Case Report

Veno-venous extracorporeal membrane oxygenation and prone ventilation for therapeutic management of COVID-19

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Background: The efficacy and safety of the combined use of veno-venous extracorporeal membrane oxygenation (ECMO) and prone ventilation are currently not known for coronavirus disease 2019 (COVID-19).

Case presentation: We report two cases in which the combination of veno-venous ECMO and prone ventilation for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia were successfully carried out. Both patients had developed severe respiratory failure due to SARS-CoV-2 pneumonia, thus requiring veno-venous ECMO. Prone ventilation was also administered safely.

Conclusion: Oxygenation and lung compliance gradually improved during prone ventilation, and both patients were successfully extubated. For patients with severe SARS-CoV-2 pneumonia who require veno-venous ECMO, the use of prone ventilation could be beneficial, and should be considered.

Key words: Acute respiratory distress syndrome, COVID-19, extracorporeal membrane oxygenation, prone ventilation, SARS-CoV-2

INTRODUCTION

AT THE END of 2019, acute respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began to spread in Wuhan, China.[1] This respiratory illness, named coronavirus disease 2019 (COVID-19), gradually spread globally, and the WHO declared COVID-19 as a pandemic in March 2020.

Prone ventilation has been reported to reduce mortality among patients with moderate-to-severe acute respiratory distress syndrome (ARDS) when used for at least 12 h daily.[2] Furthermore, veno-venous extracorporeal membrane oxygenation (ECMO) is the standard treatment for severe ARDS.[3] However, the efficacy of the combination of veno-venous ECMO and prone ventilation is currently not known. Here, we report two cases in which the combination of veno-venous ECMO and prone ventilation was successful in treating SARS-CoV-2 pneumonia.

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CASE REPORT

Case 1

A 61-YEAR-OLD MAN with a history of hypertension, diabetes, and chronic atrial fibrillation was admitted to a local hospital 9 days after developing a fever and tested positive for the SARS-Co-V-2. Fourteen days after the onset of symptoms, his respiratory status deteriorated, and he was intubated. Two days later, he was referred to our hospital to receive veno-venous ECMO.

The patient's vital signs on admission to our hospital were as follows: respiratory rate, 8 breaths/min; oxygen saturation, 96% under positive end-expiratory pressure (PEEP) of 14 cmH_2O and fraction of inspiratory oxygen (FiO_2) of 1.0; heart rate, 129 b.p.m.; and blood pressure, 137/93 mmHg using noradrenaline 0.03 μg/kg/min and vasopressin 2 units/h. The arterial blood gas analysis results were: pH 7.158; PaO_2, 84.0; and $PaCO_2$, 64.5. Laboratory data showed elevation of N-terminal pro-brain natriuretic peptide

(3,199 pg/mL) and creatinine (1.47 mg/dL). Left ventricular ejection fraction was 45% by echocardiogram and the daily urine output was approximately 300 mL. Hypoxia due to heart failure or renal failure was also considered, but we determined that SARS-CoV-2 pneumonia was the leading cause of hypoxia. Therefore, we decided to treat with veno-venous ECMO and continuous renal replacement therapy. Veno-venous ECMO was administered through the right internal jugular vein for blood drainage with a 25 French gauge (Fr) heparin-coated cannula, and the right femoral vein for blood return with a 20 Fr heparin-coated cannula. The procedure was carried out safely, and the patient experienced no complications. Computed tomography (CT) showed bilateral ground-glass opacities and bilateral dorsal consolidation (Fig. 1). After hemodynamic stabilization, prone ventilation was implemented safely from day 2 to day 4 (prone position for 17 h, supine position for 7 h). The patient's PaO_2 and lung compliance were gradually improved within 72 h of prone ventilation: PaO_2 from 70.4 to 89.2 mmHg; and lung compliance from 25 mL/cmH_2O to 32 mL/cmH_2O. The use of ECMO was stopped on day 9 (Table 1). The patient was extubated on day 13.

Case 2

Emergency medical services found a 59-year-old woman collapsed at her home. She was lethargic, and her blood pressure could not be measured. On arrival at our hospital, her vital signs were as follows: consciousness, Glasgow Coma Scale of 14 (E4V4M6); respiratory rate, 24 breaths/min; oxygen saturation, 99% with reservoir face mask at 10 L/min oxygen; blood pressure, 84/71 mmHg; heart rate, 112 b.p.m.; and body temperature, 36.8°C. The patient's laboratory data were as follows: hematocrit, 47.4%; N-terminal pro-brain natriuretic peptide, 3,325 pg/mL; creatinine, 0.82 mg/dL. The CT imaging revealed bilateral ground-glass opacities, and the patient tested positive for SARS-CoV-2. The patient had a medical history of diabetes and depression.

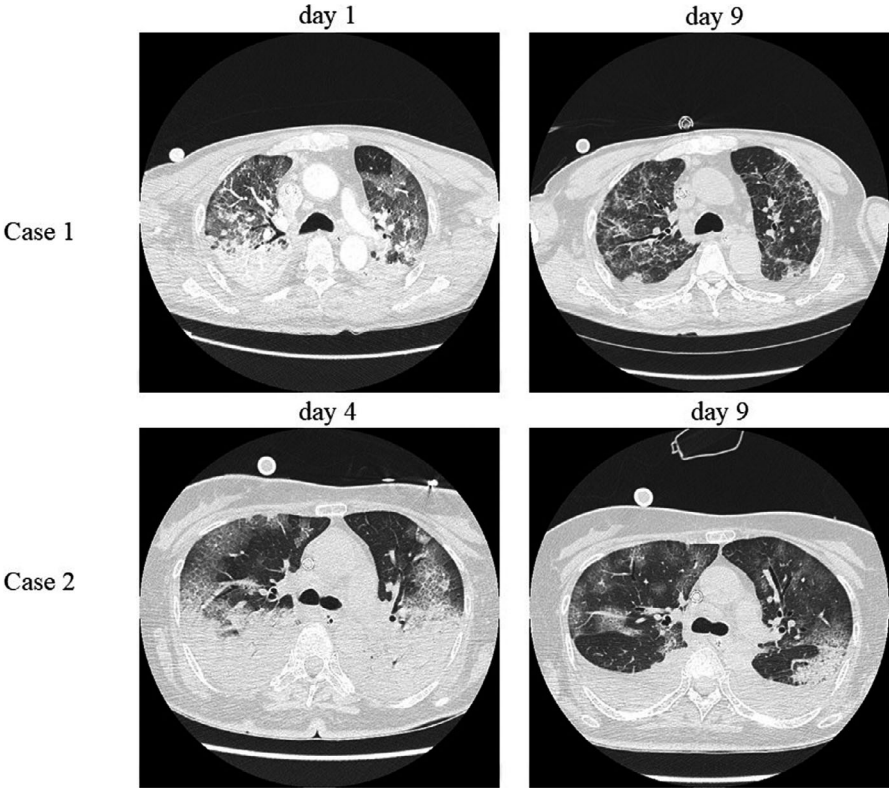

Fig. 1. Chest computed tomography scans of two patients with COVID-19 treated with veno-venous extracorporeal membrane oxygenation (ECMO) and prone ventilation. Case 1, day 1: Ground-glass opacities and bilateral dorsal consolidation were visible. Case 1, day 9: Bilateral dorsal consolidation improved. Case 2, day 4: Ground-glass opacities and bilateral dorsal consolidation were visible. Case 2, day 9: Bilateral dorsal consolidation improved and bilateral pleural effusion.

Table 1. Demographic data of two patients with COVID-19 treated with veno-venous extracorporeal membrane oxygenation (ECMO) and prone ventilation

	Case 1	Case 2
Age (years)	61	59
Sex	M	F
MV		
Total MV duration (days)	14	12
Pre-ECMO status		
P/F ratio (mmHg)	80	80.9
PEEP (cmH_2O)	14	16
Lung compliance (mL/cmH_2O)	30	22
MV duration (days)	1	2
ECMO		
ECMO duration (days)	9	6
Size of the drainage/infusion cannula (Fr)	25/20	25/20
Prone ventilation		
Duration (h)	17	17
Number of sessions	3	3
Complication	N	N
Medication		
Lopinavir/ritonavir	Y (day 1–14)	Y (day 3–15)
Favipiravir	Y (day 1–12)	Y (day 2–15)
Ciclesonide	Y (day 1–15)	Y (day 2–15)

F, female; M, male; MV, mechanical ventilation; N, no; PEEP, positive end-expiratory pressure; P/F, ratio of arterial oxygen partial pressure to the fractional inspired oxygen; Y, yes.

The day after admission, the patient's respiratory status had deteriorated, and she was intubated. The arterial blood gas analysis on day 4 was as follows: pH, 7.346; PaO_2, 64.7; and $PaCO_2$, 50.7 (FiO_2 0.8, PEEP 16 cmH_2O). The ratio of arterial oxygen partial pressure to the fractional inspired oxygen was at 80.9 and continued to decrease gradually. The patient's blood pressure was 91/68 mmHg using noradrenaline 0.1 μg/kg/min and vasopressin 2 units/h. Left ventricular ejection fraction was 50% by echocardiogram and the daily urine output was approximately 750 mL. We decided to treat the patient with ECMO. The veno-venous ECMO was established through the right internal jugular vein for blood drainage with a 25 Fr heparin-coated cannula, and the right femoral vein for blood return with a 20 Fr heparin-coated cannula. The procedure was carried out safely, and no complications occurred. The CT imaging showed a deteriorating bilateral dorsal consolidation (Fig. 1). Prone ventilation was administered safely from day 5 to day 7. The patient's PaO_2 and lung compliance were gradually improved within 72 h of prone ventilation: PaO_2 from 59.5 to 76.8 mmHg and lung compliance from 20 to 40 mL/cmH_2O. The veno-venous ECMO treatment was stopped on day 9 (Table 1). The patient was extubated on day 13.

DISCUSSION

THE GUIDELINES FOR the management of COVID-19 in mechanically ventilated adult patients with refractory hypoxemia by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine suggest the use of veno-venous ECMO. The guidelines also state optimizing the ventilation and using prone ventilation for moderate-to-severe ARDS.[4] There is no recommendation for a therapeutic combination of veno-venous ECMO and prone ventilation. Our cases show that prone ventilation is possible even when using veno-venous ECMO. The Advanced Critical Care and Emergency Center at Sapporo Medical University is a referral center for adult patients requiring ECMO in Hokkaido, Japan. The center has six beds in the intensive care unit and 22 full-time doctors. We treat approximately 10 cases of respiratory ECMO annually.

In a report of radiological date from 81 patients with COVID-19 pneumonia, CT images showed that COVID-19 pneumonia was manifested with chest abnormalities, even in asymptomatic patients, with a rapid evolution from focal unilateral to diffuse bilateral ground-glass opacities, that progressed to or coexisted with consolidations within 1–3 weeks.[5] Therefore, prone ventilation is likely to be effective in gradually decreasing the ventral alveolar distension and dorsal alveolar collapse in COVID-19 cases. In our cases, CT images after veno-venous ECMO placement showed bilateral dorsal consolidation. These findings suggest that prone ventilation could be beneficial.

There are two main safety concerns related to the use of combined veno-venous ECMO and prone ventilation for COVID-19 treatment. The first concern is tube displacement. This problem has been discussed both in veno-venous ECMO combination therapy and prone ventilation. As the blood drainage cannula and blood return cannula of ECMO have a large diameter, in the event of displacement, the risk of a fatal bleeding complication increases. Additionally, displacement could also be fatal due to the use of a discontinued ECMO machine. However, the application of prone ventilation during veno-venous ECMO has been shown to be a safe and reliable technique when undertaken in an ECMO center by trained staff and following standard procedures.[6] The second concern is the spread of SARS-CoV-2 as a result of an accidental disconnection of the intubation tube from the ventilator. There is a possibility that the virus persists through aerosol for a substantially long period,[7]

rendering the medical personnel at risk of infection. Therefore, the disconnection of the intubation tube from the ventilator must be minimized. In order to address these concerns, we assigned qualified personnel to manage the connection between the intubation tube and the ventilator and the blood drainage and return cannulas in veno-venous ECMO when patients were shifted from the spine to prone position. There was no tube displacement in either case, and the risk of spreading SARS-COV-2 was minimized. We have used air-fluidized bed when patients were shifted from the spine to prone position. By using air-fluidized bed, the shift from the spine to prone position can be carried out by four medical staff.

In conclusion, the combination therapy of veno-venous ECMO and prone ventilation is possible in patients with SARS-CoV-2 pneumonia without any complication. For severe SARS-CoV-2 pneumonia requiring ECMO, prone ventilation could be useful, as evidenced by radiographic data. Prone ventilation should be considered for use by medical personnel.

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DISCLOSURE

Approval of the research protocol: Formal ethical approval from the University Research Ethics Board was not required for the completion of this study.

Informed consent: Written informed consent for publication of this case report was obtained from the patients.
Registry and registration no. of the study: N/A.
Animal studies: N/A.
Conflict of interest: None.

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