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Extra Corporeal Membrane Oxygenation versus Standard of Care Lung Protective Strategy in Covid-19 ARDS Mechanically Ventilated Critically Ill Patients

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ABSTRACT

Background: The use of venovenous extra corporeal membrane oxygenation (VV-Ecmo) in severe hypoxemic respiratory failure from coronavirus disease 2019 has been described but reported utilization and outcomes are variable and detailed data on patient characteristics is lacking.

Objective: Our study aimed to evaluate the effect of extra-corporeal membrane oxygenation (ECMO) when compared to the traditional conventional protective lung strategy mechanical ventilation for Covid-19 ARDS associated Respiratory failure.

Patients and methods: This is a prospective study with 1:1 randomization for either to go through ECMO or keep on conventional mechanical ventilation with protective lung strategy for patient Covid-ARDS associated with respiratory failure. One hundred patients were randomized in each group.

Results: Hundred patients were in each group. Age was 48.4 ± 9.0 in the standard care mechanical ventilation group versus 47.8 ± 8.3 in the ECMO group, 54 males and 46 females in the standard care group and 59 males and 41 females in the ECMO group. Vasopressor weaning was in 40 cases in the standard care group and 64 patients in the ECMO group with a significant statistical difference in favor of the ECMO group (p-value < 0.001). Also, weaning from mechanical ventilation was 29 patients versus 66 patients in the standard care group and in the ECMO group respectively (P-value <0.001). Also the inflammatory markers like CRP, D-dimer, procalcitonin, IL-6 and ferritin were more improved in the ECMO group, more than in the standard care group with a significant statistical difference (p-value <0.001),

Conclusion: ECMO in Covid-19 ARDS respiratory failure patients was associated with weaning from mechanical ventilation & vasopressors and more improvement in the markers profile, together with the radiological point of view and arterial blood gases parameters when compared to the standard care group together with a great reduction in the length of stay in the intensive care unit with decrease in the mortality.

Keywords: ECMO, Covid-19, ARDS, Mechanical ventilation.

INTRODUCTION

Approximately 40% of Covid-19 patients admitted to the critical care unit have severe acute respiratory failure [(1-2)]. Extracorporeal membrane oxygenation (ECMO) lowers mortality in patients with Covid-19 and non-Covid-19 who experience acute respiratory failure despite receiving the best care possible from conventional mechanical ventilation by maintaining gas exchange and minimising lung injury caused by ventilation while the lung recovers [(2-6)].

Due to the limited resources available during a pandemic, reports of low survival rates in case series of Covid-19-associated acute respiratory failure treated with ECMO discouraged doctors from using it early in the pandemic, prompting some to advocate for a ban on its use in Covid-19 patients [(7)].

Early data from the extracorporeal life support organisation suggested that 40% of patients undergoing ECMO for acute respiratory failure linked to Covid-19 would die [(8)].

Despite variations in mortality rates over time and across the pandemic, many observational studies came to the conclusion that the outcomes with ECMO in patients with Covid-19-related acute respiratory failure was comparable to previous observations on the impact of ECMO in patients with other causes of acute respiratory failure [(9-14)]. In a recent study in patients with acute respiratory failure without Covid-19, it was discovered that ECMO is beneficial for patients with severe hypoxemic acute respiratory failure, which is indicated by a partial pressure of arterial oxygen to fraction of inspired oxygen (Pao2/Fio2) ratio of 80 mm Hg. At first, there was a shortage of information to inform clinical judgments regarding whether patients should get ECMO, and developed guidelines were primarily based on these findings [(3-4)].

An accepted statistical method for estimating treatment efficacy across populations in an uncontrolled context is to use prospective data to simulate a target trial [(15, 16)].

This analysis approach was a desirable addition to randomised controlled trials when performing them was difficult (e.g., due to poor enrollment rates, crossovers, stringent inclusion criteria, and lack of equipoise) [(17)]. When researching a complicated and resource-intensive technique like ECMO during a worldwide epidemic, it can provide more significant and more generalizable data [(3, 18, 19)].We compared weaning from vasopressor

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treatment in our prospective trial of people with acute respiratory failure caused by the Covid-19 virus.

Weaning from mechanical ventilation, improvement in inflammatory markers, improvement in chest x-ray & computed tomography of the chest, arterial blood gases parameters together with ICU length of stay and ICU mortality between ECMO treatment in patients with a PaO_2/FIO_2 ratio < 80 mmHg and a method of care where everyone had regular mechanical ventilation without ECMO. Additional analyses were conducted to determine whether age, pre-existing comorbidities, or the length of mechanical ventilation used prior to the use of ECMO were related to altered therapeutic efficacy.

At the end, we evaluated the effectiveness of ECMO using a variety of metrics that take into consideration the degree of acute respiratory failure or the level of mechanical ventilation that changes as a patient is admitted to critical care [20, 21].

PATIENTS AND METHODS

A prospective study of two hundred adult patients with Covid-19 related acute respiratory failure admitted in Helwan University Hospital ICU were randomized into two groups; group with the standard mechanical ventilation and another group with the ECMO started in the period of April 2020 till May 2022.

By using either the next-generation or reverse transcriptase polymerase chain reaction, all patients were shown to have SARS Cov-2 infection, together with daily chest X-ray and chest computed Tomography Inflammatory markers were done and follow-up was done for C-reactive protein, D-dimer, procalcitonin, interleukin-6 and ferritin, together with serial arterial blood gases.

Primary outcome analysis:

We compared weaning from mechanical ventilation, weaning from vasopressor support, improving of inflammatory markers like CRP, D-dimer, procalcitonin, interleukin-6 and ferritin together with radiology represented in chest x-ray and chest computed tomography. At the same time the arterial blood gases parameters where ECMO was initiated if the PaO_2/FIO_2 ratio with the therapy where patients had standard mechanical breathing without ECMO decreased below 80 mmHg. Additionally, we looked at the possibility of impact modifiers related to age, pre-existing co-morbidities (diabetes, obesity, and arterial hypertension), and length of mechanical ventilation. Also, using several time-varying indicators of the severity of the illness, we calculated the efficiency of ECMO when it was first started. A measure of the severity of acute respiratory failure was the PaO_2/FIO_2 ratio. We employed static driving pressure, which is determined by subtracting the positive end expiratory pressure from the plateau airway pressure, to indicate the degree of mechanical ventilation [22].

Secondary outcome analysis:

We compared the ICU length of stay and ICU mortality in the ECMO group versus the standard strategy mechanical ventilation.

Ethical consent:

The Ethical Institutional Review Board at Helwan University approved the study. After explaining our research objectives, written informed consents were obtained from all study participants. This study was conducted in compliance with the code of ethics of the world medical association (Declaration of Helsinki) for human subjects.

Statistical analyses

The social science statistical package was used to edit, code, tabulate, and introduce the acquired data to a computer (SPSS 25). Data were given, and the type of data gathered for each parameter was appropriately analysed. For numerical data, the mean and standard deviation. Proportion and frequency of non-numerical information. The statistical significance of the difference between the means of the two study groups was evaluated using a student T-test. The correlation between two qualitative variables was investigated using the chi-square test. P value ≤ 0.05 was regarded as significant.

RESULTS

Two hundred patients were included in the study with 87 patients were female (43.5%) and 113 patients were male (51.5%). The mean age was 48.4 ± 9.0 in the standard care group and 47.8 ± 8.3 in the ECMO group. Table (1) showed 54 males in the standard care group versus 46 females. While, in the ECMO group there was 59 males and 41 females while mean age was 48.4 ± 9.0 in the standard care group and 47.8 ± 8.3 in the ECMO group all were non-significant statistically.

Table (1): Demographic Data

		Standard of Care		ECMO		Chi-Square test		
		N	%	N	%	X^2	P-value	
Sex	Male	54	54.0%	59	59.0%	X^2=0.51	0.476	NS
	Female	46	46.0%	41	41%			
		Standard of care		ECMO		T-test		
		Mean	SD	Mean	SD	T	P-value	
Age		48.4	9.0	47.8	8.3	0.42	0.672	NS

Table (2) showed improving and weaning of vasopressor support in the ECMO group than in the standard care (64 versus 40 respectively). Also, weaning from mechanical ventilation, improvement in inflammatory markers and radiological point of view were all in favor of the ECMO group as compared to the standard care group with a highly significant statistical difference ($p < 0.001$.)

Table (2): Vasopressor weaning, mechanical ventilation weaning, inflammatory markers & radiology improvement in both groups

		Standard of Care		ECMO		Chi-Square test		
		N	%	N	%	X^2	P-value	Sig.
Sex	Male	54	54.0%	59	59.0%	X^2=0.51	0.476	NS
	Female	46	46.0%	41	41.0%			
Vasopressor requirement & weaning	Deteriorating	60	60.0%	36	36.0%	X^2=11.54	0.001	S
	Improving	40	40.0%	64	64.0%			
MV setting & weaning	Deteriorating	71	71.0%	34	34.0%	X^2=27.45	0.001	S
	Improving	29	29.0%	66	66.0%			
CRP	Deteriorating	72	72.0%	32	32.0%	X^2=32.05	<0.001	S
	Improving	28	28.0%	68	68.0%			
D-Dimer	Deteriorating	72	72.0%	33	33.0%	X^2=30.5	<0.001	S
	Improving	28	28.0%	67	67.0%			
Procalcitonin	Deteriorating	66	66.0%	47	47.0%	X^2=7.34	0.007	S
	Improving	34	34.0%	53	53.0%			
IL-6	Deteriorating	59	59.0%	33	33.0%	X^2=13.61	<0.001	S
	Improving	41	41.0%	67	67.0%			
Ferritin	Deteriorating	68	68.0%	43	43.0%	M^2=12.65	<0.001	S
	Improving	32	32.0%	57	57.0%			
Radiology	Deteriorating	63	63.0%	20	20.0%	M^2=38.08	<0.001	S
	Improving	37	37.0%	80	80.0%			

Table (3) Showed the improved arterial blood gases parameters together with hemodynamics, which were more prominent in the ECMO group versus the standard care group with a highly significant statistical difference (P-value <0.001).

Table (3): Arterial blood gases parameters & Hemodynamics improvement in both groups

		Standard of Care		ECMO		Chi-Square test		
		N	%	N	%	X^2	P-value	Sig.
PH	Deteriorating	72	72.0%	37	37.0%	X^2=24.7	<0.001	S
	Improving	28	28.0%	63	63.0%			
PCO2	Deteriorating	60	60.0%	36	36.0%	X^2=11.54	<0.001	S
	Improving	40	40.0%	64	64.0%			
PO2	Deteriorating	54	54.0%	20	20.0%	X^2=24.8	<0.001	S
	Improving	46	46.0%	80	80.0%			
HCO3	Deteriorating	72	72.0%	27	27.0%	X^2=40.5	<0.001	S
	Improving	28	28.0%	73	73.0%			
hemodynamics	Deteriorating	63	63.0%	32	32.0%	X^2=19.27	<0001	S
	Improving	37	37.0%	68	68.0%			

Table (4) showed the less duration of ICU length of stay in the ECMO group when compared to the standard care group with a mean of 17.0 ± 4.1 versus 23.5 ± 1.7 respectively with a highly significant statistical difference (p-value < 0.001).

Table (4): ICU length of stay

	Standard of Care		ECMO		t test		
	Mean	SD	Mean	SD	t	P-value	Sig.
ICU LOS	23.5	1.7	17.0	4.1	21.88	<0.001	S

Table (5) showed more survival in the ECMO group, 75 patients out of one hundred versus 25 patients out of the one hundred in the standard care group with a highly significant statistical difference p-value < 0.001.

Table (5): ICU mortality

		Standard of Care		ECMO		Chi sq		
		N	%	N	%	X^{2t}	P-value	Sig.
ICU MORTALITY	Expired	75	75.0%	25	25.0%	X2=50	<0.001	S
	Survived	25	25.0%	75	75.0%			

DISCUSSION

In our study of two hundred adult patients with Covid-19 associated with acute respiratory failure, with ECMO in those with PaO_2/FIO_2 <80 mm Hg was associated with survival 75% in the one hundred adult patients underwent ECMO versus 75% mortality in the other one hundred in the conventional standard care of mechanical ventilation without ECMO.

According to a research to rescue lung damage in severe ARDS, patients with acute respiratory distress syndrome caused by variables other than COVID-19 had a risk rate of 0.76 (95% confidence interval 0.55 to 1.04) [(3)]. Another studies discovered that patients with Covid-19-related acute respiratory failure had an adjusted hazard ratio of 0.55 (95% confidence interval 0.41 to 0.74), indicating that the identified range of values for the causal effect estimated in our analysis is consistent with evidence from previous studies. This was discovered for the same period of time following diagnosis [(23-29)].

Also we found that ECMO group carried a more favorable outcome as regards the weaning from vasopressor support, weaning from mechanical ventilation, improvement in the inflammatory markers like CRP, D-dimer, procalcitonin, interleukin-6 (IL-6) and ferritin together with the radiological point of view represented in the chest x-ray together with the chest computed tomography.

In addition, ECMO significantly improved hemodynamics and arterial blood gas values as compared to the mechanical ventilation group receiving standard care without ECMO.

Additionally, we investigated whether the duration of mechanical ventilation before the commencement of ECMO and pre-existing co-morbidities were related to changed treatment success. The effectiveness of ECMO was then evaluated using indicators that took into account the degree of acute respiratory failure or the level of mechanical ventilation.

ECMO has been proven to be useful in lowering mortality in patients with numerous co-morbidities, including Covid-19 associated with more severe obesity, diabetes, and arterial hypertension.

Our findings also call into question the notion that ECMO should be strictly limited to Covid-19 patients with a PaO_2/FIO_2 of 80 mm Hg, for at least six hours, and only during the first seven days of mechanical ventilation, as suggested by the Extra Corporeal Life Support Organization's most recent recommendations, which were based on the results of the ECMO to Rescue lung injury in severe ARDS trial [(3, 4)].

We discovered that ECMO, which could be started up to 10 days after the start of mechanical ventilation, had a positive effect. We also discovered that ECMO was linked to increased survival in patients receiving potentially harmful levels of mechanical ventilation, which most likely diminished the danger of ventilator-induced lung damage [(22)].

The findings of a previous single-country cohort study from the United States [(9)] that looked at the efficacy of ECMO in patients with Covid-19 and more severe acute respiratory failure are also presented. Earlier research on the efficacy of ECMO in treating patients with acute respiratory distress syndrome caused by variables other than Covid-19 has been supplemented and enhanced by our prospective study. Furthermore, our data adds to the current understanding of clinical criteria that may be considered prior to the commencement of ECMO, as well as parameters impacting the success of such treatment in Covid-19 patients.

Our study findings should be confirmed in subsequent randomised controlled trials with larger sample sizes and multicenter designs due to the limited time and resources available, the evolving pandemic epidemiology, and the potential transition of Covid-19 to endemicity as reliable vaccinations are more commonly available. They should be viewed as supplementary data collected in a natural environment under controllable circumstances [(31, 32)].

Our study's final results may potentially offer crucial recommendations for future study design and support the use of ECMO in patients with acute respiratory failure brought on by other illnesses, such as viral pneumonia brought on by seasonal viruses or the Middle East respiratory syndrome Coronavirus [(33-35)].

CONCLUSION

Our prospective study based on patients with Covid-19 associated with acute respiratory failure. ECMO carried a great improvement in weaning from vasopressor support, weaning from mechanical ventilation, improving in inflammatory markers, together with improving in radiological point of view represented in the chest-X-ray and chest computed tomography. In addition, ECMO reduced ICU mortality and duration of stay when compared to standard mechanical breathing without ECMO. If routinely given to carefully chosen patients who had more severe hypoxemia or were receiving greater levels of mechanical ventilation, ECMO also improved outcomes.

To reduce the risk of ECMO-related injury and to optimise the efficiency of ECMO in patients with Covid-19, considerations such as the severity of hypoxemia, before electing to start ECMO, the decision on the length and degree of mechanical ventilation should be taken.

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