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

Ko-Wei Chang, Kuang-Tso Lee, Yu-Lun Lo, Han-Chung Hu, Cheng-Ta Yang, Shu-Min Lin

Department of Thoracic Medicine, Chang Gung Memorial Hospital, Chang Gung University, School of Medicine, Taipei, Taiwan
Department of Cardiovascular, Chang Gung Memorial Hospital, Chang Gung University, School of Medicine, Taipei, Taiwan
Department of Respiratory Therapy, Chang Gung Memorial Hospital, Chang Gung University, School of Medicine, Taipei, Taiwan

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.

Keywords: COVID-19
Acute respiratory distress syndrome
Extracorporeal membrane oxygenation

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/μL, a lymphocyte count of 1148/μL, 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...
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 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 \(\text{P/F}\) ratio of 112.5 and \(\text{PaCO}_2\) of 50.9 mmHg), the prone positioning was tried on day 14, but it was held due to more severe hypoxemia after the procedure (\(\text{P/F}\) ratio of 100.3 and \(\text{PaCO}_2\) of 55.5 mmHg). Since the hypoxemia and hypercapnia were more severe (\(\text{P/F}\) ratio of 77.1 and \(\text{PaCO}_2\) 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 \(\text{FiO}_2\) 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 clinic 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 (168% 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 H7N9 in 2013 and the Middle East respiratory syndrome coronavirus in 2015. The patient featured in this paper developed ARDS after contracting H7N9 in 2013 and the Middle East respiratory syndrome coronavirus in 2015. The patient featured in this paper developed ARDS after contracting H7N9 in 2013 and the Middle East respiratory syndrome coronavirus in 2015. The patient featured in this paper developed ARDS after contracting H7N9 in 2013 and the Middle East respiratory syndrome coronavirus in 2015.

### Table 1

| Day 12 | Day 14 | Day 19 | Day 20 | Day 21 | Day 25 | Day 26 | Day 27 | Day 29 | Day 33 | Day 39 | Day 41 | Day 50 |
|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| **Ventilator setting** | | | | | | | | | | | | |
| Mode | PCV | PCV | PCV | PCV | PCV | PCV | PCV | PCV | PCV | PS | PS | PS |
| Positive end expiratory pressure (cm H\(2\)O) | 12 | 12 | 14 | 14 | 14 | 14 | 14 | 10 | 10 | 10 | 10 | 8 |
| Peak airway pressure (cm H\(2\)O) | 32 | 30 | 35 | 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 |
| Respiratory rate (/min) | 24 | 24 | 28 | 12 | 10 | 10 | 18 | 28 | 22 | 16 | 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 |
| **ECMO setting** | | | | | | | | | | | | |
| Blood flow (L/min) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Fraction of inspired oxygen (%) | 100 | 100 | 90 | 30 | 30 |
| **Laboratory Data** | | | | | | | | | | | | |
| Absolute lymphocyte count (/\(\mu\)L) | 1467 | 520 | 275 | 490 | 1255 | 1699 | 2189 | 2684 | 860 | 1047 | 1260 | 1228 |
| 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 (Vt) 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 Vt 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., Vt < 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 Vt 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 [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 (PaO₂/FiO₂ 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 management 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. 20200083B0).

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.

Financial support

No financial support.

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.

Acknowledgments

The authors thank their exceptional patient for her trust.

References

[1] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhuan, China. JAMA 2020;123(11):1061–9. https://doi.org/10.1001/jama.2020.1585
[2] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395(10223):507–13. https://doi.org/10.1016/S0140-6736(20)30211-7
[3] Noah MA, Peel GJ, Finney SJ, Griffiths MJ, Harrison DA, Grieve R, et al. Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A(H1N1). JAMA 2011;306(15):1659–68. https://doi.org/10.1001/jama.2011.1471
[4] Huang L, Zhang W, Yang Y, Wu W, Lu W, Xue H, et al. Application of extracorporeal membrane oxygenation in patients with severe acute respiratory distress syndrome induced by avian influenza A (H7N9) viral pneumonia: national data from the Chinese multicentre collaboration. BMC Infect Dis 2018;18:1(22). https://doi.org/10.1186/s12879-017-2903-x
[5] Alshahrani MS, Sindi A, Alshamsi F, Al-Omari A, El Tahan M, Alahmadi B, et al. Extracorporeal membrane oxygenation for severe Middle East respiratory syndrome coronavirus infection. Intensive Care Med 2020;46(6):941–50. https://doi.org/10.1007/s00134-020-05949-1
syndrome coronavirus. Ann Intensive Care 2018;8(1):3. https://doi.org/10.1186/s13613-017-0350-x

[6] Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, et al. Extracorporeal Life Support O. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization Registry. Lancet 2020;396(10257):1071–8. https://doi.org/10.1016/S0140-6736(20)32008-0

[7] Shaefi S, Brenner SK, Gupta S, O’Gara BP, Krajewski ML, Charytan DM, et al. STOP-COVID I. Extracorporeal membrane oxygenation in patients with severe respiratory failure from COVID-19. Intensive Care Med 2021;47(2):208–21. https://doi.org/10.1007/s00134-020-06331-9

[8] Fan E, Brodie D, Slutsky AS. Acute respiratory distress syndrome: advances in diagnosis and treatment. JAMA 2018;319(7):698–710. https://doi.org/10.1001/jama.2017.21907

[9] Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators, Davies A, Jones D, Bailey M, Beca J, Bellomo R, et al. Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome. JAMA 2009;302(17):1888–95. https://doi.org/10.1001/jama.2009.1535

[10] Gao Y, Li T, Han M, Li X, Wu D, Xu Y, et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. J Med Virol 2020;92(7):791–6. https://doi.org/10.1002/jmv.25770

[11] Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020;46(5):846–8. https://doi.org/10.1007/s00134-020-05991-x

[12] Risnes I, Wagner K, Ueland T, Molines T, Aukrust P, Svennevig J. Interleukin-6 may predict survival in extracorporeal membrane oxygenation treatment. Perfusion 2008;23(3):173–8. https://doi.org/10.11177/0267659108097382

[13] Barbaro RP, Odetola FO, Kidwell KM, Paden ML, Bartlett RH, Davis MM, et al. Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. Ann J Respir Crit Care Med 2015;191(8):894–901. https://doi.org/10.1164/rccm.201409-16340C

[14] Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, et al. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. Pulmonology 2021;27:328–37. https://doi.org/10.1016/j.pulmoe.2020.10.013

[15] Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 2021;397(10270):220–32. https://doi.org/10.1016/S0140-6736(20)32656-8

[16] Chu IC, Chuang LP, Lee SW, Lin YJ, Chang CJ, Li HH, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome: propensity score matching. Membranes 2021;11(6):393.