Awake Extracorporeal Membrane Oxygenation in Coronavirus Disease 2019 Patients Without Invasive Mechanical Ventilation

OBJECTIVES/BACKGROUND: Extracorporeal membrane oxygenation is used as rescue therapy for patients with acute respiratory distress syndrome in whom conventional therapy has failed prior to an Extra Corporeal Membrane Oxygenator to rescue Lung Injury in Severe Acute Respiratory Distress Syndrome trial. Since then, extracorporeal membrane oxygenation has been incorporated as part of the standard treatment algorithm in many centers for patients with severe acute respiratory distress syndrome. Since the emergence of coronavirus disease 2019 in early 2020, extracorporeal membrane oxygenation has been used effectively as rescue therapy and as a bridge to recovery in some patients with refractory respiratory failure.

DESIGN, SUBJECT, AND INTERVENTION: We present a 38-year-old male healthcare worker diagnosed with coronavirus disease 2019 and progressed to critical condition with severe surgical emphysema on a high-flow nasal cannula with Fio2 100%, a flow of 40 L/min, and a maximum oxygen saturation of 88%. He was successfully treated by applying awake extracorporeal membrane oxygenation, without a need for invasive mechanical ventilation, to avoid worsening barotrauma and hemodynamic compromise potentially induced by positive pressure ventilation.

MAIN RESULTS AND CONCLUSIONS: To our knowledge, this is one of the first cases to be reported in the literature on the use of awake extracorporeal membrane oxygenation as a “treatment” for barotrauma due to severe acute respiratory distress syndrome in a coronavirus disease 2019 patient, without the need for invasive mechanical ventilation. In selected patients with severe respiratory failure, awake extracorporeal membrane oxygenation can be used as a salvage treatment and obviate the need for invasive mechanical ventilation.

KEY WORDS: acute respiratory distress syndrome; awake; coronavirus disease 2019; extracorporeal membrane oxygenation; mechanical ventilation

Since 2009 and based on the findings from the conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure trial (1), extracorporeal membrane oxygenation (ECMO) has become increasingly common in the management of patients with severe acute respiratory distress syndrome (ARDS). Based on experience from the H1N1 (2) and Middle East respiratory syndrome coronavirus pandemics (3), ECMO is known to improve survival in patients with severe ARDS secondary to viral pneumonia (4). Since the emergence of coronavirus disease 2019 (COVID-19) in early 2020, ECMO has been used in patients with COVID-19 pneumonia in whom maximum conventional therapy on mechanical ventilation (MV) failed (5–10). However, it is mainly initiated in patients while they are on MV. Here, we present a case of applying ECMO as a treatment modality in awake patients with severe ARDS secondary to COVID-19,
obviating the need for invasive MV. Written informed consent was acquired from the patient for publication of this case report.

**CASE PRESENTATION**

In early July 2020, a 38-year-old male healthcare worker presented to the emergency department (ED) of a private hospital complaining of fever, productive cough, and shortness of breath for 3 days prior to presentation. He had no history of any previous medical illnesses. He was 188 cm tall and weighed 122 kg (body mass index: 34.5 kg/m²; body surface area: 2.49 m²). He had never used any illicit drugs or an inhaler. On arrival at the ED, the patient's vital signs were as follows: blood pressure: 125/83 mm Hg, heart rate: 90 beats/min; respiratory rate: 20 breaths/min, and oxygen saturation: 85% on room air. His chest examination revealed bilateral coarse crepitation in the lower and middle zones of the lungs. His chest radiograph (CXR) in the ED revealed bilateral opacification in the lower and middle zones of the lungs (Fig. 1A). The following laboratory findings were significant: ferritin 1,340 ng/mL (20–250 ng/mL), lactate dehydrogenase 465 U/L (140–280 U/L), WBC 13 × 10⁹/L (4.5–11.0 × 10⁹/L), C-reactive protein 195.5 mg/L (< 10 mg/L), d-dimer 0.62 µg/mL (< 0.4 µg/ml), and hemoglobin 11.1 g/dL (13.5–17.5 g/dL). His nasal swab severe acute respiratory syndrome coronavirus 2 polymerase chain reaction test was positive. The patient was admitted to the ward and put on oxygen therapy 2–4 L/min via nasal cannula. On day 1 after admission, the patient's condition deteriorated, and his oxygen requirement increased to 7 L/min via a face mask, with an oxygen saturation in the low 80 seconds. The rapid response team was activated, and the patient was shifted to the ICU for close monitoring. Repeat CXR showed surgical emphysema, mild pneumomediastinum, minimal left pneumothorax, right pneumothorax, exaggerated bronchovascular markings, and bilateral dense widespread inhomogenous patchy opacities of consolidations (Fig. 1B). The patient was started on steroids and broad-spectrum antibiotics. The patient was seen by on-call thoracic surgery team, and bilateral chest tubes were inserted and confirmed by CXR (Fig. 1C) and connected to an underwater seal system, with a negative pressure of 20 cm H₂O initiated on both sides. On day 2, the patient oxygen requirement increased to 15 L/min with a nonrebreather mask. Despite inserting two chest tubes with 40 cm negative pressure suction, the surgical emphysema and pneumothoraces increased. A high-flow nasal cannula was initiated with 100% Fio₂ and a flow rate of 40 L/min. Prone positioning was performed, but patient oxygenation did not improve (oxygen saturation [Sao₂] 88%).

On day 3 post admission, the regional ECMO team was consulted to evaluate the patient and to transfer him to the regional ECMO center. After full evaluation of the patient's condition, taking into consideration the

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**Figure 1.** Chest radiographs. **A,** Initial chest radiograph in emergency department (ED): bilateral opacification in the lower and middle zones of the lungs. **B,** Chest radiograph on day 2 post admission: surgical emphysema, mild pneumomediastinum, minimal left pneumothorax, right pneumothorax, exaggerated bronchovascular markings, and bilateral dense, widespread, inhomogeneous patchy opacities of consolidations. **C,** Chest radiograph on day 2 after left chest tube insertion on 40 cm H₂O negative pressure suction. Bilateral pneumothoraces and surgical emphysema are still present. R in the figure represents the right side of the patient.
worsening surgical emphysema and pneumothoraces and discussion with the thoracic surgery team to confirm that there was no surgical intervention that could be offered for his condition, the patient was counseled regarding the option of inserting a venovenous-ECMO without intubation and MV, with all the pros and cons discussed. Using mild conscious sedation and local anesthesia in the presence of the anesthesia consultant, in case of a need for an emergency airway, the patient was placed on venovenous-ECMO using both femoral veins (fem-fem venovenous-ECMO) with no acute complication using a Cardiohelp Device with an CARDIOHELP System 7.0 L ECMO membrane oxygenator (Getinge AB, Göteborg, Sweden). Because the patient was fully awake and conscious, the cannulation options were explained to him (including the fem-jugular approach), and based on his preferences, a fem-fem approach was chosen, mainly for comfort and free neck mobility.

The initial ECMO settings were as follows: Fio2 100%, sweep gas of 4 L/min, and ECMO flow of 3.5 L/min. Patient vital signs were stable, and his Sao2 reached 100%. The patient was weaned to a nonrebreather mask at 12 L/min. After confirming the cannula placement by x-ray and assuring patient stability, the patient was transported by the regional ECMO team via ambulance and transferred to the regional ECMO center (~30 kilometers away).

In the regional ECMO center, the patient was stabilized and started on treatment for COVID-19 as per the Saudi Ministry of Health Protocol for Patients Suspected of/Confirmed with COVID-19 (11), which included heparin infusion, broad-spectrum antibiotics (piperacillin/tazobactam 4.5 g IV tid, favipiravir 1,800 mg bid 1 day then 800 mg bid for 10 d), and dexamethasone 6 mg daily. Pan cultures were taken. The chest drains were checked by the thoracic surgery team and kept on negative 40 cm H2O connected to the underwater seal systems. CT of the chest with IV contrast was performed and revealed no pulmonary embolism, bilateral moderate pneumothoraces, pneumomediastinum, and bilateral diffuse ground glass opacities with consolidation and air bronchogram with interlobular septal thickening (Fig. 2A).

Although the patient was on ECMO, the patient was kept conscious without any sedation. He was awake, alert, fully oriented, and cooperating. He received daily physiotherapy in his ICU bed, which included upper and lower limb muscle strengthening and power exercises, chest physiotherapy by the respiratory therapy team, including chest tapping and incentive spirometry. To optimize chest physiotherapy, specifically incentive spirometry, the patient was receiving paracetamol 1 g IV four times a day regular and morphine 2–4 mg IV every 4 hours as needed to relieve his COVID-related and chest tube–induced pleuritic chest pain and maximize the use of incentive spirometry. Patient oxygenation was maintained on a high-flow nasal cannula most of the time and periodically with bilevel positive airway pressure (BiPAP) with the following settings: BiPAP 12 cm H2O and expiratory peak airway pressure 5 cm H2O as needed when the patient complained of dyspnea or was tachypnea. The oxygen requirement was titrated to keep his Sao2 between 88% and 92% while on venovenous-ECMO with Fio2 100% and a sweep of 4 L/min. During his ICU stay, because he was anxious and irritable, brain CT was performed to rule out any major events, and it was negative. He was started on anxiolytics (quetiapine 50 mg by mouth bid).

**Figure 2.** CT. A, CT of the chest with IV contrast on day 3 post extracorporeal membrane oxygenation cannulation: no pulmonary embolism, bilateral moderate pneumothoraces, pneumomediastinum, and bilateral diffuse ground glass opacities with consolidation and an air bronchogram with interlobular septal thickening. B, CT of the chest 6 mo later showed dramatic improvement of his lung tissue with minimal residual ground glass appearance in the bilateral lower lung zones.
The patient continued to improve, and he was weaned slowly from ECMO support, with a target oxygen level of greater than 90%. He was successfully decannulated under mild conscious sedation on the 22nd day from presentation (total ECMO run 18 d). The next day after decannulation, the patient was on a 3 L nasal cannula with oxygen saturation of 94% and a normal arterial blood gas reading (pH: 7.4, Pco2: 39, Po2: 72, Hco3: 28, lactate: 2). The patient was doing well and moving. He was discharged from the ICU and transferred back to his primary hospital on the 29th day after presentation (5 d after decannulation). He had a smooth recovery and was discharged home 54 days after his primary presentation (32 d from decannulation off ECMO). His repeated CT of the chest 6 months later showed dramatic improvement of his lung tissue with minimal residual ground glass appearance in the lower lung zones bilaterally (Fig. 2B). He returned to work 5 months after his primary presentation (3 mo from discharge).

DISCUSSION AND CONCLUSIONS

Patients with COVID-19 pneumonia have an unpredictable course, as they can deteriorate rapidly and require major interventions and ICU care. MV with a high ventilatory setting in patients with severe ARDS is well known to be associated with barotrauma and hemodynamic compromise (12). After exhausting conventional therapy, ECMO can be used in some patients as a bridge to recovery, with the main goal of buying time for the medications to slow the disease process and systematic inflammatory response and, at the same time, decreasing potential harm from the high setting required on the mechanical ventilator (5–10). However, it has only been initiated in intubated patients.

Prior to the COVID pandemic, awake ECMO was successfully used in the management of patients with moderate-to-severe ARDS (13). In this small series, most patients were not intubated because they were immunocompromised, and ECMO was used as a treatment modality for moderate-to-severe ARDS to avoid the side effects related to intubation (mainly infection and barotrauma), with a good outcome of 80% survival to home discharge.

During the COVID-19 pandemic, several authors have reported the use of awake ECMO as a management strategy for patients with severe ARDS. Tang et al (14) reported a case of “Awake ECMO” in Wuhan, China. This patient was a 49-year-old woman who was intubated on the 14th day of admission and mechanically ventilated, continued to deteriorate and required venovenous-ECMO support on the 16th day of admission (2 d after intubation). She was then extubated on venovenous-ECMO (27th day after admission or 9 d after the initiation of ECMO). She was doing well and eventually was weaned from ECMO on the 35th day after admission (17 d on ECMO). However, this patient was intubated before ECMO and was extubated on ECMO.

A group at Methodist Hospital in San Antonio, led by Jeffrey DellaVolpe, advocated the initiation of early ECMO and placed seven to eight patients on ECMO prior to MV (15), according to an interview conducted on Rebel emergency medicine on May 31, 2020 (16). However, they have not yet published this work in the medical literature, and there are few details about the patient selection criteria.

Maintaining spontaneous breathing in patients has its pros: 1) the dorsal part of the diaphragm is preferentially moved, leading to optimal ventilation-perfusion matching; 2) chest wall expansion guarantees optimal functional residual capacity; 3) ventilator-induced diaphragm dysfunction is avoided; 4) the negative effects of positive pressure ventilation on venous return and hemodynamics are avoided; and 5) the risk of bacterial infection induced by MV is decreased (17).

However, ECMO is a resource-intensive intervention that is associated with major complications. Several authors have looked in the economic impact of the use of venovenous-ECMO in patients with severe ARDS. In a article by Barrett et al (18), the authors compared venovenous-ECMO with conventional lung-protective ventilation strategy and found out that the use of venovenous-ECMO resulted in of gain of at least 5 life years and an incremental cost-effectiveness ratio was ~36,000 Canadian dollars/quality-adjusted life year. The utilization of ECMO should be balanced against available resources and surge capacity of a pandemic, which was highlighted elegantly in the Extracorporeal Life Support Organization COVID-19 Interim Guidelines (10). Although, our patient could have been managed by intubation and MV, the negative effect of positive pressure ventilation in the presence of severe barotrauma and air leak cannot be ignored (12).
To our knowledge, we have presented one of the first cases to be published in the medical literature on the successful use of ECMO as a “treatment” for barotrauma and mechanical complications (pneumothorax and surgical emphysema) due to severe ARDS in an awake patient with COVID-19 pneumonia, without the need for MV. Patients with severe respiratory failure and air leakage are at risk of developing hemodynamic compromise and worsening barotrauma that is associated with deep sedation and the positive pressure ventilation required for mechanically invasive ventilation. During past pandemics, no cases of ECMO being used as the primary treatment modality, without the need for MV, were reported. Based on our experience in this case, we were able to demonstrate that awake ECMO can be initiated in nonintubated patients with COVID-19 pneumonia and moderate-to-severe ARDS. Although we have successfully treated this patient, this is the only case we have treated in this manner, and we do not recommend the routine use of ECMO in patients with ARDS until further evidence on this topic is published. This management approach is experimental, very expensive, associated with major complications and can only be initiated in selected patients who are cooperative in the presence of an experienced team.

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REFERENCES

1. Peek GJ, Mugford M, Tiruvoipati R, et al; CESAR trial collaboration: Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): A multicentre randomised controlled trial. Lancet 2009; 374:1351–1363
2. Davies A, Jones D, Bailey M, 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
3. Alshahrani MS, Sindi A, Alshamsi F, et al; Extracorporeal membrane oxygenation for severe middle east respiratory syndrome coronavirus. Ann Intensive Care 2018; 8:3
4. Combes A, Hajage D, Capellier G, 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
5. Schmidt M, Hajage D, Lebreton G, et al; Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: A retrospective cohort study. Lancet Respir Med 2020; 8:1121–1131
6. Barbaro RP, MacLaren G, Boonstra PS, 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
7. ELSO: ELSO Guidance Document: ECMO for COVID-19 Patients With Severe Cardiopulmonary Failure, 2020. Available at: https://www.elso.org/Portals/0/Files/pdf/ECMO%20for%20COVID%2019%20Guidance%20Document.Final%2003.24.2020.pdf. Accessed April 04, 2020
8. MacLaren G, Fisher D, Brodie D; Preparing for the most critically ill patients with COVID-19: The potential role of extracorporeal membrane oxygenation. JAMA 2020; 323:1245–1246
9. Savarimuthu S, BinSaeid J, Harky A: The role of ECMO in COVID-19: Can it provide rescue therapy in those who are critically ill? J Card Surg 2020; 35:1298–1301
10. Shekar K, Badulak J, Peek G, 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
11. Health SMo: Saudi MoH Protocol for Patients Suspected of/Confirmed With COVID-19. 2021. Available at: https://www.moh.gov.sa/Ministry/MediaCenter/Publications/Documents/MOH-therapeutic-protocol-for-COVID-19.pdf. Accessed April 30, 2021
12. Heller RDD: Barotrauma and Mechanical Ventilation. Available at: https://www.ncbi.nlm.nih.gov/books/NBK545226/. Accessed March 20, 2021
13. Hoeper MM, Wiesner O, Hadem J, et al: Extracorporeal membrane oxygenation instead of invasive mechanical ventilation in patients with acute respiratory distress syndrome. *Intensive Care Med* 2013; 39:2056–2057
14. Tang J, Li W, Jiang F, et al: Successfully treatment of application awake extracorporeal membrane oxygenation in critical COVID-19 patient: A case report. *J Cardiothorac Surg* 2020; 15:335
15. MedPage-Today: Should ECMO Come Before Intubation for COVID-19? 2020. Available at: https://www.medpagetoday.com/infectiousdisease/covid19/89562. Accessed March 20, 2021
16. REBEL-EM: COVID-19 in the ICU, ECMO Early, & Steroids With Jeff Dellavolpe, MD. 2020. Available at: https://rebelem.com/rebel-cast-ep83-covid-19-in-the-icu-ecmo-early-steroids-with-jeff-dellavolpe-md/. Accessed March 20, 2021
17. Langer T, Santini A, Bottino N, et al: "Awake" extracorporeal membrane oxygenation (ECMO): Pathophysiology, technical considerations, and clinical pioneering. *Crit Care* 2016; 20:150
18. Barrett KA, Hawkins N, Fan E: Economic evaluation of venovenous extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *Crit Care Med* 2019; 47:186–193