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**2022 Symposium Presentation**

# Extracorporeal Membrane Oxygenation Therapy in COVID-19 Patients with Acute Respiratory Distress Syndrome

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Patients with coronavirus disease of 2019 (COVID-19) may present with a wide range of symptoms ranging from asymptomatic to critically ill. Approximately 10-14% of patients require hospitalization. Those individuals requiring hospitalization can deteriorate rapidly with worsening hypoxemia or new-onset pneumonia, resulting in 20-30% of patients developing acute respiratory distress syndrome (ARDS).

When refractory to medical management, severe ARDS secondary to other illnesses has been successfully treated with extracorporeal membrane oxygenation (ECMO). We completed a comprehensive literature review of ECMO utilization for patients with severe COVID-19 who were unresponsive to critical care management. Of the 1419 patients with a reported diagnosis of COVID-19-related ARDS requiring ECMO therapy, 53.6% were discharged alive, 8.4% remained on ECMO in the intensive care unit, and 43.0% are deceased. These results are similar to the discharge rate of 60% for patients with non-COVID-related ARDS treated with ECMO. Data reported by the Extracorporeal Life Support Organization notes that 49% of patients with COVID-19 ARDS were discharged alive, 38% of whom were discharged home or to a long-term facility, and 11% were discharged to another hospital. In summary, using ECMO to treat patients with severe ARDS unresponsive to critical care management yields similar results in both non-COVID and COVID-related ARDS.

**Keywords:** coronavirus, acute respiratory distress syndrome, extracorporeal membrane oxygenation**Background**

Critical care management of acute respiratory distress syndrome (ARDS), independent of the cause, relies on respiratory support ranging from a nasal cannula to full mechanical ventilation and eventually extracorporeal membrane oxygenation (ECMO) therapy if hypoxemia is refractory to medical management.<sup>1</sup> The coronavirus pandemic has incited alarm within communities worldwide. Many clinicians initially questioned the efficacy of utilizing ECMO as a treatment for severe coronavirus disease (COVID)-related ARDS that is unresponsive to critical care management. Factors that contributed to this uncertainty include the constantly evolving and spreading of the virus, the

wide range of symptoms that can result from infection, delay of diagnostic test availability, misinformation concerning symptoms, and the overall uncertainty of health care resources.

**ECMO Considerations in Patients with ARDS Secondary to COVID-19***ECMO in ARDS for Respiratory Management*

ECMO is recommended as supportive therapy for cardiac and/or respiratory failure refractory to medical management. ECMO is considered to have a positive risk/benefit when patients have persistently decreased PaO<sub>2</sub>/ FiO<sub>2</sub> of less than 80 mmHg for more than 6 hours, less than 50 mmHg for greater

than 3 hours, or if the pH is less than 7.25 with a PaCO<sub>2</sub> greater than 60 mmHg for more than 6 hours despite adequate FiO<sub>2</sub> and positive end expiratory pressure settings. Kassirian et al summarize the appropriate respiratory management for hypoxemic respiratory failure in figures.<sup>2</sup>

### *When to Start ECMO Treatment*

Every day of mechanical ventilation before ECMO initiation is associated with an increased odds of mortality. In a study by Kunavarapu et al, those who survived post-ECMO support were, on average, initiated on treatment earlier ( $11.4 \pm 4.8$  days) as compared to those patients that died ( $14.4 \pm 5.5$  days) ( $P = .047$ ).<sup>3</sup> The total number of days spent on ECMO support also significantly affects mortality outcomes. The survival group spent  $10.7 \pm 16.6$  days on ECMO while the deceased group averaged  $20.9 \pm 16.8$  days on support ( $P = .001$ ). One explanation for the difference in survival is the high incidence of ventilator-associated morbidity and mortality in patients with ARDS, which ECMO may mitigate. Alternatively, the number of days spent on ECMO support may be a marker of disease severity.<sup>3</sup> Overall, earlier ECMO intervention increases the survival odds of ARDS that is unresponsive to critical care.

### *Indications vs Contraindications for ECMO*

Recommended indications for the use of ECMO include refractory hypoxemia, use of mechanical ventilation for < 7 days, risk of death greater than 50%, severe air leak syndrome, and a diagnosis of severe myocarditis or cardiogenic shock.<sup>4</sup>

Absolute contraindications include significant comorbidities from which a patient cannot recover. These include severe immunosuppression, sepsis with bacteremia, contraindications to systemic anticoagulation, severe multiple organ failure, severe aortic dissection, acute intracerebral hemorrhage, irreversible severe brain injury, critical congenital heart defects, chronic lung disease, and lethal chromosomal anomalies.<sup>4</sup> Relative contraindications also include an age of 65 years or older, a body mass index > 30 kg/m<sup>2</sup>, prolonged ventilatory support, frailty, allo-sensitization with prolonged waitlist time, and limitations in vascular access.<sup>4</sup> During the early phase of the COVID-19 pandemic, the Extracorporeal Life Support Organization (ELSO) recommended prioritizing young, previously healthy patients with only a single organ failure for ECMO support, as they may derive the maximum benefit.<sup>5</sup> As clinical experience continued to evolve, these priorities were relaxed based on program experience and increased access to health care resources.

### *Type of ECMO for COVID ARDS*

Veno-venous ECMO provides total gas exchange and the easiest access in patients with COVID-related ARDS. Veno-arterial ECMO is recommended for patients with COVID-related myocarditis, and atrio-pulmonary access has an

advantage in patients with pulmonary hypertension and associated right ventricular dysfunction.<sup>6</sup>

### *Complications of ECMO*

Complications of ECMO therapy in patients with both COVID-related ARDS and non-COVID ARDS include hemorrhage, arterial and venous thrombosis, infection, liver failure, and acute kidney injury.<sup>7,8</sup> Survivors of ECMO were significantly less likely than non-survivors to experience renal failure ( $P = .007$ ), cannula site bleeding ( $P = .037$ ), septic shock ( $P = .130$ ), and systemic inflammatory response ( $P = .013$ ).<sup>7</sup> However, patients on ECMO secondary to COVID-related ARDS were significantly more likely to experience thromboembolic events ( $P = .031$ ), specifically pulmonary artery embolism ( $P = .008$ ), than non-COVID ECMO patients.<sup>8</sup>

### *ECMO Results in COVID-related ARDS*

Based on the review of the literature, 53.6% (760/1419) of patients initiated on ECMO support secondary to COVID-related ARDS were discharged alive, but 8.4% remained on ECMO in the intensive care unit. There is an associated 38% mortality on ECMO with 539 out of 1419 patients deceased.<sup>3,7,8,9,10</sup> This data was compared to the ELSO database and found to be similar. ELSO currently reports that 49% (4754/9685) of patients treated with ECMO for COVID-related ARDS were discharged alive. Of these 49%, half were discharged home or to an acute care facility, a quarter went to another hospital, and a quarter was discharged to a long-term acute care facility or unspecified location.<sup>10,11</sup> Despite limited resources and personnel during the pandemic, this mortality rate is similar to the 34%–39% mortality rate reported for patients with non-COVID-related ARDS on ECMO support.<sup>7</sup>

### *Ongoing Research*

An open-label, randomized, controlled trial is currently underway in patients on ECMO support with COVID-19 pneumonia and moderate-to-severe ARDS.<sup>12</sup>

### *Current Recommendations*

ECMO should be used in patients with COVID-related ARDS when the severe respiratory failure is refractory to other therapies.<sup>5</sup> Current indications for ECMO in patients with ARDS secondary to COVID-19 should not be different than other ARDS cases but should be based on the availability of open beds, equipment, and access to skilled personnel.

### **How do these concepts impact clinical practice?**

To summarize, ECMO is an appropriate treatment option for patients with ARDS secondary to COVID-19, but only after standard critical care management is used. Ideally, ECMO should be started before an extended trial of

mechanical ventilation. Complications of ECMO are consistent among all causes of ARDS with a slightly increased risk of experiencing thromboembolic events, specifically pulmonary artery embolism, in patients with COVID-19. A comprehensive review indicates that ECMO therapy increases the number of patients discharged alive and should be utilized more consistently in COVID-19 ARDS.

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