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

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

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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.

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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_T, ml/kg PBW	5.4 (4.7–6.0)	6.0 (5.7–6.4)	—	6.0 (5.3–7.1)
PEEP, cm H_2O	10 ± 4.1	14 (12–14)	14 (12–16)	15 (14–18)
Driving pressure, cm H_2O	15 (14–18)	18 (16–21)	—	15 (11–18)
Static compliance, ml/cm H_2O	22 (18–28)	22 (18–26)	—	28 (21–36)
Pa_{O_2}/FI_{O_2}	87 (64–99)	60 (54–68)	72 (59–94)	72 (61–90)
Pa_{CO_2}, 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_{O_2}/FI_{O_2}; *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_{O_2}/FI_{O_2}, potentially obviating the need for ECMO, especially considering that the median driving pressure was only 15 cm H_2O.

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. ■

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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 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

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