Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Cardiothoracic and Vascular Anesthesia 35 (2021) 2467–2470

Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Case Report

Acute Respiratory Distress Syndrome Treated With Awake Extracorporeal Membrane Oxygenation in a Patient With COVID-19 Pneumonia

Tong Li, MD*, Peng-Fei Yin, MM†, Ang Li, BS†, Maxwell R. Shen, BS, MBBS‡, Yong-Xing Yao, MD†,[1]

*Department of Intensive Care Unit, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

†Department of Anesthesia, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

‡Zhejiang University School of Medicine, Hangzhou, China

Key Words: extracorporeal membrane oxygenation; COVID-19; 2019-coronavirus pneumonia; acute respiratory distress syndrome; awake ECMO

Since the first outbreak of coronavirus disease 2019 (COVID-19) in December 2019, which was caused by severe acute respiratory syndrome coronavirus 2, the disease has spread worldwide over the past months and become a global pandemic.[1] Although most infections are mild, severe impairment of the respiratory system and acute respiratory distress syndrome (ARDS) may develop in patients with preexisting comorbidities such as hypertension, diabetes, and other lung diseases. Extensive use of mechanical respiratory support and extracorporeal membrane oxygenation (ECMO) has helped to reduce the case fatality rate of COVID-19 to less than 2% in some regions.[2] However, various related complications, including pneumothorax, thrombosis, ventilator-associated infection, ventilator-induced lung injury, systemic inflammation, and neurologic complications may emerge during the use of conventional mechanically ventilated ECMO.[3] In recent years, ECMO without mechanical ventilation (MV) and sedation (awake ECMO) has been used in several subset populations.[4] Similar to conventional ECMO, awake ECMO also notably improves oxygenation; awake ECMO exempts MV and avoids the complications associated with prolonged sedation and tracheal intubation. Awake and fully mobile ECMO has proven to be beneficial in patients with ARDS induced by pneumocystis pneumonia, immunocompromised patients, and patients requiring extracorporeal life support.[5-7] However, the use of awake ECMO has not been reported in ARDS patients secondary to COVID-19 pneumonia. In this case report, the authors managed a case of ARDS resulting from COVID-19 pneumonia with awake ECMO.

Case Report

An 80-year-old female patient was admitted to the authors' intensive care unit for severe bilateral pneumonia. Thoracic radiography showed diffuse whiteout of the lungs, and computed tomography (CT) showed bilateral multiple ground-glass opacities (Fig 1, A and B). Her main symptoms were persistent fever, cough, and shortness of breath for seven days. Her laboratory tests indicated a C-reactive protein concentration of 51.20 mg/dL, with normal coagulation profile (D-dimer, 953 μg/L) and serum enzyme levels. A complete blood count revealed leukocytosis (13,500/dL), with neutrophil predominance (94.6%) and a low lymphocyte count (200/dL). The nasal and pharyngeal swab specimens tested positive

Informed consents were obtained for publishing the details of the report and the photograph.

[1]Address correspondence to Yong-Xing Yao, MD, Department of Anesthesia, First Affiliated Hospital, Zhejiang University School of Medicine, 79 Qingchun Rd, Hangzhou, 310003, P. R. China.

E-mail address: yaoyongxing@zju.edu.cn (Y.-X. Yao).

https://doi.org/10.1053/j.jvca.2020.11.017

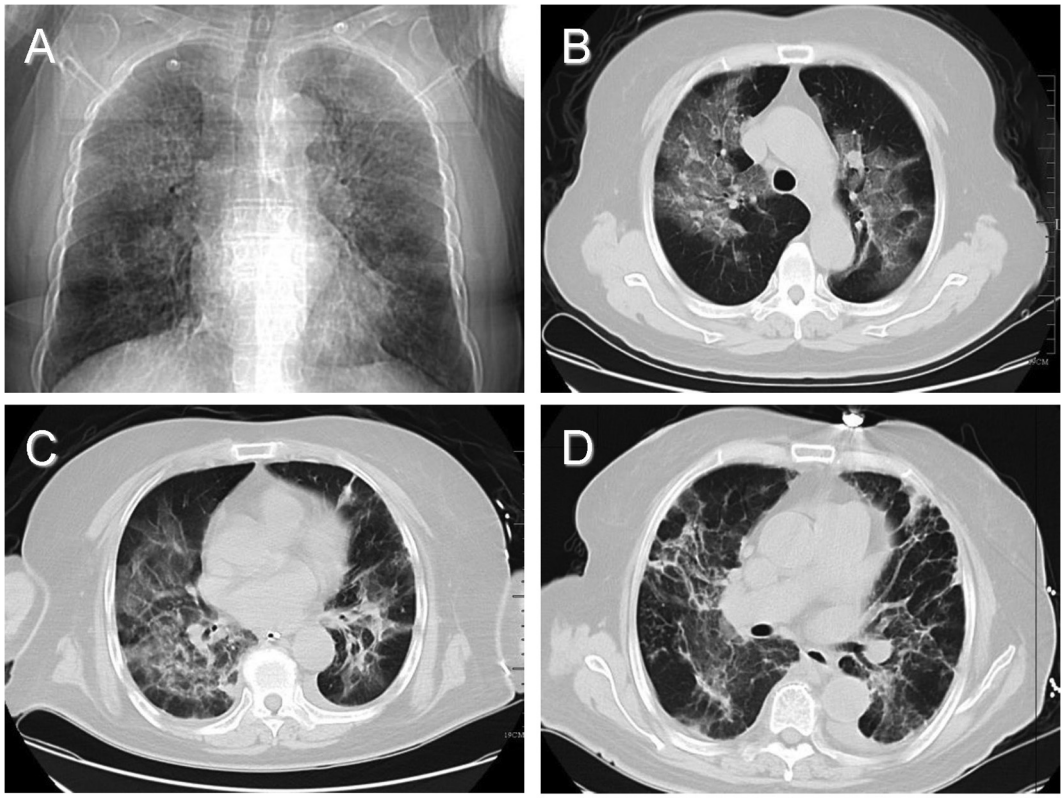

Fig 1. Timeline of thoracic computed tomography. (A, B) Multiple ground-glass opacities in both the lungs. (C) Progressed inflammation after five days of symptomatic treatment. (D) Lung inflammation improved after 10 days of extracorporeal oxygenation support.

for COVID-19 and negative for influenza A and B viruses; adenovirus; respiratory syncytial virus; and parainfluenza virus 1, 2, and 3. Initial arterial blood gas (ABG) analysis was performed, which showed a pH of 7.44, PaO_2 of 62.4 mmHg, $PaCO_2$ of 30.7 mmHg, and a low PaO_2/fraction of inspired oxygen (F_IO_2) ratio with an F_IO_2 of 50%. High-flow oxygen therapy via the nasal cannula under a mask was initiated with the goal of maintaining her oxygen saturation (SpO_2) above 90%.

In an isolated room, the patient received intensive monitoring, antiviral therapy (arbidol, 0.2 g/8 h, orally), and recombinant human aerosolized interferon alfa-1b (0.1 million U, 4 times a day via inhalation) for five days. Enoxaparin (4,000 U, subcutaneous, once a day) was administered from day four to day 16. Despite receiving supportive and respiratory care, such as back percussions, prone positioning, and sputum drainage, her respiratory function deteriorated further. Her respiratory rate (RR) was 33 breaths/min, and the PaO_2/FIO_2 ratio decreased to less than 80. A repeat thoracic CT scan showed progressive inflammation (Fig 1, C). Subsequently, her PaO_2 declined to 53.4 mmHg, with an F_IO_2 of 100%. Emergency endotracheal intubation, facilitated by neuromuscular blocking agents coupled with MV under sedation with propofol and dexmedetomidine infusions, was performed. Respiratory parameters were set using pressure-control ventilation mode, with 30 cmH_2O, positive end-expiratory pressure of 10 cmH_2O, and tidal volume of 250 mL, with the goal of maintaining her SpO_2 at 95%. After four days of MV, her pulmonary function improved and F_IO_2 was reduced from 75% to 50%, with an RR of 18-to-20 breaths/min. Her SpO_2 stabilized at 96% to 98% (PaO_2/F_IO_2 ratio of 214; $PaCO_2$, 37.5 mmHg). She was conscious and responsive. She was extubated and switched to high-flow oxygen therapy, with an F_IO_2 of 50%. However, her pulmonary function was undulant, and on the sixth day after extubation, her PaO_2 declined to 51 mmHg despite an F_IO_2 of 90%, with an RR of 30 breaths/min. The patient was reintubated and sedated by propofol infusion. The ABG analysis showed a pH of 7.48, PaO_2 of 61.2 mmHg (F_IO_2 of 100%), and $PaCO_2$ of 33.6 mmHg. Despite recruitment maneuvers, prone positioning, optimal ventilation setting, and use of neuromuscular blocking agents for 24 hours, the pressure remained as high as 30 cmH_2O, with a tidal volume of 150 mL, and her PaO_2/FIO_2 remained below 70, together with ongoing signs and symptoms of respiratory distress. Therefore, percutaneous venovenous ECMO (BE-PLS 2050, Maquet, Germany) was initiated. The ECMO was conducted with a dual cannula from the right femoral vein (24F) into the abdominal inferior vena cava as the drainage cannula and the right internal jugular vein (19F) as the return cannula (Fig 2), with an initial flow rate of 3.5 L/min. Cannulae were fixed using a self-adhesive bandage along the patient's neck. The blood coagulation parameter was maintained at a target of 60 seconds activated partialthromboplastin time using unfractionated heparin infusion as prophylaxis against thrombi formation. An intravenous infusion of norepinephrine (3 μg/min) was titrated to maintain a stable blood pressure. Two hours

Fig 2. Cannula fixation. Cannulae fixed with self-adhesive bandage along the patient's neck (photo belongs to a separate patient).

later, she regained consciousness. She was hemodynamically stable, and norepinephrine was discontinued. The ABG analysis showed the following: $PaCO_2$, 31.7 mmHg; PaO_2, 69.2 mmHg ($PaO_2/F_IO_2 = 221$). After a comprehensive evaluation, she was extubated and received awake ECMO support. The flow rate was adjusted to 60 mL/kg/min, with air flow/blood flow of 0.8 to 1:1. After extubation, the patient was not breathless and had an RR of 20 breaths/min. She was in a good mental state and could feed herself. She received plasma (300 mL) from a convalescent donor who recovered from COVID-19, and two days later, her COVID-19 test result was negative. Her blood test showed a hemoglobin level of 8.5 g/dL; thus, packed red blood cells (400 mL) were administered. After 10 days of ECMO support, the patient's pulmonary function improved. Her ABG analysis showed the following: PaO_2, 99 mmHg (F_IO_2, 30%); $PaCO_2$, 37 mmHg; and SpO_2, 98%. Her temperature was normal, with a heart rate of 77 beats/min and an RR of 22 breaths/min. Thoracic CT demonstrated a significant improvement in ground-glass opacification from her previous scan (Fig 1, D). Based on her condition, the weaning process began while maintaining continuous assessment. The patient tolerated weaning well, with a gradual reduction in the ECMO blood flow rate. On complete suspension, her ABG analysis showed the following: PaO_2, 72 mmHg (F_IO_2, 30%); $PaCO_2$, 45 mmHg; SpO_2, 94% with stable hemodynamic parameters (blood pressure: 157/62 mmHg, heart rate: 76 beats per minute). The patient was weaned successfully off ECMO and recuperated under supportive care. The subsequent therapy period was uneventful. She was discharged from the hospital after 10 days of additional therapy, with ABG analysis showing a $PaCO_2$ of 34 mmHg and PaO_2 of 102 mmHg with an F_IO_2 of 30%.

Discussion

COVID-19 is an emerging, rapidly evolving pandemic. Profound hypoxemia and acute lung failure, the main causes of death, are the prominent features of ARDS, resulting in a subset of critical COVID-19 pneumonia patients.[1] Despite the wide use of MV, the mortality rate is as high as 80% in intubated populations.[8] ECMO has become an alternative therapy for prolonging patient life and allowing time for lung recovery, especially in severe ARDS resulting from COVID-19.[9,10] However, conventional ECMO is conducted under MV and sedation; various complications may emerge during prolonged MV and sedation, including pneumothorax, increased risk of infection, ventilator-induced lung injury, systemic inflammation, and neurologic complications.[11,12] In addition, pneumonia and ARDS caused by COVID-19 show an unusual pattern of disease progression. Lung inflammation and tissue destruction arise from the lower airways and involve the alveoli, and features of pulmonary edema and hyaline membrane formation cause a restrictive lung pattern.[13]

In recent years, awake ECMO has been used in selected cases of ARDS and has proved advantageous. The strong rationale for using awake ECMO over conventional mechanically ventilated ECMO is that awake ECMO avoids intubation and MV, results in minimal stress, has no synchronization issues, and requires no sedatives. These parameters help avoid complications such as ventilator-induced lung injury, ventilator-associated infections, and delirium secondary to prolonged sedative usage. While providing time for lung recovery, awake ECMO permits spontaneous breathing, self-feeding, and active functional rehabilitation, which are all essential for post-ECMO recuperation.[4] In the authors' patient, the premature extubation caused the gradual deterioration of pulmonary function, suggesting that inflammation persisted even after four days of respiratory support.

The indications to initiate ECMO in COVID-19 have been suggested in a previous publication; namely, PaO_2/F_IO_2 of < 50 mmHg for three hours or more, $PaO_2/F_IO_2 < 80$ mmHg for six hours or more, or an arterial pH lower than 7.25 with a $PaCO_2$ of ≥ 60 mmHg for six hours.[14] In the present patient, after reintubation and respiratory support for 24 hours, profound hypoxemia was still evident, which prompted the initiation of venovenous ECMO. Subsequently, an awake ECMO strategy was adopted. After extubation, the patient was able to communicate with her relatives and medical staff, and to feed herself the following day. Throughout the duration of her treatment under awake ECMO, early physiotherapy was initiated with passive and active movements progressing to daily ambulation without obvious discomfort. At the same time, preventive strategies and class III precautions as recommended for ECMO in COVID-19 were followed. The medical team

donned face shields and disposable drapes in addition to the surgical masks and gloves, as recommended by the Chinese Society of Anesthesiology.[15]

Conclusions

The use of awake ECMO in critically ill patients who respond poorly to MV may be a promising therapeutic strategy for managing patients with ARDS due to COVID-19 pneumonia. However, this warrants further investigation.

Conflict of Interest

None.

References

1 Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020;46:846–8.

2 Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–20.

3 Combes A, Hajage D, Capellier G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. N Engl J Med 2018;378:1965–75.

4 Langer T, Santini A, Bottino N, et al. "Awake" extracorporeal membrane oxygenation (ECMO): Pathophysiology, technical considerations, and clinical pioneering. Crit Care 2016;20:150.

5 Stahl K, Seeliger B, Hoeper MM, et al. "Better be awake"—a role for awake extracorporeal membrane oxygenation in acute respiratory distress syndrome due to Pneumocystis pneumonia. Crit Care 2019;23:418.

6 Schmidt M, Schellongowski P, Patroniti N, et al. Six-month outcome of immunocompromised patients with severe acute respiratory distress syndrome rescued by extracorporeal membrane oxygenation. An international multicenter retrospective study. Am J Respir Crit Care Med 2018;197:1297–307.

7 Abrams D, Garan AR, Brodie D. Awake and fully mobile patients on cardiac extracorporeal life support. Ann Cardiothorac Surg 2019;8:44–53.

8 Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. Lancet Respir Med 2020;8:475–81.

9 Henry BM. COVID-19, ECMO, and lymphopenia: A word of caution. Lancet Respir Med 2020;8:e24.

10 Augoustides JG. Extracorporeal membrane oxygenation – Crucial considerations during the coronavirus crisis. J Cardiothorac Vasc Anesth 2020;34:1720–2.

11 Keller SP. Contemporary approaches in the use of extracorporeal membrane oxygenation to support patients waiting for lung transplantation. Ann Cardiothorac Surg 2020;9:29–41.

12 Hoyler MM, Flynn B, Iannacone EM, et al. Clinical management of venoarterial extracorporeal membrane oxygenation. J Cardiothorac Vasc Anesth 2020;34:2776–92.

13 Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420–2.

14 Mikkelsen ME, Vernick W, Gutsche J. Extracorporeal membrane oxygenation during the coronavirus disease 2019 pandemic. Crit Care Med 2020;48:1389–91. https://doi.org/10.1097/CCM.0000000000004507; [e-pub ahead of print].

15 Gong Y, Cao X, Mei W, et al. Anesthesia considerations and infection precautions for trauma and acute care cases during the COVID-19 pandemic: Recommendations from a task force of the Chinese Society of Anesthesiology. Anesth Analg 2020;131:326–34.