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## Journal Pre-proof

Poor survival with extracorporeal membrane oxygenation in acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19): Pooled analysis of early reports

Brandon Michael Henry, Giuseppe Lippi

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**Poor Survival with Extracorporeal Membrane Oxygenation in Acute  
Respiratory Distress Syndrome (ARDS) due to Coronavirus Disease 2019  
(COVID-19): pooled analysis of early reports**

**Brandon Michael Henry<sup>1</sup>, Giuseppe Lippi<sup>2</sup>**

<sup>1</sup>Cardiac Intensive Care Unit, The Heart Institute, Cincinnati Children's Hospital Medical Center, Ohio, USA

<sup>2</sup>Section of Clinical Biochemistry, Department of Neuroscience, Bio. medicine and Movement, University of Verona, Verona, Italy

\* *Corresponding author.*

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**Corresponding Author:**

Brandon Michael Henry, M.D.  
Cardiac Intensive Care Unit  
The Heart Institute  
Cincinnati Children's Hospital Medical Center  
3333 Burnet Avenue, Cincinnati, Ohio, 45229, USA  
Email: Brandon.henry@cchmc.org

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*Dear Editor,*

The novel coronavirus disease 2019 (COVID-19) can induce acute respiratory distress syndrome (ARDS), which can progress to refractory pulmonary failure. In such cases, extracorporeal membrane oxygenation (ECMO) may be considered as a rescue therapy. In a study of ECMO for ARDS in patients with Middle East Respiratory Syndrome Coronavirus (MERS-CoV), a similar coronavirus disease emerged in 2012, a significant decrease of in-hospital mortality rate and length of intensive care unit (ICU) stay was found in patients treated with ECMO compared to those managed with conventional therapy [1]. However, with COVID-19, concerns have been raised about high mortality rate observed in an early report which included data on ECMO in infected patients [2]. It has been suggested that the compounded immunologic insult by both infection and extracorporeal circuit may counterbalance or even offset survival benefits [2]. In this article, we aimed to evaluate ECMO mortality as reported in early COVID-19 epidemiological studies.

An electronic search of Medline (PubMed interface), Scopus and Web of Science, was executed employing the keywords “mortality” OR “death” OR “ECMO” AND “coronavirus 2019” OR “COVID-19” OR “2019-nCoV” OR “SARS-CoV-2”, between 2019 and present time (i.e., March 13, 2020). No language restrictions were applied. The title, abstract and full text of all articles captured with these search criteria were assessed, and those reporting the rate of mortality in COVID-19 patients receiving ECMO were included in pooled analysis. The reference list of all identified studies was also analyzed (forward and backward citation tracking) to detect additional articles.

Data on the number of patients with ARDS and treated with ECMO, and the mortality rate for each was extracted. The obtained data was pooled using a random effects model, with estimation of odds ratio (OR) and its 95% confidence interval (95% CI) for mortality in patients

with or without ECMO support. Statistical analysis was performed using MetaXL, software Version 5.3 (EpiGear International Pty Ltd., Sunrise Beach, Australia). The study was carried out in accordance with the declaration of Helsinki and local legislation.

Overall, 87 articles were initially identified based on our electronic and reference search, which after screening by title, abstract, and full text, 83 were excluded for the following reasons: not related to COVID-19 (n=27), review articles (n=9), did not provide relevant data (n=37), and editorials (n=10). Thus, a total of 4 studies [3–6] were finally included in our pooled analysis, comprising 562 COVID-19 patients, 234 (41.6%) of which developed ARDS. All studies were from China. Table 1 presents essential study characteristics.

Among the 234 ARDS patients, 17 (7.2%) underwent ECMO. The mortality rate was 94.1% in the ECMO patients and 70.9% in conventional therapy patients. The results of the pooled analysis is presented in Figure 1. The pooled odds of mortality in ECMO versus conventional therapy was not significantly different (OR: 2.00, 95%CI: 0.49-8.16). There was no observable heterogeneity ( $I^2=0\%$ , Cochran's Q, p-value=0.99).

The results of this analysis using currently available literature would suggest that ECMO does not seemingly produce either harm or benefit in COVID-19 patients progressing to ARDS. A few limitations shall be noted, however. Patients may have variable levels of ARDS severity, with those receiving ECMO being potentially more critically ill in some cases, which may have impacted the mortality rates. Nonetheless, the mortality rate in the conventional therapy group was relatively high (70.9%). Data on baseline characteristics and disease courses were not provided on ECMO patients. Lastly, the sample size of ECMO patients was considerably small (n=17). However, when compared to the largest report of MERS patients receiving ECMO (n=17), COVID-19 patients seem to have substantially higher mortality to-date (94.1% vs.

65.0%), raising questions about real utility of ECMO in this outbreak [1]. Further research is urgently needed. We encourage authors of future COVID-19 reports to provide more data specifically on the ECMO patients in order to aid in optimal patient selection in a limited resource setting.

## References

- [1] Alshahrani MS, Sindi A, Alshamsi F, Al-Omari A, Tahan ME, Alahmadi B, et al. Extracorporeal membrane oxygenation for severe Middle East respiratory syndrome coronavirus. *Annals of Intensive Care* 2018;8. <https://doi.org/10.1186/s13613-017-0350-x>.
- [2] Henry B. COVID-19, ECMO, and lymphopenia: a word of caution. *Lancet Respiratory Medicine* 2020. [https://doi.org/10.1016/S2213-2600\(20\)30119-3](https://doi.org/10.1016/S2213-2600(20)30119-3)
- [3] Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* 2020. <https://doi.org/10.1007/s00134-020-05991-x>.
- [4] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine* 2020;0. [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).
- [5] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020.
- [6] Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, 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.

<https://doi.org/10.1001/jamainternmed.2020.0994>.

**Table 1. Characteristics of Included Studies**

Authors	Age (yrs): *	# of patients: n= (# ARDS patients)	Conventional ARDS Therapy: n=	Conventional ARDS Therapy Survivors: n (%)	ECMO: n=	ECMO - Survivors: n (%)
<i>Ruan Q et al. 2020</i>	Survivors: 67 (15-81) Non- Survivors: 50 (44-81)	150 (62)	55	7 (12.7%)	7	0 (0%)
<i>Wu et al. 2020</i>	51 (43-60)	210 (84)	83	40 (48.2)	1	0 (%)
<i>Yang X et al. 2020</i>	59.7 (13.3)	52 (35)	29	9 (31.0%)	6	1 (16.6%)
<i>Zhou F et al. 2020</i>	56.0 (46.0- 67.0)	191 (59)	5	9 (16.1%)	3	0 (0%)

\*Data presented as mean (SD) or median (IQR). ARDS – Acute Respiratory Distress Syndrome

**Figure 1. Forest Plots for Odds of Mortality in COVID-19 Patients Receiving of ECMO Therapy versus Conventional Therapy.**