

An Extracorporeal Membrane Oxygenation First Strategy in COVID-19 Acute Respiratory Distress Syndrome

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COVID-19 can be associated with acute respiratory distress syndrome, which increases the likelihood of morbidity and mortality. Ventilator-induced lung injury is a known complication of mechanical ventilation (MV) and can further compound lung injury and recovery. Escalation to extracorporeal membrane oxygenation can be required in patients who deteriorate on MV. We report our experience with complete avoidance of MV using an ECMO First strategy deployed in an awake nonintubated COVID-19 patient with severe pneumonia. ASAIO Journal 2021; 67;1097–1099

Key Words: ECMO, COVID-19, ARDS, pneumonia, ventilator-induced lung injury

Since December 2019, there have been over 150 million SARS-CoV-2 virus confirmed cases and 3.1 million confirmed deaths in the COVID-19 pandemic. The majority of COVID-19 patients develop only mild or uncomplicated illness. Among patients hospitalized with COVID-19, roughly 50% require ICU admission, 13% need invasive mechanical ventilation (MV), and 12% die.¹ As of April 2021, 6,500 patients on MV have been placed on extracorporeal membrane oxygenation (ECMO) for COVID-19 with an in-hospital survival as approximately 50%.²

Ventilator-induced lung injury (VLI) is a known complication of MV in COVID-19 patients, despite the use of lung protective strategies.³ An increased incidence of barotrauma has been reported in COVID patients on MV, which can further compound the ability to provide effective MV.⁴ Additional morbidity associated with MV includes hemodynamic decline, delirium, and critical illness myopathy secondary to the high-sedation requirements and prolonged use of neuromuscular blocker agents utilized to achieve adequate oxygenation.

Conventionally, veno-veno ECMO has been selectively employed in the management of COVID patients who fail MV. In contradistinction to early Chinese reports, large recent series have shown improved survival rates of 46–62% in patients treated with escalation of care from MV to VV-ECMO.^{5,6}

Given the theoretical additive effects of ventilator-associated morbidity and COVID-19 lung injury, an “ECMO First” approach, that is, bypassing the use of MV and selecting

ECMO as the first therapy, is an attractive hypothesis. This is particularly applicable to patients with COVID pneumonia who are (a) at high risk of decompensation with intubation but will accept awake ECMO and (b) where positive pressure ventilation is problematic due to severe barotrauma and air leaks syndromes. We describe our successful experience with an “ECMO First” strategy in a patient who refused MV.

Clinical Case

A 57 years old male with a history of DM2, hyperlipidemia, and a remote history of prostate cancer presented to the ER with a 9 day history of fever, chills, and generalized weakness. COVID-19 pneumonia was diagnosed, and he was discharged home with Levaquin and steroids. Four days later, he presented with fever, chills, dry cough, and shortness of breath. The chest x-ray and CT showed severe multifocal infiltrates (Figure 1). On examination, he was alert and oriented with an oxygen saturation of 84% on room air, breathing 25–30 breaths per minute and a heart rate of 113 bpm. He was initially admitted to telemetry, placed on 12 L Oxymizer with an improvement in O₂ saturation of 93%. ABGs are shown in (Figure 2). His biomarkers on admission and day 3 are shown in Table 1. He was started on dexamethasone, ceftriaxone, azithromycin, and remdesivir. Over the subsequent 2 days, his oxygen requirements continued to deteriorate on high-flow nasal cannula (HFNC). He was started on diuretics and placed in prone position with minimal improvement. He was transferred to the ICU for evaluation. The patient refused intubation but consented to ECMO if his respiratory status declined. On day 3 of his hospitalization, with a PaO₂ of 39 on 40 L 100% + 15 L nonrebreather, the multidisciplinary team agreed to proceed with ECMO.

Percutaneous cannulation took place bedside in the ICU, using ultrasound and x-ray guidance. The patient remained awake for the procedure and received fentanyl and versed in addition to lidocaine as a local anesthetic. A 25 Fr multistage drainage cannula was placed in the left common femoral vein terminating at the intrahepatic inferior vena cava (IVC) and a 21 Fr single stage return cannula was placed *via* the right common femoral vein terminating at the IVC/right atrial junction. A 7,500-unit heparin bolus was administered during the cannulation before initiation of ECMO. The initial blood flow was 3.5 L/min, and sweep gas flow was 3.5 L/min at 100% FiO₂. Adjustments to these parameters were made daily based on serial arterial blood gas readings. Bivalirudin was used for anticoagulation with a PTT goal of 50–70 seconds, which was the clinical protocol used in this patient population. His oxygen saturation and arterial blood gases immediately improved and over the next few days, he was able to wean his HFNC support, eat more, talk to his wife on the phone and work with physical therapy. By day 4 on ECMO, he was walking in his room with therapy on 15 L HFNC and sweep of 1 on ECMO.

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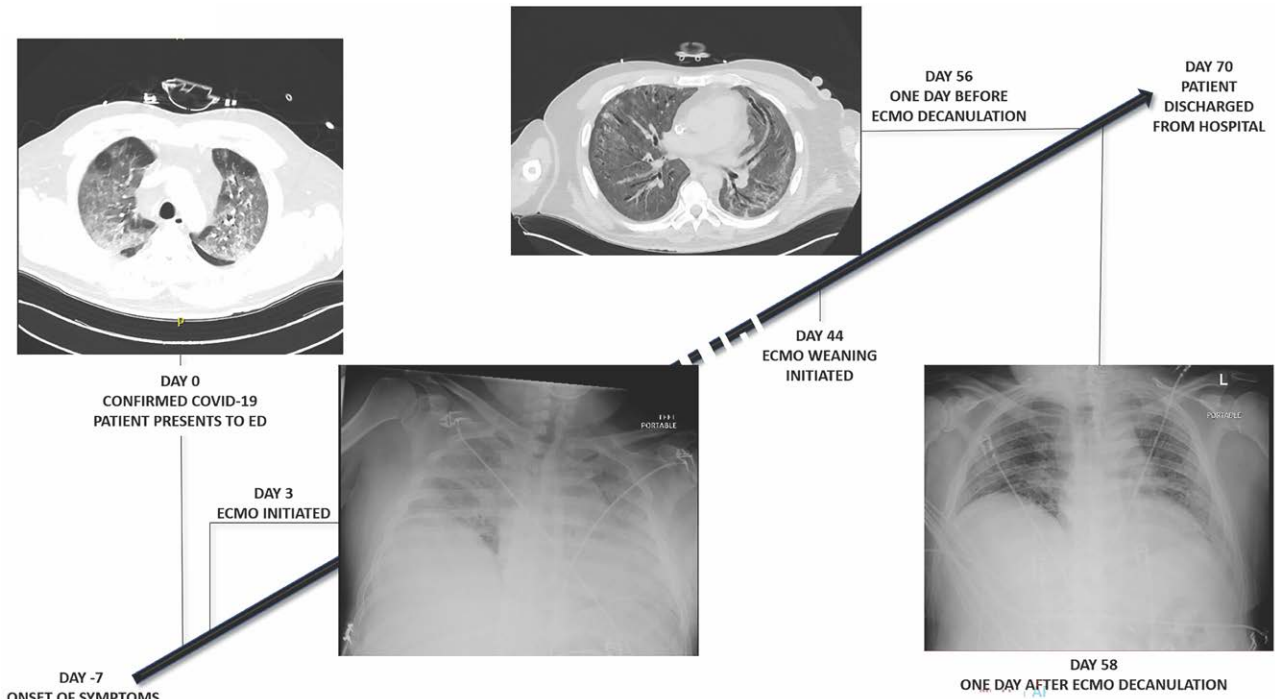


Figure 1. Timeline of treatment.

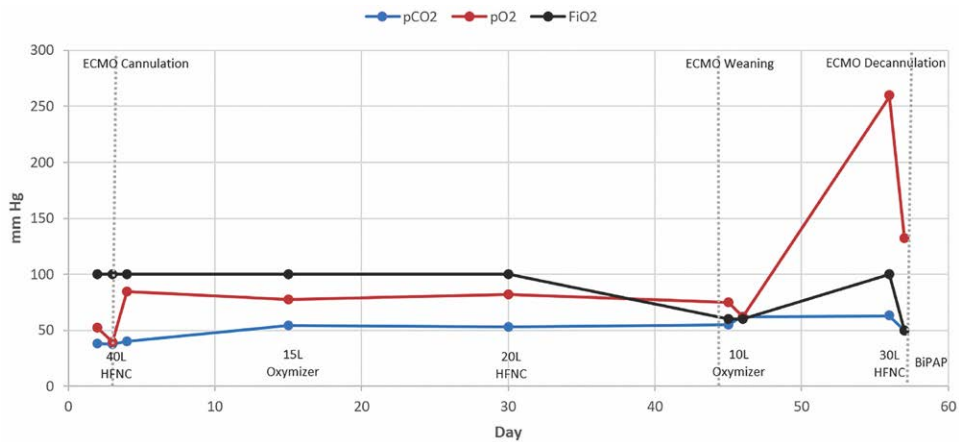


Figure 2. Select ABG and FiO₂ values during hospitalization.

Table 1. Biomarkers Upon Admission and Before Cannulation

Test Performed	Reference Values	Day 1	Day 3
		Hospital Admission	Before ECMO Cannulation
Fibrin degradation fragment (D dimer)	<0.50 mass/vol	0.79	1.74
CRP	<10 mg/L	256	155
Ferritin (adult male)	20–250 ng/mL	N/A	1,050
LDH	140–280 units/L	448	609
Lactic acid	0.5–1 mmol/L	2.9	1.7
Platelet count	150,000–450,000 platelets/ μ L	257,000	347,000
IL-6*	< 1.5 pg/mL	39 (10/27)	N/A

*This test has not been FDA cleared or approved. This test has been authorized by FDA under an EUA for use by authorized laboratories. CRP, C-reactive protein; ECMO, extracorporeal membrane oxygenation; IL-6, interleukin-6; LDH, lactic acid dehydrogenase; N/A, not available.

By ECMO day 10, he was transitioned to a 30 Fr dual-lumen cannula (Crescent, Medtronic) placed in the left subclavian vein. On day 22, his course was complicated by a spontaneous gastrointestinal bleed. An EGD documented a duodenal ulcer, erosive gastritis, and an esophageal ulcer that were clipped. By day 44, ECMO weaning trials began by turning off the sweep gas while increasing his supplemental oxygen. During these trials, he was encouraged to continue his usual therapy routine to gauge his readiness to decannulate from ECMO. After 54 days on VV-ECMO, he was decannulated with noticeable improvement of CT and CXR (Figure 1) and placed on 5L NC. He was discharged to a rehab facility on hospital day 70 and was discharged home after 1 week.

Discussion

The management of severe acute respiratory distress syndrome (ARDS) related to COVID-19 continues to evolve. ECMO can be utilized to minimize VLI associated with MV, improve systemic oxygen delivery, and prevent the downward spiral associated with hypoxemia in severe ARDS. Our case demonstrates that use of ECMO alone can rapidly correct profound hypoxia while avoiding MV-associated VLI and barotrauma to an already injured COVID-19 lung (Figure 2). By avoiding MV altogether, patients can avoid prolonged sedation, participate in pulmonary toilet management, physical therapy, and communicate with their family, which helps them maintain a positive psychological outlook. Our ECMO First approach allowed for a patient with severe ARDS to avoid the ventilator and return home with minimal complications.

The ECMO First concept is employed in the field of lung transplantation, where VV-ECMO is an accepted “lung-assistance” strategy for patients deteriorating while awaiting lung transplantation.⁷ Although this strategy has demonstrated a profound improvement of patients’ overall status before lung transplantation and avoids the ongoing barotrauma of MV, the role of ECMO before intubation in acute respiratory failure has not been established. While there is experience of successful deployment of ECMO as salvage therapy, there is relatively little data about earlier deployment in patients not yet requiring MV.

An April 2020 COVID-19 pandemic series of 5,700 patients hospitalized with COVID-19 in the New York City Area stated that 1,151 (20%) required MV.⁸ The mortality of patients requiring MV has been reported around 50%; however, reporting of outcomes has been inconsistent, with many patients not reaching a definitive outcome at the time of analysis.⁹ In addition to the risk of VLI from ongoing MV, the intubation process itself is high-risk, especially in the COVID population. Major adverse events including cardiovascular instability, severe hypoxia, or cardiac arrest occurred after intubation in 45% of critically ill (non-COVID) patients requiring intubation.¹⁰ Additionally, intubation in COVID-19 places the intubating team at risk of exposure through potential aerosolization. By utilizing ECMO before MV, the risk of mechanical damage to the lungs and the risk of peri-arrest with intubation are reduced but must be weighed against the risks of ECMO itself.

Evidence is emerging about the development of fibrotic lung injury after resolution of COVID infection.¹¹ There are an increasing number of COVID-19 pneumonia cases that have “recovered” but have compromised pulmonary function. In its severe form this necessitates long-term oxygen dependency

and the possibility of lung transplantation. An evaluation of how the utilization of “ECMO First,” and removing the potential for additional MV associated with lung injury, will impact the response to injury remains unknown and needs to be evaluated.

The use of ECMO First may have some disadvantages: a decrease in airway clearance; an increased risk of bleeding secondary to anticoagulation, embolism, and misadventure during cannulation. Wider use of an ECMO First strategy is limited by access to a facility employing ECMO as a therapeutic modality, the costs involved for equipment and training, and personnel availability for the required labor-intensive patient monitoring and care. Finally, there exists the possibility of a selection bias as there is currently insufficient evidence to support whether patients selected for awake ECMO would not improve on MV alone. Further studies will be needed to assess the efficacy of this approach.

Summary

We describe our favorable experience using an ECMO First strategy without MV in a patient with severe COVID-19 related lung injury. In select patients, this approach can be considered. Further randomized studies comparing ECMO following MV *versus* an ECMO First strategy are needed.

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