ethical Committee decision No: 178). The principles of human experimentation set out in the Helsinki Agreement adopted in 1975 were complied with. Moreover, permission was received from the Turkish Ministry of Health for the anonymous analysis of the recorded patient data. After receiving ethics permission, patients who were followed up in the intensive care unit between April 2020 and May 2021, who were positive for polymerase chain reaction (PCR), diagnosed with COVID-19 and underwent ECMO were retrospectively screened.

Demographic data of the patients, beginning time of ECMO treatment and ECMO durations, ECMO type, type of cannula used, intubation times, intensive care hospitalization times were analyzed from the Hospital Information Management System.

Inclusion criteria were determined as Covid-positive patients aged 18–65 years, who were not pregnant, who received PCR test positivity, who received COVID-19 pneumonia, and who received ECMO treatment. Exclusion criteria were determined as >18, years of age and pregnant women.

Statistical Analysis

Statistical analyzes were performed using SPSS 15.0 for Windows. Descriptive criteria were presented as mean and standard deviation, median and min-max values. Conformity of the data to normal distribution was checked with the Kolmogorov-Smirnov test. Mann-Whitney U test was used for normally distributed parametric values when conditions were not met for the comparison of continuous variables between discharged and deceased patients. Significance level was taken as $p<0.05$.

RESULTS

As a result of the statistical analysis, no statistically significant difference was found between the groups in terms of demographic data. Demographic data are shown in Table 1. Among the patients with ARDS who underwent ECMO, 4 were females and 24 were males. Mean body mass index (BMI) of the patients was found to be 31.1±3.3.

As a result of the statistical analysis, when hemodynamic parameters were compared, no statistically significant difference was found between the groups. Comparison of hemodynamic parameters are shown in Table 2. All patients needed high doses of inotropic agents.

Of the 28 Covid-19 patients who underwent ECMO, 25 (89.3%) died. Eight patients left ECMO, but only 3 of the patients who left ECMO were discharged. As a result of the statistical analysis, no statistically significant difference was found in terms of the onset of ECMO after intubation ($p=0.62$). Mean ECMO time applied to the patients was determined as 10.6±9.6 days. Comparison of intubation and ECMO times are shown in Table 3.

Lung protective ventilation was maintained during ECMO support in all patients, and lung protective mechanical ventilation was continued in 3 patients after weaning from ECMO. All patients had P/F levels below 80. Computed tomography scans showed the typical ground glass appearance and consolidations were reduced. The level of PEEP gradually decreased during weaning from ECMO and afterwards during weaning from mechanical ventilation. After improvement of native lung functions (FIO_2 <0.5, PEEP <10 cmH_2O, peak inspiratory pressure in pressure-controlled ventilation [PIP] <25 cm H_2O), ECMO flow was gradually reduced to 2.0 L/min.

Three patients with VV ECMO support who could be weaned off were stopped after gradually decreasing flow and oxygen support from ECMO. Unfortunately, 5 patients were lost after

Table 1. Comparison of demographic data

	Dead patient Mean±SD Median (min-max)	Discharge Mean±SD Median (min-max)	Total Mean±SD Median (min-max)	p
Age	58.6±5.7 59.0 (52–66)	48.0±7.0 45.0 (43–56)	54.6±7.9 55.0 (43–66)	0.19
Weight	93.6±11.1 88.0 (85–110)	85.0±5.0 85.0 (80–90)	90.4±9.8 86.5 (80–110)	0.48
Size	169.2±8.6 168.0 (158–180)	173.3±7.6 175.0 (165–180)	170.8±7.9 171.5 (158–180)	0.99
BMI	32.6±1.4 32.7 (31.2–34.0)	28.5±4.2 27.8 (24.7–33.1)	31.1±3.3 31.9 (24.7–34.0)	0.48

SD: Standard deviation; BMI: Body mass index

Table 2. Comparison of hemodynamic parameters

	Dead patient Mean±SD Median (min-max)	Discharge Mean±SD Median (min-max)	Total Mean±SD Median (min-max)	p
Systolic blood pressure	128.8±31.7 140.0 (80–162)	112.7±31.8 130.0 (76–132)	122.8±30.5 131.0 (76–162)	0.28
Diastolic blood pressure	77.6±18.1 78.0 (50–97)	67.0±20.8 78.0 (43–80)	73.6±18.5 78.0 (43–97)	0.57
Heart rate	93.6±20.6 88.0 (73–124)	94.7±21.6 87.0 (78–119)	94.0±19.4 87.5 (73–124)	0.62
SPO_2	84.2±7.6 88.0 (76–91)	66.7±23.2 78.0 (40–82)	77.6±16.4 80.0 (40–91)	0.15

Table 3. Comparison of intubation and ECMO times

	Dead patient Mean±SD Median (min-max)	Discharge Mean±SD Median (min-max)	Total Mean±SD Median (min-max)	p
ECMO times	9.7±9.8 6.0 (1–38)	18.0±3.5 20.0 (14–20)	10.6±9.6 7.5 (1–38)	0.06
Between Intubation and ECMO time	4.0±3.6 3.0 (0–15)	2.7±2.1 2.0 (1–5)	3.9±3.5 3.0 (0–15)	0.62

ECMO: Extracorporeal membrane oxygenation

weaning from ECMO, the remaining patients with VV ECMO were lost while still on ECMO. Among the patients who could be weaned off ECMO, 5 of them died due to cardiac rhythm disorders and hypotension.

Three (% 10.7) of 28 VV ECMO supported patient's blood gas values were at normal ranges but due to long intubation duration and increased secretion, they needed tracheostomy and they were discharged from ICU unit to the ward with tracheostomy cannula. These three weaned off ECMO and were discharged from hospital without any neurologic or ischemic pathology.

DISCUSSION

As a result of the statistical analysis performed in our study, no statistically significant difference was found be-

tween the groups in terms of demographic data. Of the patients with ARDS who underwent ECMO, 4 were females and 24 were males. Mean body mass index (BMI) of the patients was 31.1±3.3.

There are some questions about when and for which indications ECMO therapy should be started in COVID-19. Some guidelines recommend the use of ECMO after standard therapy.[11] Some authors use ECMO early before MODS or severe ventilator-related lung injury because studies suggest that early initiation of ECMO in ARDS may be beneficial.[12,13] As a result of the statistical analysis performed in our study, when the patients who were discharged and those who died were compared, mean time to start ECMO treatment after intubation was 3.9±3.5 days, and no statistically significant difference was found (p=0,62). Mean ECMO time applied to the patients was determined as 10.6±9.6 days. In our study, ECMO treatment was started early in patients who developed ARDS and were treated with all conventional treatments.

Information on COVID-19 is increasing, and the role of ECMO is being studied at various specialist centers. In these centers, ECMO tends to save the critically ill. Yang et al.[14] have studied 52 critically ill patients and administered ECMO therapy to six of them. Of these patients, 67% had ARDS, and only one out of 6 patients who underwent ECMO survived more than 28 days. Li et al.[15] have administered ECMO therapy to eight out of 16 of their COVID-19 patients. Four of them died (50%) and three of them left ECMO but continued to receive mechanical ventilation support (37.5%). Only one patient left ECMO within 28 days. Zhan et al.,[16] noticing early on that mechanical ventilation was inadequate, have reported a low-risk case who was treated with ECMO within hours after intubation. This patient recovered and was discharged within 40 days. Henry et al.[17] have studied 234 cases of COVID-19-related ARDS in China, of whom 17 (7.25%) received ECMO. Although the severity of ARDS and the timing of the ECMO intervention have not been not specified, the study has shown a 94.1% mortality rate in ECMO patients compared to 70.9% in conventional patients, bearing in mind that patients with severe ARDS are more likely to undergo ECMO.

In our study, 25 (89.3%) of 28 Covid-19 patients who underwent ECMO died. Eight patients weaned from ECMO. Three patients with VV ECMO support weaned from ECMO after flow and oxygen support were gradually reduced. Unfortunately, 5 patients died after weaning from ECMO, other patients who received VV ECMO treatment died while on ECMO. Of the patients eligible for ECMO, 5 died due to cardiac arrhythmias and hypotension.

As regards direct pulmonary artery flow improving oxygenation and ventilation using dual cannula and early mobilization after weaning from the ventilator, Liu et al.[18] have reported that there are several advantages such as low complication rate associated with cannula. In our study, dual cannulation was applied in two cases, but we could not reach sufficient support for oxygenation in these patients. The patient's oxygen saturation could not be increased to 90%. Thereupon, one patient died due to multi-organ failure, and we decided to change the cannulas to the femoral and internal jugular veins in the other patient, and blood gas measurements improved. This patient was subsequently weaned from ECMO. In other patients, right internal jugular vein and right femoral vein were cannulated under ultrasound guidance, and we did not encounter any complications during catheterization.

While in conventional practice, VV-ECMO circuits usually involve cannulation of two vessels (double cannulation), it is now possible to use a single cannula for VV-ECMO support. Double cannulation technique may be the first choice for VV-ECMO given its ease of implantation and efficiency. Dual cannula is an attractive option for outpatient VV-ECMO programs, but more complex implantation and higher costs have limited its widespread use.[19] ECMO is a salvage treatment for critically ill patients that requires the participation of an experienced and disciplined team.

Disclosures

Ethics Committee Approval: The study was approved by the Istanbul Medipol University Non-interventional Clinical Research Ethics Committee (No: 178, Date: 18/02/2021).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer reviewed.

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