



**HAL**  
open science

# Appraising the Real-Life Need for Extracorporeal Membrane Oxygenation during the COVID-19 Pandemic

Pineton de Chambrun, Daniel Brodie, Alain Combes

## ► To cite this version:

Pineton de Chambrun, Daniel Brodie, Alain Combes. Appraising the Real-Life Need for Extracorporeal Membrane Oxygenation during the COVID-19 Pandemic. *American Journal of Respiratory and Critical Care Medicine*, 2021, 204 (1), pp.2 - 4. 10.1164/rccm.202104-0897ed . hal-03290283

**HAL Id: hal-03290283**

<https://hal.sorbonne-universite.fr/hal-03290283v1>

Submitted on 19 Jul 2021

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

modality for the treatment of IgE-mediated allergies, including those to various foods, animal danders, insects, venoms, drugs, and aeroallergens. ■

**Author disclosures** are available with the text of this article at [www.atsjournals.org](http://www.atsjournals.org).

Kari C. Nadeau, M.D., Ph.D.  
Sean N. Parker Center for Allergy and Asthma Research  
Stanford University  
Stanford, California

ORCID ID: 0000-0002-2146-2955 (K.C.N.).

## References

1. Nelson HS. The evolution of allergy immunotherapy. *Ann Allergy Asthma Immunol* 2021;126:357–366.
2. Shamji MH, Singh I, Layhadi JA, Ito C, Karamani A, Kouser L, et al. Passive prophylactic administration with a single dose of anti-Fel d 1 monoclonal antibodies REGN1908–1909 in cat allergen-induced allergic rhinitis: a randomized, double-blind, placebo-controlled trial. *Am J Respir Crit Care Med* 2021;204:23–33.
3. Orengo JM, Radin AR, Kamat V, Badithe A, Ben LH, Bennett BL, et al. Treating cat allergy with monoclonal IgG antibodies that bind allergen and prevent IgE engagement. *Nat Commun* 2018;9:1421.
4. Dhami S, Agarwal A. Does evidence support the use of cat allergen immunotherapy? *Curr Opin Allergy Clin Immunol* 2018;18:350–355.
5. Grönlund H, Saarne T, Gafvelin G, van Hage M. The major cat allergen, Fel d 1, in diagnosis and therapy. *Int Arch Allergy Immunol* 2010;151:265–274.
6. Patel D, Couroux P, Hickey P, Salapatek AM, Laidler P, Larche M, et al. Fel d 1-derived peptide antigen desensitization shows a persistent treatment effect 1 year after the start of dosing: a randomized, placebo-controlled study. *J Allergy Clin Immunol* 2013;131:103–109, e101–107.
7. Circassia Pharmaceuticals. Circassia announces top-line results from cat allergy phase III study. 2016 [accessed 2021 March 10]. Available from: <https://www.circassia.com/media/press-releases/circassia-announces-top-line-results-from-cat-allergy-phase-iii-study/>.
8. Alvarez-Cuesta E, Cuesta-Herranz J, Puyana-Ruiz J, Cuesta-Herranz C, Blanco-Quirós A. Monoclonal antibody-standardized cat extract immunotherapy: risk-benefit effects from a double-blind placebo study. *J Allergy Clin Immunol* 1994;93:556–566.
9. Kanagaratham C, El Ansari YS, Lewis OL, Oettgen HC. IgE and IgG antibodies as regulators of mast cell and basophil functions in food allergy. *Front Immunol* 2020;11:603050.
10. Alvaro-Lozano M, Akdis CA, Akdis M, Alviani C, Angier E, Arasi S, et al. EAACI allergen immunotherapy user's guide. *Pediatr Allergy Immunol* 2020;31:1–101.
11. Celebi Sözüner Z, Mungan D, Cevhertas L, Ogulur I, Akdis M, Akdis C. Tolerance mechanisms in allergen immunotherapy. *Curr Opin Allergy Clin Immunol* 2020;20:591–601.
12. Lin C, Lee IT, Sampath V, Dinakar C, DeKruyff RH, Schneider LC, et al. Combining anti-IgE with oral immunotherapy. *Pediatr Allergy Immunol* 2017;28:619–627.

Copyright © 2021 by the American Thoracic Society



## Appraising the Real-Life Need for Extracorporeal Membrane Oxygenation during the COVID-19 Pandemic

The coronavirus disease (COVID-19) has become the leading cause of acute respiratory distress syndrome (ARDS) worldwide since January 2020. In a recent meta-analysis of 69 studies including 57,420 adult patients requiring invasive mechanical ventilation for COVID-19, the overall case fatality rate was estimated as 45% (95% confidence interval [CI], 39–52%) (1) and was higher than in the LUNG-SAFE cohort (40%; 95% CI, 38–42%) (2). Since the publication of the EOLIA trial (3) and its *post hoc* Bayesian analysis (4), venovenous extracorporeal membrane oxygenation (ECMO) has increasingly been used for patients with severe ARDS. As the COVID-19 pandemic drastically increased the demand for ECMO, data on the outcomes of this very specific population were eagerly awaited. In the largest series published to date, including 1,035 patients with COVID-19 from the Extracorporeal Life Support Organization registry, originating from 213 hospitals in 36 countries (5), the estimated 90-day probability of mortality was 37%

(95% CI, 34–40%). It was 36% (95% CI, 27–48%) in a cohort of 83 ECMO-treated patients at the Paris-Sorbonne University hospitals in France (6). More recently, the 60-day mortality rate of 190 ECMO-treated patients with COVID-19–related ARDS in 55 centers in the United States was 33% (7). The authors performed an emulated target trial in this cohort, comparing patients initiated on ECMO in the first 7 days of ICU admission with those who did not receive ECMO, with lower mortality in the ECMO group (hazard ratio, 0.55; 95% CI, 0.41–0.74). These three cohorts reported early results with a significant proportion of patients without a final disposition at the end of follow-up. Moreover, these studies did not capture the overall proportion of mechanically ventilated patients with COVID-19 that required ECMO support at a regional or national level.

In this issue of the *Journal*, Diaz and colleagues (pp. 34–43) report the results of a population-based study focusing on patients with COVID-19–related ARDS treated with ECMO during the first wave of the pandemic in Chile (8). This is indeed the first cohort study evaluating the need for ECMO in COVID-19–related ARDS at a national level, in a country that has developed a coordinated national ECMO program (9, 10), using data from comprehensive national databases of mechanically ventilated and ECMO-treated patients. During the study period, 13 ECMO centers were commissioned by the Chilean National Advisory Commission to provide ECMO in adult patients with COVID-19.

Ⓐ This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License 4.0 (<https://creativecommons.org/licenses/by-nc-nd/4.0/>). For commercial usage and reprints, please contact Diane Gern ([dgerm@thoracic.org](mailto:dgerm@thoracic.org)).

Originally Published in Press as DOI: 10.1164/rccm.202104-0897ED on April 23, 2021

**Table 1.** Recent Cohorts of Patients with COVID-19 with Severe ARDS Supported by VV-ECMO

Study	Diaz et al. (8)	Schmidt et al. (5)	Barbaro et al. (6)	Shaefi et al. (7)
Country	Chile	France	International	United States
Number of patients	85	83	1,035	190
Age, yr	48 (41–55)	49 (41–56)	49 (41–57)	49 (41–58)
Sex, F, %	16	27	26	28
Pre-ECMO parameters				
RESP score	3 (1–5)	4 (2–5)	—	3 (1–5)
SOFA score	10 (7–12)	12 (9–13)	—	—
Time from MV to ECMO, d	4 (2–7)	4 (3–6)	4 (2–6)	2 (0–5)
Prone positioning, %	92	94	60	71
Neuromuscular blockers, %	94	96	72	78
V <sub>T</sub> , ml/kg PBW	5.4 (4.7–6.0)	6.0 (5.7–6.4)	—	6.0 (5.3–7.1)
PEEP, cm H <sub>2</sub> O	10 ± 4.1	14 (12–14)	14 (12–16)	15 (14–18)
Driving pressure, cm H <sub>2</sub> O	15 (14–18)	18 (16–21)	—	15 (11–18)
Static compliance, ml/cm H <sub>2</sub> O	22 (18–28)	22 (18–26)	—	28 (21–36)
Pa <sub>O<sub>2</sub></sub> /Fi <sub>O<sub>2</sub></sub>	87 (64–99)	60 (54–68)	72 (59–94)	72 (61–90)
PaCO <sub>2</sub> , mm Hg	58 (47–71)	57 (50–68)	60 (50–74)	55 (46–66)
Time on ECMO, d	16 (10–27)	20 (10–40)	14 (8–23)	16 (10–23)
Time in the ICU, d	40 (21–57)	36 (23–60)	—	31 (20–43)
Time in hospital, d	50 (24–69)	—	27 (16–43)	39 (28–53)
60-d mortality, %	38	31	—	33
90-d mortality, %	39	36	37	—

*Definition of abbreviations:* ARDS = acute respiratory distress syndrome; COVID-19 = coronavirus disease; MV = mechanical ventilation; PBW = predicted body weight; PEEP = positive end-expiratory pressure; RESP = Respiratory Extracorporeal Membrane Oxygenation Survival Prediction; SOFA = Sequential Organ Failure Assessment; VV-ECMO = venovenous extracorporeal membrane oxygenation. Continuous variables are expressed as means ± SDs or medians (interquartile range, 25–75).

Members of the Commission evaluated and authorized the procedure and the referral to ECMO centers, including mobile ECMO. Patient selection criteria and ECMO management were based on the initial Extracorporeal Life Support Organization COVID-19 guidelines (11). The authors used the Chilean databases to identify all mechanically ventilated and ECMO-supported patients with COVID-19 between March 3, 2020, and August 31, 2020. The age-adjusted cumulative incidences of ECMO use were 0.42 per 100,000 population, 14.89 per 100,000 COVID-19 cases, and 1.2% per mechanically ventilated patients with COVID-19, respectively, which represents twice the frequency observed in a 3-month period in Australia and New Zealand during the 2009 influenza A (H1N1) pandemic (12).

The authors also provide a detailed description of 85 of the 94 patients who received ECMO with follow-up until March 3, 2021. Patients were cannulated early after intubation, and most of them had received neuromuscular blockers (94%) and prone positioning (92%) before ECMO. The median durations of ECMO, ICU, and hospital length of stay were 16 (interquartile range [IQR], 10–27), 40 (IQR, 21–57), and 50 (IQR, 24–69) days, respectively. Interestingly, late cannulation (>10 days of invasive mechanical ventilation before ECMO) was not associated with a higher mortality, in contrast to previous observations in ECMO for non-COVID-19-related ARDS (13, 14) as well as for ECMO in patients with COVID-19 (6, 15). At the end of the follow-up period, the mortality rate was 39%, similar to that reported in previous COVID-19 ECMO cohorts (5–7) (see Table 1). It should again be noted that all ECMO survivors were discharged home in this Chilean series, whereas other cohorts have reported estimated mortality rates, with the outcome of some patients remaining unknown at the end of follow-up. However, this result should be analyzed in the context of a somewhat milder severity of ARDS at the time of ECMO

initiation (lower driving pressure and higher Pa<sub>O<sub>2</sub></sub>/Fi<sub>O<sub>2</sub></sub>; see Table 1). It should also be noted that positive end-expiratory pressure was markedly lower before ECMO in this Chilean cohort than in the other three (Table 1). Setting positive end-expiratory pressure at a higher degree might have recruited more collapsed lung and improved Pa<sub>O<sub>2</sub></sub>/Fi<sub>O<sub>2</sub></sub>, potentially obviating the need for ECMO, especially considering that the median driving pressure was only 15 cm H<sub>2</sub>O.

Although many questions remain, including the most appropriate indications for ECMO in this setting, as well as longer-term outcomes of patients who received ECMO for COVID-19 (for instance, functional, neuropsychological, and long-term mortality), this is nonetheless important population-level data offering numerous insights into the use of ECMO during the pandemic. Furthermore, Diaz and colleagues should be commended for achieving excellent outcomes with ECMO for COVID-19 under such difficult circumstances. It stands to reason that a substantial portion of their success may have derived from the comprehensive coordination of a national system for deploying ECMO across all of Chile: a model for other countries to follow. ■

**Author disclosures** are available with the text of this article at [www.atsjournals.org](http://www.atsjournals.org).

Pineton de Chambrun, M.D.  
*Institute of Cardiometabolism and Nutrition,  
 Sorbonne Université  
 Paris, France*

and  
*Institut de Cardiologie,  
 Sorbonne Université Hôpital Pitié-Salpêtrière, and  
 Paris, France*

Daniel Brodie, M.D.  
Department of Medicine,  
Columbia University College of Physicians & Surgeons,  
New York, New York

and  
Center for Acute Respiratory Failure,  
New York-Presbyterian Hospital/Columbia University,  
New York, New York

Alain Combes, M.D., Ph.D.  
Institute of Cardiometabolism and Nutrition,  
Sorbonne Université  
Paris, France

and  
Institut de Cardiologie,  
Sorbonne Université Hôpital Pitié-Salpêtrière, and  
Paris, France

ORCID ID: 0000-0002-6030-3957 (A.C.).

## References

1. Lim ZJ, Subramaniam A, Ponnappa Reddy M, Blecher G, Kadam U, Afroz A, et al. Case fatality rates for patients with COVID-19 requiring invasive mechanical ventilation: a meta-analysis. *Am J Respir Crit Care Med* 2021;203:54–66.
2. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al.; LUNG SAFE Investigators; ESICM Trials Group. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA* 2016;315:788–800.
3. Combes A, Hajage D, Capellier G, Demoule A, Lavoué S, Guervilly C, et al.; EOLIA Trial Group, REVA, and ECMONet. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *N Engl J Med* 2018;378:1965–1975.
4. Goligher EC, Tomlinson G, Hajage D, Wijeyesundera DN, Fan E, Jüni P, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome and posterior probability of mortality benefit in a *post hoc* Bayesian analysis of a randomized clinical trial. *JAMA* 2018;320:2251–2259.
5. Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, et al.; Extracorporeal Life Support Organization. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. *Lancet* 2020;396:1071–1078.
6. Schmidt M, Hajage D, Lebreton G, Monsel A, Voiriot G, Levy D, et al.; Groupe de Recherche Clinique en REanimation et Soins intensifs du Patient en Insuffisance Respiratoire aiguë (GRC-RESPIRE) Sorbonne Université; Paris-Sorbonne ECMO-COVID investigators. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. *Lancet Respir Med* 2020;8:1121–1131.
7. Shaefi S, Brenner SK, Gupta S, O’Gara BP, Krajewski ML, Charytan DM, et al.; STOP-COVID Investigators. Extracorporeal membrane oxygenation in patients with severe respiratory failure from COVID-19. *Intensive Care Med* 2021;47:208–221.
8. Diaz RA, Graf J, Zambrano JM, Ruiz C, Espinoza JA, Bravo SI, et al., National Advisory Commission for Adult ECMO. Extracorporeal membrane oxygenation for COVID-19-associated severe acute respiratory distress syndrome in Chile: a nationwide incidence and cohort study. *Am J Respir Crit Care Med* 2021;204:34–43.
9. Torres JP, O’Ryan M, Herve B, Espinoza R, Acuña G, Mañalich J, et al. Impact of the novel influenza A (H1N1) during the 2009 autumn-winter season in a large hospital setting in Santiago, Chile. *Clin Infect Dis* 2010;50:860–868.
10. Ugarte S, Arancibia F, Soto R. Influenza A pandemics: clinical and organizational aspects: the experience in Chile. *Crit Care Med* 2010;38(4 Suppl):e133–e137.
11. Shekar K, Badulak J, Peek G, Boeken U, Dalton HJ, Arora L, et al.; ELSO Guideline Working Group. Extracorporeal life support organization coronavirus disease 2019 interim guidelines: a consensus document from an international group of interdisciplinary extracorporeal membrane oxygenation providers. *ASAIO J* 2020;66:707–721.
12. Davies A, Jones D, Bailey M, Beca J, Bellomo R, Blackwell N, et al; Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators. Extracorporeal membrane oxygenation for 2009 influenza A(H1N1) acute respiratory distress syndrome. *JAMA* 2009;302:1888–1895.
13. Schmidt M, Zogheib E, Rozé H, Repesse X, Lebreton G, Luyt C-E, et al. The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *Intensive Care Med* 2013;39:1704–1713.
14. Schmidt M, Bailey M, Sheldrake J, Hodgson C, Aubron C, Rycus PT, et al. Predicting survival after extracorporeal membrane oxygenation for severe acute respiratory failure: the Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score. *Am J Respir Crit Care Med* 2014;189:1374–1382.
15. Supady A, Taccone FS, Lepper PM, Ziegler S, Staudacher DL; COVEC-Study Group. Survival after extracorporeal membrane oxygenation in severe COVID-19 ARDS: results from an international multicenter registry. *Crit Care* 2021;25:90.

Copyright © 2021 by the American Thoracic Society



## 🔔 I Don't Want My Algorithm to Die in a Paper Detecting Deteriorating Patients Early

In this issue of the *Journal*, Pimentel and colleagues (pp. 44–52) report a retrospective evaluation of a new model (Hospital-wide Alerting via Electronic Noticeboard [HAVEN]) for predicting deteriorating ward

Ⓢ This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License 4.0 (<https://creativecommons.org/licenses/by-nc-nd/4.0/>). For commercial usage and reprints, please contact Diane Gern (dgern@thoracic.org).

Originally Published in Press as DOI: 10.1164/rccm.202102-0459ED on March 18, 2021

patients using vital signs, laboratory measurements, demographics, and historical diagnostic coding (1). The standard metrics of accuracy are impressive (e.g., a c-statistic of 0.901). Accepting nine false alarms for every one true positive, HAVEN will identify more than 40% of cardiac arrests or unplanned ICU admissions within the preceding 48 hours and provide as much as 12-hour notice for more than 25%. This is twice the rate of the best of the alphabet soup of competitors (NEWS, LAPS-2, eCART, and several friends) (2–4).

But predictive scores with nice acronyms are two-a-penny. So why should we care? Because, reading the report carefully, this is a score that