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CASE REPORT

Weaning from Venovenous Mode Extracorporeal Membrane Oxygenation in Coronavirus Disease 2019-Related Respiratory Distress Syndrome

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The coronavirus disease-2019 (COVID-19) has caused a worldwide pandemic. Approximately 5% of victims develop severe acute respiratory distress syndrome (ARDS), and some require extracorporeal membrane oxygenation (ECMO). However, weaning patients with COVID-19-related ARDS from ECMO are challenging. Here, we report a COVID-19 case with severe ARDS that received venovenous ECMO to maintain adequate gas exchange for more than 4 weeks. We performed prolonged prone position ventilation and airway pressure release ventilation, and the patient was successfully weaned off ECMO.

Key words: Acute respiratory distress syndrome, airway pressure release ventilation, coronavirus disease-2019, extracorporeal membrane oxygenation, prone position ventilation

INTRODUCTION

Since the disease outbreaks, critical care for the coronavirus disease-2019 (COVID-19) has been widely discussed, and approximately 5% of COVID-19 patients develop acute respiratory distress syndrome (ARDS).[1] Extracorporeal membrane oxygenation (ECMO), which allows the lung to rest at minimal ventilator settings to prevent further lung injury and act as a last resort in patients with severe hypoxemia and hypercapnia, is a treatment option for patients with ARDS who are refractory to optimal ventilator management. A systematic review reported that in-hospital mortality in selected patients receiving ECMO support for COVID-19-related ARDS (C-ARDS) was 37.1%. This study suggests that venovenous ECMO (VV-ECMO) outcomes were similar between COVID-19 and non-C-ARDS, with increased age as a mortality risk factor.[2] Recently, a retrospective multicenter study confirmed that the survival of selected patients with C-ARDS was comparable to that of patients with non-C-ARDS.[3]

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However, the Extracorporeal Life Support Organization and Surviving Sepsis Campaign Guidelines recommend that ECMO should only be considered in carefully selected patients with C-ARDS due to the resource-intensive nature of ECMO and the need for experienced centers and health-care workers. The complications of ECMO, such as thromboembolic events, bleeding, bloodstream infection, and neurological injury, increase with prolonged usage. Patients who are appropriately liberated from ECMO need to be able to maintain adequate respiratory effort and gas exchange with reduced ECMO pump flow and gas flow. However, approximately 40% of COVID-19 patients with VV-ECMO require prolonged usage for more than 3 weeks.[2] As weaning from ECMO in patients with C-ARDS is challenging, novel strategies are warranted.

Herein, we describe a patient with C-ARDS who received VV-ECMO to maintain adequate gas exchange for 4 weeks. Combined prolonged prone position ventilation (PPV) and airway pressure release ventilation (APRV) modes of

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mechanical ventilation were successfully performed to wean the patient from VV-ECMO.

CASE REPORT

A 66-year-old male was admitted for fever and dyspnea that had persisted for 2 days. He had received adjuvant chemotherapy for rectal cancer 10 days prior. Chest radiography revealed ground-glass opacities in both lower lobes. Nucleic acid amplification testing of a nasopharyngeal swab sample for severe acute respiratory syndrome coronavirus 2 RNA was positive. His initial vital signs were as follows: body temperature – 37.8°C, blood pressure – 136/60 mmHg, heart rate – 88 beats/min, respiratory rate – 28 breaths/min, and saturation – 99% under 100% fraction of inspired oxygen (FiO_2). Laboratory data showed the following: white blood cells count – 20,700 μL, C-reactive protein – 2.57 mg/dL, D-dimer – 1.83 mg/L, ferritin – 899 ng/mL, lactate dehydrogenase (LDH) – 586 U/L, and lactate – 1.3 mmol/L [Table 1].

We administered intravenous remdesivir (200 mg stat and 100 mg/day for 9 days), dexamethasone (5 mg/day for 10 days), and tocilizumab (400 mg stat) for COVID-19 infection. Enoxaparin (40 mg/day) was administered to prevent thromboembolic events. Empiric antibiotics, with meropenem and clarithromycin, were also administered. One day later, oxygenation rapidly deteriorated, and the endotracheal tube was intubated. The initial mechanical ventilator settings were as follows: peak inspiratory pressure – 22 cmH_2O; respiratory rate – 18 breaths per minute (breaths/min); positive end-expiratory pressure – 10 cmH_2O; and FiO_2 of 80% under pressure control mode. His initial tidal volume was approximately 325 mL with a compliance of 30 L/cmH_2O, a resistance of 10 cmH_2O/L/sec, and P/F ratio of approximately 120–140. On day 3, the P/F ratio dropped to 80.7. PPV was attempted with a poor response. Laboratory data were as follows: white blood cells – count 17,040 μL; C-reactive protein – 15.46 mg/dL; D-dimer – >20 mg/L; ferritin – 2952 ng/mL; LDH – 1017 U/L; and lactate – 1.0 mmol/L [Table 1]. Therefore, a VV-ECMO was performed. The initial ECMO settings were as follows: blood flow – 2.9 L/min, gas flow – 3.5 L/min, and FiO2 – 100%. However, after ECMO, the dynamic compliance and tidal volume remained impaired [Figure 1].

A computed tomography of the chest was performed on day 14 and revealed ground-glass opacities and

Table 1: Patient's laboratory data on admission (day 1), on extracorporeal membrane oxygenation (day 3) and before weaning from extracorporeal membrane oxygenation (day 38)

Laboratory analysis	Admission (day 1)	On ECMO (day 3)	Before weaning from ECMO (day 38)	Reference value
Leukocyte (/mm^3)	20,700	17,040	8330	4500–11,000
Hemoglobin (g/dL)	13.7	8.5	10.1	13.5–18.0
Platelet count (/mm^3)	212,000	92,000	130,000	150,000–400,000
D-dimer (mg/L)	1.83	>20	4.61	<0.50
Creatinine (mg/dL)	0.5	0.9	1.1	0.7–1.2
Aspartate aminotransferase (U/L)	64	86	42	<40
Alanine aminotransferase (U/L)	32	24	11	<40
LDH (U/L)	586	1017	302	140–270
C-reactive protein (mg/dL)	2.57	15.46	1.33	<0.80
Procalcitonin (ng/mL)	0.15	0.56	N/A	<0.05
Ferritin (ng/mL)	899	2952	1928	30–400
Lactate (mmol/L)	1.3	1.0	1.2	0.5–2.2
Arterial gas				
pH value	7.467	7.402	7.426	7.350–7.450
$PaCO_2$ (mmHg)	33.7	41.7	49.4	35–45
PaO_2 (mmHg)	146.6	80.7	104.9	75–100
HCO_3 (mmol/L)	24.6	26.2	32.8	21–28
SpO_2 (%)	99.8	95.6	98.3	95–98
Compliance	34	23	18	
Resistant	8	13	15	
P/F ratio	146.6	80.7	262.25	

LDH=Lactate dehydrogenase; ECMO=Extracorporeal membrane oxygenation; P/F ratio=Horowitz index for lung function (PaO_2/FiO_2)

consolidations over the bilateral lung regions, especially over the dorsal part [Figure 2]. Although the challenging circumstances of a severe pandemic, the limited availability of hospital resources has placed a considerable burden on the usual PPV for this patient. Through the literature review, we discovered that researchers have found that prolonged PPV yielded comparable outcomes to usual PPV while causing no significant additional complications. Therefore, prolonged PPV was used instead.[4,5] The first course of prolonged PPV was administered with VV-ECMO on day 17 [Figure 3]. After PPV, both tidal volume and oxygenation were improved, and resupination was performed on day 23. We tapered down the setting until mating target ventilator support criteria performed a sequential daily weaning trial and reduced ECMO FiO_2 –21% to maintain a SpO_2 >90% for 24–48 h, of ECMO. However, the trial could only be maintained for 6–8 h and was then forced to be discontinued due to oxygenation after resupination on day 26.

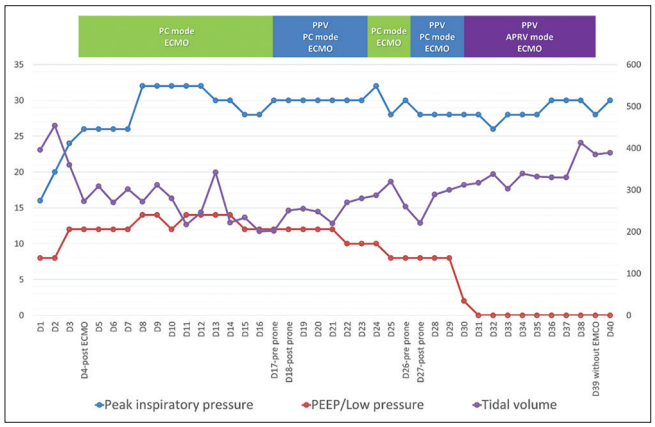

Figure 1: The patient's ventilator setting and trend graph of tidal volume under different strategies

We performed again on day 27 [Figures 1 and 4]. Although the patient's condition had improved with the use of PPV under ECMO, we suspected that poor oxygenation in returning to the supine position might result from recollapse of the lungs. Under prolonged PPV, a ventilation strategy with APRV was used from day 31. The initial APRV settings were as follows: high airway pressure (P_{high}) of 28 mm H2O, low airway pressure (P_{low}) of 0 mm H_2O, inspiratory time (T_{high}) of 3s, and expiratory time (T_{low}) of 0.5s. We adjusted the P_{high} to maintain a tidal volume of 6–8 mL/kg. Thigh was adjusted based on his $PaCO_2$ and pH values to maintain a pH >7.25 and PaCO2 <60 mmH_2O. The patient's tidal volume had significantly improved. The carbon dioxide clearance and oxygenation remained while we tapered down the setting of VV-ECMO. On day 39, the resupination was repeated. We maintained the APRV mode, and ECMO was successfully weaned off on day 40. Follow-up chest computed tomography on day 45 revealed significant improvement in the dorsal part of the bilateral lungs [Figure 2].

DISCUSSION

We present a case of C-ARDS that required prolonged VV-ECMO to maintain adequate oxygenation. Combining prolonged PPV and APRV modes of mechanical ventilation were used for successful weaning from ECMO.

The lung computed tomography images of the present case showed typical ARDS features, including lung collapse and consolidation in the dorsal region and hyperinflation of the

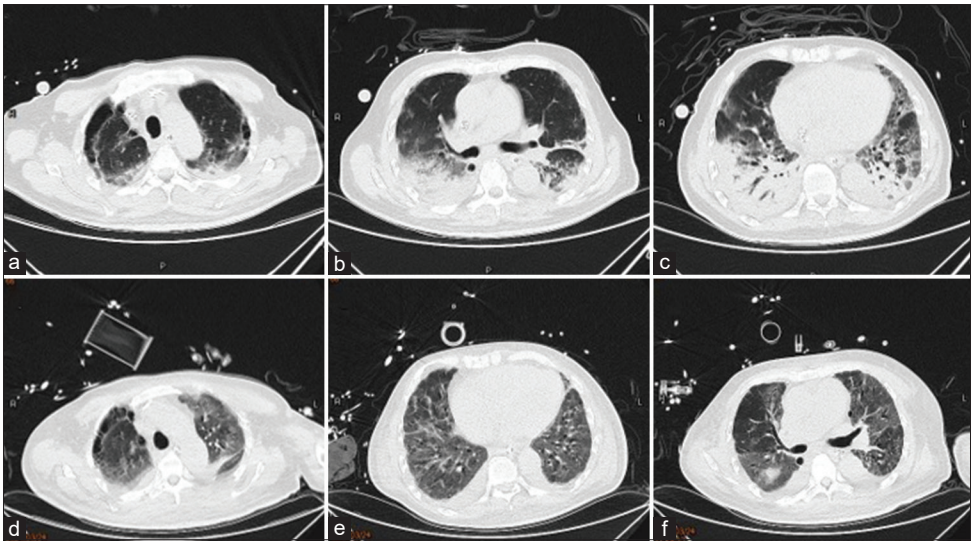

Figure 2: (a-c) Computed tomography of chest on day 14 before prolonged prone. (d-f) Computed tomography of chest on day 45 after weaning ECMO. ECMO = Extracorporeal membrane oxygenation

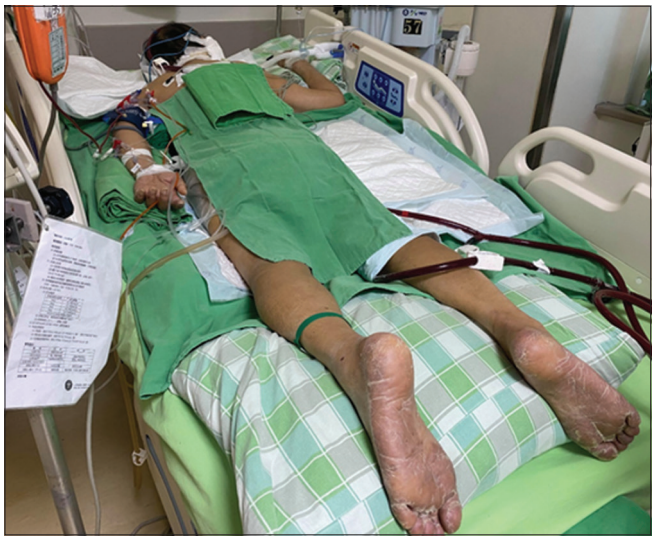

Figure 3: Our patient with the use of prone position during venovenous extracorporeal membrane oxygenation

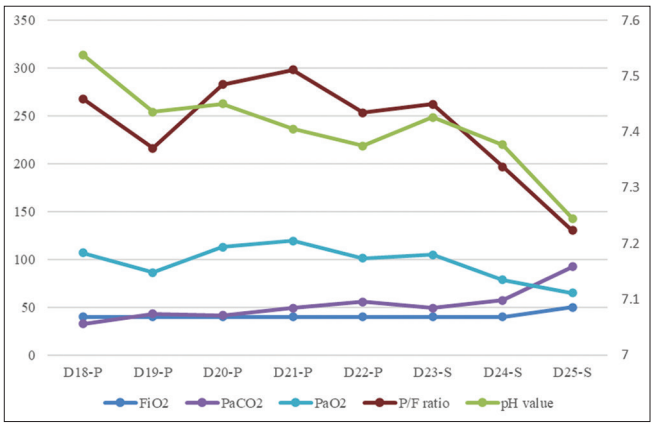

Figure 4: The patient's FiO_2, PaO_2, $PaCO_2$, P/F ratio, and pH value after resupination. P/F ratio=Horowitz index for lung function (PaO_2/FiO_2)

ventral region. PPV could result in more homogeneous inflation and ventilation distribution, improved ventilation-perfusion matching, and attenuated periodic recruitment reduction at the interface between the dorsal and ventral regions, which rescue hypoxemia and prevent ventilator-induced lung injury. PPV has been adopted for COVID-19 or ARDS or other causes.[5] Considering the burden of usual PPV for health-care workers, prolonged PPV is feasible and relatively safe for treating critically ill COVID-19 patients with ARDS.[4] A previous study showed that PaO_2/FiO_2 recorded in the supine position after a prolonged PPV was significantly higher than that of the standard method, while it did not increase the incidence of skin lesions.[4]

ECMO provides an alternative for patients with ARDS because conventional mechanical ventilation fails to maintain adequate gas exchange. The combination of PPV and ECMO may offer additional clinical advantages through the optimization of ventilation and perfusion matching.[6,7] A retrospective study of 168 ECMO patients reported that PPV improved survival.[8] Another multicenter cohort study also showed that the application of PPV in ARDS patients on VV-ECMO improved oxygenation and reduced hospital mortality by 20%.[7]

Airway pressure-release ventilation (APRV) is a pressure-controlled, intermittent mandatory ventilation mode with a short intermittent release phase, allowing the release of partial lung volume and spontaneous breathing at a high level of pressure. The long duration of inspiration (T_{high}) and high constant airway pressure (P_{high}) ensure the recruitment of alveolar units. PPV and APRV share the same conception of recruiting consolidated lungs by different mechanisms, and in theory, the combination of the two strategies might have a synergic effect.[9] Early application of APRV may reduce the duration of mechanical ventilation in ARDS. A prospective randomized intervention study showed that APRV during PPV is feasible for the treatment of patients with acute lung injury. APRV after 24 h appears to enhance oxygenation improvement in response to PPV.[10]

For the patient, the goal of treatment was to minimize the risk of ECMO-related complications by early weaning off ECMO. However, we discovered that the conventional ventilation strategy was insufficient for this patient. We used APRV to keep the alveoli open and maintain oxygenation. In a meta-analysis, using APRV may have improved oxygenation on day 3 and contributed to a reduction in the length of stay in the intensive care unit.[11] A case series study reported on a select subgroup of ARDS patients with PPV who used APRV. All five patients had improved oxygenation after APRV, and three patients were extubated within 72 h of turning supine.[9] In addition to the improvement in alveolar recruitment, the period of airway pressure reduction during the release phase of APRV is short, thus minimizing repetitive alveolar collapse. Although future trials are needed to determine the heterogeneous use of combinations of PPV and APRV in clinical practice, the strategies of "Open the lung" and "Never let the lung collapse" may be beneficial to weaning from prolonged ECMO usage in COVID-19 patients with severe ARDS.

There are some difficult-to-clarify parts in this case report. First, our patient underwent the fourth cycle of adjuvant chemotherapy for colorectal cancer and there have been discussions on cancer treatment for COVID-19-diagnosed patients before the pandemic. An article published in The Lancet stated that the mortality from COVID-19 in cancer patients appears to be principally driven by age, gender, and comorbidities. They found no evidence that cancer patients receiving cytotoxic chemotherapy or other anticancer treatment had a higher risk of death from COVID-19 disease compared to those not receiving aggressive treatment for cancer.[12] Indeed, due to the weakened immune system caused by tumor growth and anticancer treatment, cancer patients are

considered a highly vulnerable group, with a higher risk of severe clinical events such as ICU admission, invasive ventilation, or death than noncancer patients.

Second, the efficacy of VV-ECMO in cancer patients suffering from severe respiratory failure remains ambiguous. A retrospective multicenter analysis has revealed that the disease status, low platelet count, and elevated lactate levels are unfavorable prognostic indicators that should be taken into consideration when deciding whether to proceed with VV-ECMO.[13] The ELSO 2021 Interim Guidelines for VV-ECMO in adult patients list "anticipated nonrecovery without a viable decannulation plan" as the only absolute contraindication and deem "immunosuppression" a relative contraindication. Despite these guidelines, the use of VV-ECMO in cancer patients with respiratory failure remains uncertain and further investigation is warranted.

CONCLUSION

For patients with prolonged VV-ECMO use due to C-ARDS, the application of prolonged PPV and APRV of mechanical ventilation can be a feasible strategy for weaning from ECMO.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent form. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for disease control and prevention. JAMA 2020;323:1239-42.
2. Ramanathan K, Shekar K, Ling RR, Barbaro RP, Wong SN, Tan CS, *et al.* Extracorporeal membrane oxygenation for COVID-19: A systematic review and meta-analysis. Crit Care 2021;25:211.
3. Vigneshwar NG, Masood MF, Vasic I, Krause M, Bartels K, Lucas MT, *et al.* Venovenous extracorporeal membrane oxygenation support in patients with COVID-19 respiratory failure: A multicenter study. JTCVS Open 2022;12:211-20.
4. Carsetti A, Damia Paciarini A, Marini B, Pantanetti S, Adrario E, Donati A. Prolonged prone position ventilation for SARS-CoV-2 patients is feasible and effective. Crit Care 2020;24:225.
5. Guérin C, Albert RK, Beitler J, Gattinoni L, Jaber S, Marini JJ, *et al.* Prone position in ARDS patients: Why, when, how and for whom. Intensive Care Med 2020;46:2385-96.
6. Zaaqoq AM, Barnett AG, Griffee MJ, MacLaren G, Jacobs JP, Heinsar S, *et al.* Beneficial effect of prone positioning during venovenous extracorporeal membrane oxygenation for coronavirus disease 2019. Crit Care Med 2022;50:275-85.
7. Giani M, Martucci G, Madotto F, Belliato M, Fanelli V, Garofalo E, *et al.* Prone positioning during venovenous extracorporeal membrane oxygenation in acute respiratory distress syndrome. A multicenter cohort study and propensity-matched analysis. Ann Am Thorac Soc 2021;18:495-501.
8. Guervilly C, Prud'homme E, Pauly V, Bourenne J, Hraiech S, Daviet F, *et al.* Prone positioning and extracorporeal membrane oxygenation for severe acute respiratory distress syndrome: Time for a randomized trial? Intensive Care Med 2019;45:1040-2.
9. Varpula T, Jousela I, Niemi R, Takkunen O, Pettilä V. Combined effects of prone positioning and airway pressure release ventilation on gas exchange in patients with acute lung injury. Acta Anaesthesiol Scand 2003;47:516-24.
10. Zhou Y, Jin X, Lv Y, Wang P, Yang Y, Liang G, *et al.* Early application of airway pressure release ventilation may reduce the duration of mechanical ventilation in acute respiratory distress syndrome. Intensive Care Med 2017;43:1648-59.
11. Othman F, Alsagami N, Alharbi R, Almuammer Y, Alshahrani S, Ismaeil T. The efficacy of airway pressure release ventilation in acute respiratory distress syndrome adult patients: A meta-analysis of clinical trials. Ann Thorac Med 2021;16:245-52.
12. Lee LY, Cazier JB, Angelis V, Arnold R, Bisht V, Campton NA, *et al.* COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: A prospective cohort study. Lancet 2020;395:1919-26.
13. Kochanek M, Kochanek J, Böll B, Eichenauer DA, Beutel G, Bracht H, *et al.* Veno-venous extracorporeal membrane oxygenation (vv-ECMO) for severe respiratory failure in adult cancer patients: A retrospective multicenter analysis. Intensive Care Med 2022;48:332-42.