Effect of Extracorporeal Membrane Oxygenation in Treatment of COVID-19 Patient with Acute Respiratory Distress Syndrome

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Abstract
Coronavirus disease 2019 (COVID-19) is a contagious infection caused by the newly discovered severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel virus causing from very mild symptoms to severe symptoms associated with high morbidity and mortality. The most common symptoms of COVID-19 are fever, dry mouth and tiredness, sore throat, headache, loss of taste or smell, diarrhea, conjunctivitis, and sometimes a skin rash. In severe cases, some patients require mechanical ventilator support in a prone position to improve their oxygenation. In extreme cases, despite all the above measures, patients are required to have extracorporeal membrane oxygenation (ECMO) support to improve oxygenation. The two most common types of ECMO are veno-arterial (VA) and veno-venous (VV). This case report presents a positive outcome when VV-ECMO was used in COVID-19 patients with acute respiratory distress syndrome at the hospital’s field intensive care unit.

Keywords: COVID-19; Dyspnea; Extracorporeal Membrane Oxygenation; Hypoxia, Respiratory Distress Syndrome.

Introduction
In December 2019, an outbreak of unexplained pneumonia occurred in Wuhan, China. On January 7, 2020, the causative pathogen was identified as a novel coronavirus, currently named SARS-CoV-2. The illness caused by this virus, coronavirus disease 2019 (COVID-19), spread swiftly around the globe, and on March 11, 2020, the World Health Organization (WHO) declared COVID-19 as a pandemic.1,2

COVID-19 has thus transmitted from Wuhan to the rest of the world, and more than 51 million people have been infected, with 93,508 (1%) becoming critically ill and suffering from acute respiratory distress syndrome (ARDS) about 1 week after the onset. The WHO recently named this disease, COVID-19.3 The therapies of the most severe patients include intravenous antibiotics, antiviral administration, oxygen therapy, and mechanical ventilation. While the clinical manifestations of the virus might vary in severity, it is widely known that the cardiorespiratory system is the principal infection point of the virus, with ARDS and shock being possibilities.4,5 Also, they can present with shortness of breath (SOB) and decrease the oxygen level in the blood.
(desaturation-low SpO₂), requiring oxygen therapy. Critical patients can rapidly progress to ARDS, which can lead to multiple organ failures and high mortality rates.⁵

Multiple major health organizations recommend the use of extracorporeal membrane oxygenation (ECMO) support for COVID-19-related acute ARDS. The initial reports of ECMO use in patients with COVID-19 were reporting its high morbidity and mortality, but yet there are not enough cohort studies regarding this treatment modality outcome in patients with COVID-19.⁶

This case report presents the treatment of a patient with severe COVID-19 using ECMO at the hospital’s Field Intensive Care Unit (FICU) in Bahrain defense force (BDF) hospital. In FICU, this study showed a good example of early use of ECMO in COVID-19 associated with a good outcome. This experience revealed that the early application of ECMO could successfully treat ARDS in severe COVID-19 patients.

Case Report

A 33-year-old morbidly obese male [body mass index (BMI) of 38 kg/m²] was admitted to the hospital’s FICU in BDF Hospital on October 20, 2020, as a case of COVID-19 after a positive nasopharyngeal swab on October 19, 2020, with symptoms of cough and SOB with normal body temperature (36.7°C).

On admission, the patient was drowsy, but obeying commands. Blood pressure (BP) was normal 130/60 mmHg, accompanied with tachycardia, tachypnoea, slightly febrile, and low oxygen saturation. Heart rate (HR), respiratory rate (RR), SpO₂, and temperature were 100 bpm, 25 breaths/min, 85% on room air (RA), and 37.4°C, respectively.

The patient was maintained on 15 L fraction of inspired oxygen (FiO₂) through a non-rebreather (NRB) face mask, maintaining saturation of 97%. Chest examination was normal, with bilaterally equal chest movements. Chest was clear with no added sounds upon auscultation. Chest x-ray (CXR) showed bilateral lung infiltration (Figure 1).

Blood routine examination showed: white blood cells (WBC), 11×10⁹ L⁻¹; lymphocyte (LYM) 4.9×10⁹ L⁻¹. Liver function analyses showed: aspartate aminotransferase (AST), 61 U/L; alanine aminotransferase (ALT), 51 U/L; lactate dehydrogenase (LDH), 563 U/L. Renal function values were: blood urea nitrogen (BUN), 8.3 mmol/L; creatine kinase (CK), 193 mmol/L. Inflammatory reaction marker values were: procalcitonin (PCT), 0.51 ng/ml; C-reactive protein (CRP), 105 mg/L. Arterial blood gas (ABG) analysis values were: pH, 7.37; PCO₂ 59 mmHg; PO₂ 43 mmHg; and HCO₃⁻ 34 mm/L.

The patient was managed as per the hospital’s protocol for treatment, which included low molecular weight heparin Enoxaparin injection (Clexane, Sanofi) (80 mg) subcutaneous every 12 h, intravenous steroid injection (dexamethasone 8 mg) once per day for 10 days, convalescent plasma once per day for 2 days, antiviral injection (Remdesivir 200 mg stat dose) followed by 100 mg once daily for another 4 days, antibiotic injection [Ceftriaxone (Rocephin, Roche) 2 g] once daily for 10 days.

Hours later, the patient started to deteriorate, and became tachypnoeic with RR 42 breaths/min, and hypoxic with SpO₂ 85%. CXR was repeated and showed worsening of lung infiltration (Figure 2).
Patient’s NRB face mask was removed, and was maintained on high-flow nasal cannula (HFNC) with the setting of FiO₂ 1.0 flow 60 L/min and temperature of 37°C.

Six hours later, the patient’s ROX Index was estimated (blood oxygen level (spo2) in arterial blood gas, divided by FiO2 and divided by respiratory rate of the patient). This index is used to predict the risk of intubation (Normal value: >4.88). The patient’s ROX Index was 2.5, which indicated the failure of HFNC and the need to intubate the patient by connecting to a mechanical ventilator to improve the oxygenation. The patient was intubated with a volume mode of ventilation (protective lung ventilation strategy) with plateau pressure of 20 mmHg.

Moreover, the patient was started on infusions for sedation and muscle relaxation and was maintained in a prone position with the setting of ventilator support [VC-AC mode (Volume Control/Assist Control) with FiO₂, 100%; positive end-expiratory pressure (PEEP), 15 mmHg; RR, 30 breaths per min; tidal volume (TV), 380 ml; inspiratory time (Tinsp), 0.65 s]. Furthermore, recruitability index (RI)(an index that shows the lung tolerance to high pressure by the ventilator) was calculated to be zero, which indicated that the lungs were not tolerating the high PEEP. Therefore, PEEP was reduced to 10 mmHg.

One hour later, ABG was repeated and revealed pH 7.40, PCO₂ 56 mmHg, PO₂ 56 mmHg, and HCO₃ 34 mmol/L. Four hours later, ABG showed pH 7.42, PCO₂ 45 mmHg, PO₂ 55 mmHg, and HCO₃ 36 mmol/L. The patient was started on veno -venous (VV) ECMO through the femoral and the right internal jugular vein (Figure 3).

After heparinization, the ECMO support was started at O₂ flow 4 L/min, FiO₂ 1.0, and airflow 11 LL/min. Oxygen saturation was improving as it was increased significantly. ABG values were pH 7.55, PCO₂ 36 mmHg, PO₂ 83 mmHg, and HCO₃ 31 mmol/L. Later on, the patient was started on heparin infusion to keep activated partial thromboplastin time (APTT) between 45 and 60 s.

As the patient’s oxygenation improved, the ventilator setting weaned gradually on VC-AC mode with FiO₂ to 40%, TV 210 ml, Tinsp 1.3 s, RR 8 breaths/min, and PEEP 10 mmHg. No complications were reported (e.g., hemorrhage, thrombus, or pneumothorax) during ECMO support treatment, apart from mild epistaxis, which ceased spontaneously. Later, CXR showed left lung collapse (Figure 4). As a response, chest physiotherapy was started by a respiratory therapist, and bronchoscopy was done, which revealed mucus plugs, which were washed out. Repeated CXR showed improvement in left lung (Figure 5). After 2 weeks, the patient improved and was weaned from ECMO, and the patient was decannulated and extubated. After the patient was extubated, HFNC was started and was

![Figure 3: Frontal chest x-ray post ECMO insertion with almost complete infiltration of both lungs.](image1)

![Figure 4: Frontal chest x-ray shows complete left lung whiteout.](image2)

![Figure 5: Frontal chest x-ray post bronchoscopy with interval improvement of the left lung collapse.](image3)
weaned gradually to RA. The patient was discharged from the hospital after two negative nasopharyngeal swabs. CT (Computed tomography) of the chest without contrast at the discharge time showed bilateral lung fibrosis, although the patient was comfortable and maintained oxygenation (Figures 6 A & B).

Figure 6 (A&B): CT HRCT (High-resolution computed tomography)

Discussion
ECMO is one of the extracorporeal lung assist (ECLA) technologies, which is used to replace the cardiopulmonary function of patients, to improve lung function, to improve oxygenation of the whole organs, and to remove carbon dioxide from the body (CO2) while treating the primary disease.7-9

The Extracorporeal Life Support Organization (ELSO) reports on July 25, 2020, confirmed that 1,972 COVID-19 cases had been supported with ECMO, and 55% of discharged patients were alive (753 out 13,650). As a treatment for severe respiratory failure with ECMO requires specialized knowledge and training, the number of patients annually supported with ECMO is positively associated with the survival rate.10

Most COVID-19 patients experience no or only mild symptoms and recover with no or minimal supportive care. The severe form of COVID-19 usually presents in the form of severe SOB, low SPO2, and sometimes a high level of carbon dioxide (CO2) about 1 week after the onset of the disease. Moreover, a severe form of COVID-19 can deteriorate rapidly to ARDS, and subsequently, multiple organ failures or death. Mortality rates as high as 4.3% have been reported.5,11,12

The presented case is the second case at the hospital’s FICU and the geographical region of Bahrain, where ECMO was used for the COVID-19 patient. The first case with ECMO treatment was in June 2020 at the hospital’s FICU. In this case, the patient had delayed presentation, and was successfully weaned from ECMO and was decannulated. On the other hand, tracheostomy was carried out as the patient was very weak, and it was difficult to wean from a mechanical ventilator. Unfortunately, this patient developed massive pneumothorax in both lungs, arrested, and expired.

The patient was effectively treated by ECMO in FICU as it was introduced in the early course of the disease. The patient was referred after 4 days from initial symptoms of the disease, which progressed to a severe form after 5 days.

The patient’s condition was assessed early in the FICU and was diagnosed as a severe form of COVID-19 complicated by ARDS; all efforts towards treatment (like steroids, antivirals, antibiotics, and even mechanical ventilation) failed to improve the oxygenation.

After the discussion with the ECMO team, ECMO was initiated and effectively improved the patient’s oxygenation, and CO2 level remained within normal. In addition, vital organ functions (heart, liver, and kidney) were not affected by the disease.

The authors agree with a meta-analysis study by Vaquer et al., which stated that early ECMO support could protect the oxygen supply of organs and avoid damage to the lungs caused by long-term application of excessively high mechanical ventilation conditions. This meta-analysis helped the authors to determine the appropriate time to initiate ECMO.11,12

In this case, the authors selected VV-ECMO as the patient had only respiratory problems without cardiac diseases. In ECMO management, coagulation function was monitored as the patient was on heparin infusion in addition to regular ABG with CXR to detect and to prevent possible complications, such as hemorrhage, thrombus, and pneumothorax, which could develop during ECMO treatment. Daily blood investigations to monitor vital organ functions, such as kidney, liver, and early detection of infection (if any) were performed.
**Conclusion**

ECMO treatment is strongly recommended at the early stage in severe COVID-19 patients from this successful experience. During ECMO treatment, coagulation function and blood gas profile of the patient needs to be regularly monitored to determine the period of ECMO usage.

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