



Successful management of COVID-19 induced acute respiratory distress syndrome by extracorporeal membrane oxygenation with 1-year follow-up: A case report



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ABSTRACT

Coronavirus 2019 (referred to as COVID-19) has infected millions of people throughout the world. This paper reports on a case of COVID-19-induced acute respiratory distress syndrome (ARDS) in which the patient was administered extracorporeal membrane oxygenation (ECMO) to deal with refractory hypoxia. The patient recovered from ARDS following ECMO treatment. In 1-year follow-up, the muscle weakness persisted, and the pulmonary vital capacity recovered sooner than diffusion capacity.

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Background

Coronavirus 2019 (SARS-CoV-2), which causes the disease now known as COVID-19, has infected millions of people throughout the world, and the World Health Organization (WHO) has declared it a public health emergency. Recent papers have listed the clinical manifestations as fever, cough, and dyspnea with the appearance of characteristic viral pneumonitis in radiological images [1]. Most infected patients experience mild to moderate pneumonia; however, roughly 10% of patients develop acute respiratory distress syndrome (ARDS) [2]. ARDS is characterized by severe hypoxemia refractory to mechanical ventilation with an extremely high mortality rate. Extracorporeal membrane oxygenation (ECMO) is the ultimate respiratory support method aimed at improving the oxygenation and ventilation of patients [3]. It is also meant to facilitate the implementation of ultra-lung-protective ventilation strategies to minimize ventilator-induced lung injury and improve clinical outcomes. Emerging evidence has suggested that ECMO is an effective treatment for ARDS resulting from viral pneumonia, including H1N1,

H7N9, and MERS [3–5]. A recent report of Extracorporeal Life Support Organization Registry revealed that the 90-day mortality rate was 38.0% in 1035 patients [6]. Another study demonstrated that ECMO may reduce mortality in severe hypoxemic COVID-19 patients [7]. However, the characteristics and course of disease were not clearly addressed, and the long-term consequences of pulmonary function were not reported. In this report, we describe the first successful use of ECMO in Taiwan for the treatment of a patient with severe COVID-19-associated ARDS with 1-year follow-up pulmonary function tests.

Case presentation

On January 29, 2020, a 68-year-old hypertensive female was admitted to a tertiary hospital due to a fever that had persisted for a period of five days. Prior to hospitalization, the patient had tested positive for influenza at a clinic; however, the nasopharyngeal swab used for polymerase chain reaction (PCR) tested negative for influenza on the day of hospitalization. A chest X-ray revealed bilateral peripheral patchy-like infiltration (Fig. 1), and laboratory data revealed a white blood cell count of 8200/ μ L, a lymphocyte count of 1148/ μ L, and elevated C-reactive protein (CRP) levels (186.19 mg/L). The fever persisted and pneumonia progressed even under treatment with levofloxacin and oseltamivir. Acute hypoxic respiratory failure occurred on the 11th day after admission, and the intubation

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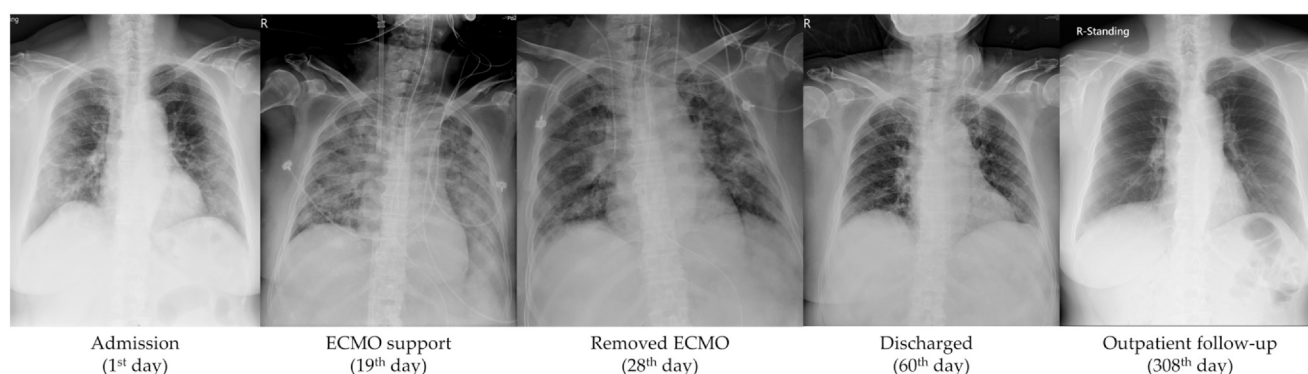


Fig. 1. Chest X-ray in different period. ECMO: Extracorporeal membrane oxygenation.

with mechanical ventilation was arranged. Midazolam and cisatracurium infusion were prescribed for ventilator synchrony. At that time, there were no confirmed cases of COVID-19 infection in Taiwan. Despite reporting no contact or cluster history, a nasopharyngeal swab for PCR tested positive for SARS-CoV-2 on February 17. Due to refractory respiratory failure ($\text{PaO}_2/\text{FiO}_2$ ratio [P/F ratio] of 112.5 and PaCO_2 of 50.9 mmHg), the prone positioning was tried on day 14, but it was held due to more severe hypoxemia after the procedure (P/F ratio of 100.3 and PaCO_2 of 55.5 mmHg). Since the hypoxemia and hypercapnia were more severe (P/F ratio of 77.1 and PaCO_2 of 83.4 mmHg), veno-venous extracorporeal membrane oxygenation (ECMO) was introduced on the 19th day after admission.

Following ECMO treatment, ultra-lung-protective ventilation was implemented with a tidal volume (V_t) < 4 ml/Kg. Chest X-rays indicated obvious improvements on the 3rd day after initiating ECMO (Fig. 1). Six days after ECMO initiation, ECMO FiO_2 was gradually decreased. Table 1 lists the ventilator settings and ECMO parameters. ECMO was halted on the 27th day after admission (i.e., treatment duration of 9 days).

Following the removal of ECMO, the patient was gradually weaned off the ventilator, eventually being liberated on the 40th day after admission. On the 50th day after admission, three consecutive PCR assays from nasopharyngeal swabs tested negative for SARS-CoV-2. The patient was transferred to the recovery ward on the 53rd day after admission and discharged on the 63rd day.

The patient received regular outpatient clinics follow-up for 12-month. She still complained of muscle weakness during exercise. However, her daily life activity return to normal and the cognition was normal without depression or distress. The pulmonary function test showed progressively improvement. The forced vital capacity (FVC) was 2.67 L (108% of predict value) in 2-month, 2.90 L (117% of

predict value) in 7-month, and 3.88 L (163% of predict value) in 10-month follow-up periods; respectively. The forced expiratory volume in one second (FEV1) were 2.42 L (122% of predict value) in 2-month, 2.55 L (129% of predict value) in 7-month, and 3.23 L (169% of predict value) in 10-month follow-up periods; respectively. The 6 min walking test was done in 10-month after respiratory failure. The results revealed the walking distance was 440 m with significant oxygen desaturation during exercise (from 98% before exercise to 88% after exercise).

Discussion

Randomized trials have clearly demonstrated that interventions, such as lung protective ventilation, prone ventilation, and neuromuscular blocking agents, can reduce the risk of mortality among patients with ARDS [8]. However, for some patients, these conventional measures fail to maintain oxygenation at a sufficient level, thereby necessitating other rescue therapies (e.g., ECMO). During the 2009 H1N1 influenza pandemic, ECMO proved highly effective in treating refractory respiratory failure in cases of severe ARDS [9]. Emerging evidence supports the use of ECMO in cases of severe hypoxemia resulting from viral diseases, such as avian influenza H7N9 [4] and the Middle East respiratory syndrome coronavirus [5]. The patient featured in this paper developed ARDS after contracting viral pneumonia with respiratory failure. Multiple organ dysfunction often occurs in cases where mechanical ventilation and maintaining the patient in a prone position are insufficient to deal with hypoxemia. V-V ECMO provides pulmonary support in cases where gas exchange is severely compromised, while protecting the lungs from damage, and giving lung tissue a chance to rest and recover.

Table 1
Ventilator and extracorporeal membrane oxygenation (ECMO) settings, laboratory data.

	Day 12	Day 14	Day 19	Day 20	Day 21	Day 25	Day 26	Day 27	Day 29	Day 33	Day 35	Day 39	Day 41	Day 50
Ventilator setting														
Mode	PCV	PCV	PCV	PCV	PCV	PCV	PCV	PCV	PCV	PCV	PS	PS	PS	NC
Positive end expiratory pressure (cm H ₂ O)	12	12	14	14	14	14	14	10	10	10	10	8	8	
Peak airway pressure (cm H ₂ O)	32	30	35	30	30	30	28	34	28	28	22	16	16	
Fraction of inspired oxygen (%)	100	80	90	70	40	40	50	55	45	40	35	35	35	32
Respiratory rate (/min)	24	24	28	12	10	10	18	28	22	16	22	27	25	
Tidal volume (ml/kg PBW)	9.2	7.7	5.0	4.0	4.2	6.7	4.5	7.2	7.0	7.0	8.7	9.4	6.4	
ECMO setting														
Blood flow (L/min)				3.5	3.5	3.5	3.5	3.5						
Air flow (L/min)				4	4	4	4	0						
Fraction of inspired oxygen (%)				100	100	90	30	0						
Laboratory Data														
Absolute lymphocyte count (/μL)	1467	520	275	490	1255	1699	2189	2684	860	1047	1260	1228	1806	2220
C-reactive protein (mg/L)	227.6	282.2	118.0				191.6	201.3	136.7	81.4	72.8	45.6	83.8	11.6
Interleukin-6 (pg/ml)					56.5		116.0			21.6			59.0	15.0

ECMO: extracorporeal membrane oxygenation; NC: nasal cannula; PBW: predict body weight; PCV: pressure control ventilation; PS: pressure support.

Ventilator-induced lung injury (VILI) is a major contributor to morbidity and mortality in cases of ARDS. During ARDS management, it is reasonable to reduce tidal volume (V_t) and airway pressure below the current standard of care to minimize the risk of VILI. One ventilator strategy aimed at protecting the lungs involves a V_t of 6 ml/kg and a plateau airway pressure of ≤ 30 cmH₂O. This approach has demonstrated survival benefits in cases of ARDS. Recent research has also indicated that implementing ECMO in conjunction with ultra-lung-protective ventilation (e.g., $V_t < 4$ ml/kg and plateau airway pressure < 25 cmH₂O) is superior to conventional management in treating patients with the most severe forms of ARDS. The patient in this study received ultra-lung-protective ventilation during ECMO support with a V_t of 4 ml/kg of predicted body weight. Nonetheless, further studies will be required to identify the best strategies by which to optimize mechanical ventilation.

In the present case, the increased serum levels of CRP and IL-6 appeared to be correlated with the severity of the illness, whereas the lymphocyte count was inversely correlated. Other researchers have also reported a positive correlation between IL-6 and CRP serum levels and the severity of COVID-19 infection [10]. Note also that IL-6 levels were significantly higher in non-survivors than in survivors [11]. During ECMO treatment, survivors presented a marked and rapid decline in IL-6 plasma levels, whereas non-survivors presented persistently elevated IL-6 levels throughout the observation period [12]. Notably, a similar pattern of enhanced CRP levels was observed in non-survivors. Furthermore, lymphocyte count has been associated with increased disease severity in COVID-19 [1,11]. Patients who have died from COVID-19 have also presented significantly lower lymphocyte counts than did survivors [10]. Many biomarkers for severity have been investigated in recent studies; however, IL-6, CRP, and lymphocyte count deserve further assessment with subjects stratified by age, comorbidities, illness severity, and outcomes.

ECMO is a resource-intensive, highly specialized, and expensive form of life support with considerable risk of complications, such as hemorrhage and nosocomial infection. ECMO is a good choice for critically ill patients when adequate resources are available; however, resources are often limited during pandemics. During large-scale outbreaks, administrators can expect a lack of ECMO equipment, suitably trained staff, and suitably equipped isolation rooms. Note also that the experience of staff and the volume of cases can have a profound effect on survival rates. One recent study reported that centers that deal with > 30 ECMO cases/year had better survival rates than did centers with < 6 cases/year [13]. Our institute operates as an ECMO center, with more than 100 cases of venoarterial and venovenous ECMO annually. At this institution, the decision to initiate ECMO cannulation is made by the treating intensivist and cardiac surgeon. The criteria for ECMO initiation in severe ARDS patients were persistent hypoxemia (PaO_2/FiO_2 ratio < 80 mm Hg) for at least 6 h despite aggressive mechanical ventilation support as positive end-expiratory pressure (PEEP) > 10 cm H₂O or peak inspiratory pressure > 35 cm H₂O. The exclusion criteria were (1) age < 20 years, (2) malignancies with poor prognosis within 5 years, (3) significant underlying comorbidities or severe multiple organ failure refractory to treatment [16]. During the current COVID-19 pandemic, it is crucial that diagnoses be confirmed rapidly and all suspected cases undergo quarantine to slow the spread of disease. It is also important to provide the resources for oxygen therapy, pulse oximeter monitoring, and mechanical ventilation. However, more clinical experience about the use of ECMO in COVID-19 patients is needed to provide the information about the benefits of ECMO in COVID-19 patients. Prospective study is mandatory to evaluate the impact of ECMO therapy in COVID-19 patients with severe ARDS and refractory hypoxemia.

The pulmonary function test in our patient showed progressively improvement of FVC and FEV1, but significant oxygen desaturation was noted during 6 min walking test and borderline walking distance in 10-month later. The long-term outcomes of COVID-19

patients with severe ARDS were not well delineated. A meta-analysis study demonstrated that diffusion capacity was impaired in 1–3 months after discharge [14]. Another study found that impaired diffusion capacity and muscle weakness persisted even after 6-month follow-up [15]. The persistent muscle weakness and exercise induced desaturation by 6-minute walk test in our patient seems compatible with previous report. In addition, the FVC and FEV1 recovered sooner than diffusion capacity.

In conclusion, ECMO is a feasible treatment choice for cases of oxygenation failure among COVID-19 patients with ARDS. ECMO should be considered refractory to conventional managements and could be combined with ultra-lung-protective ventilation to prevent lung injury. Note, however, that ECMO should be used with caution, based on the limited availability of medical resources during the current pandemic. Moreover, the pulmonary diffusion capacity was impaired more severe than vital capacity in COVID-19 patients with severe ARDS.

Ethics approval

The local Institutional Review Boards for Human Research at Linkou Chang-Gung Memorial Hospital approved this study (No. 202000833B0).

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRediT authorship contribution statement

Ko-Wei Chang: Data curation, Writing – original draft. **Kuang-Tso Lee:** Data curation. **Yu-Lun Lo:** Data curation. **Han-Chung Hu:** Data curation. **Cheng-Ta Yang:** Supervision. **Shu-Min Lin:** Writing – review & editing.

Declaration of Competing Interest

The authors report no declarations of interest.

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