CASE REPORT

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Successful Use of Prone Positioning in Severe Acute Respiratory Distress Syndrome After 44 Days of Veno-Venous Extracorporeal Membrane Oxygenation: A Case Report

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ABSTRACT

Introduction: Prone positioning is conventionally done early in patients with acute respiratory distress syndrome (ARDS), regardless of concurrent treatment with veno-venous extracorporeal membrane oxygenation (V-V ECMO). Its benefits in later phase of disease are less studied. We report a patient with severe ARDS who underwent prone positioning after 44 days of treatment with V-V ECMO.

Case Presentation: A 49-year-old man with severe ARDS following SARS-CoV2 infection was placed under V-V ECMO support as rescue for refractory hypoxemia despite mechanically ventilation with muscle relaxants and prone positioning. His illness was complicated with multiple episodes of hospital-acquired pneumonia and gastrointestinal bleeding requiring transfusions, resulting in failure in weaning ECMO therapy. He underwent five consecutive prone positioning sessions starting from day 44 of ECMO support, which results in improvement in gas exchange and lung mechanics. After 77 days, he could be liberated from the ECMO and continued to improve after his hospital discharge.

Conclusion: Prone positioning may serve as a potential treatment in patients receiving V-V ECMO, even in those who have been supported for longer period.

Keywords: acute respiratory distress syndrome$_1$, case report$_2$, extracorporeal membrane oxygenation$_3$, prone position$_4$, SARS coronavirus 2$_5$.

Introduction

Prone positioning is a widely used treatment in patients with moderate to severe acute respiratory distress syndrome (ARDS) (1). It is recommended to be performed early in the course of the disease, as the patients are more likely to respond favorably to the procedure (2). In ARDS patients who are concurrently treated with veno-venous extracorporeal membrane oxygenation (V-V ECMO), prone positioning has also been used in those who have refractory hypoxemia, and those who failed ECMO weaning attempts (3, 4). Previous reports mostly concern treatments performed early after the ECMO use, and limited evidence exists for the benefits in patients who are late in their ECMO runs. Here we report successful use of prone positioning in a 49-year-old man with severe ARDS after 44 days of V-V ECMO treatment.

Case Description

A 49-year-old man with non-insulin dependent diabetes mellitus and obesity (height 170 cm, body mass index 38.7 kg/m^2) presented to another hospital with non-productive cough. He had mild hypoxemia which was correctable with low-flow oxygen therapy. The chest radiograph was notable for faint bilateral ground-glass opacities in the middle and lower lung fields (Figure 1A). His nasal swab was positive for SARS-CoV2. His symptoms initially improved after treated with oral favipiravir and intravenous dexamethasone. On day 9 of hospital admission, he developed shortness of breath along with progressive hypoxemia. He was intubated and transferred to our hospital after 11 days of admission.

Upon admission to our unit, he was markedly tachypneic and hypoxemic. The pulse oximetry (SpO_2) was 84-86% despite mechanically ventilated with fraction of inspired oxygen (FiO_2) of 1.0. The initial chest radiograph at our hospital showed ground-glass opacities bilaterally at lung bases (Figure 1B). His sputum and, later, blood culture were positive for multidrug-resistant *Pseudomonas aeruginosa*, for which he was given intravenous colistin. Dexamethasone was also discontinued after a total of 10-day course, and changed to 100-200 mg of intravenous hydrocortisone daily, which was continued throughout his illness. He was diagnosed with severe ARDS and was deeply sedated, paralyzed and immediately placed in prone position. The ratio of arterial oxygen partial pressure to fraction of inspired oxygen (PaO_2/FiO_2) increased minimally from 61.2 to 115 after the first prone positioning, so V-V ECMO was initiated. A 26-French drainage cannula was placed to the right femoral vein and a 21-french return cannula to the right internal jugular vein (Figure 1C). After initial ECMO flow of 4.0 liter per minute (LPM), he was ventilated with tidal volume 260 ml (4 ml/kg PBW), respiratory rate 10 breaths per minute and positive end-expiratory pressure 12 cmH_2O. His lung mechanics and chest radiographs initially improved thereafter.

However, his hospital course was complicated with recurrent episodes of hospital-acquired pneumonia with septic shock and massive lower gastrointestinal bleeding due to cytomegaloviral colitis. He was treated with prolonged courses of antibiotics, together with multiple colonoscopies and blood transfusions. During the ECMO run, his SpO_2 could be consistently maintained above 90% with V-V ECMO flow around 3.2-3.8 LPM. However, the PaO_2/FiO_2 were consistently around 120-170 mmHg despite the support and attempts to wean V-V ECMO were unsuccessful due to severe hypoxemia. Moreover, when tidal volume was increased to 6 ml/kg PBW, the driving pressure were extremely high at 28 cmH_2O. The computerized tomography of his chest at this time showed diffuse ground-glass opacities and consolidation with minimal traction bronchiectasis, along with stable pneumomediastinum (Figure 2). The decision to perform another prone positioning was made on day 44 of ECMO use, as the bleeding has been successfully stopped and he was hemodynamically stable for several days. Upon placing the patient into prone position, the ECMO flow dropped precipitously from 3.4 to 1.7 LPM with frequent drainage catheter chattering. Higher chest and hip supports were place to raise the abdomen above the mattress, which restored his ECMO flow to around 2.3-2.7 LPM. Despite lower ECMO flow, his oxygenation stabilized without the need to increase ventilatory support throughout the prone session. He underwent five more 16-hour sessions of prone positioning, which resulted in improvement in the lung mechanics and chest radiographs (Figure 1D-1E, and Table 1). Muscle relaxants were discontinued after 6 sessions of prone positioning and ECMO was explanted after 77 days. He underwent intensive rehabilitation and was then discharged from the hospital after 147 days, with home ventilator therapy.

At 1 year after ECMO decannulation, his chest radiograph was remarkable for mild fibrosis which showed no sign of progression (Figure 1F). Home ventilator treatment could be safely discontinued. He could tolerate daily physical activities including walking without the need for oxygen therapy. He was also able to return to his office work as before the illness. Home oxygen therapy via low-flow oxygen cannula was intermittently used for more strenuous activities.

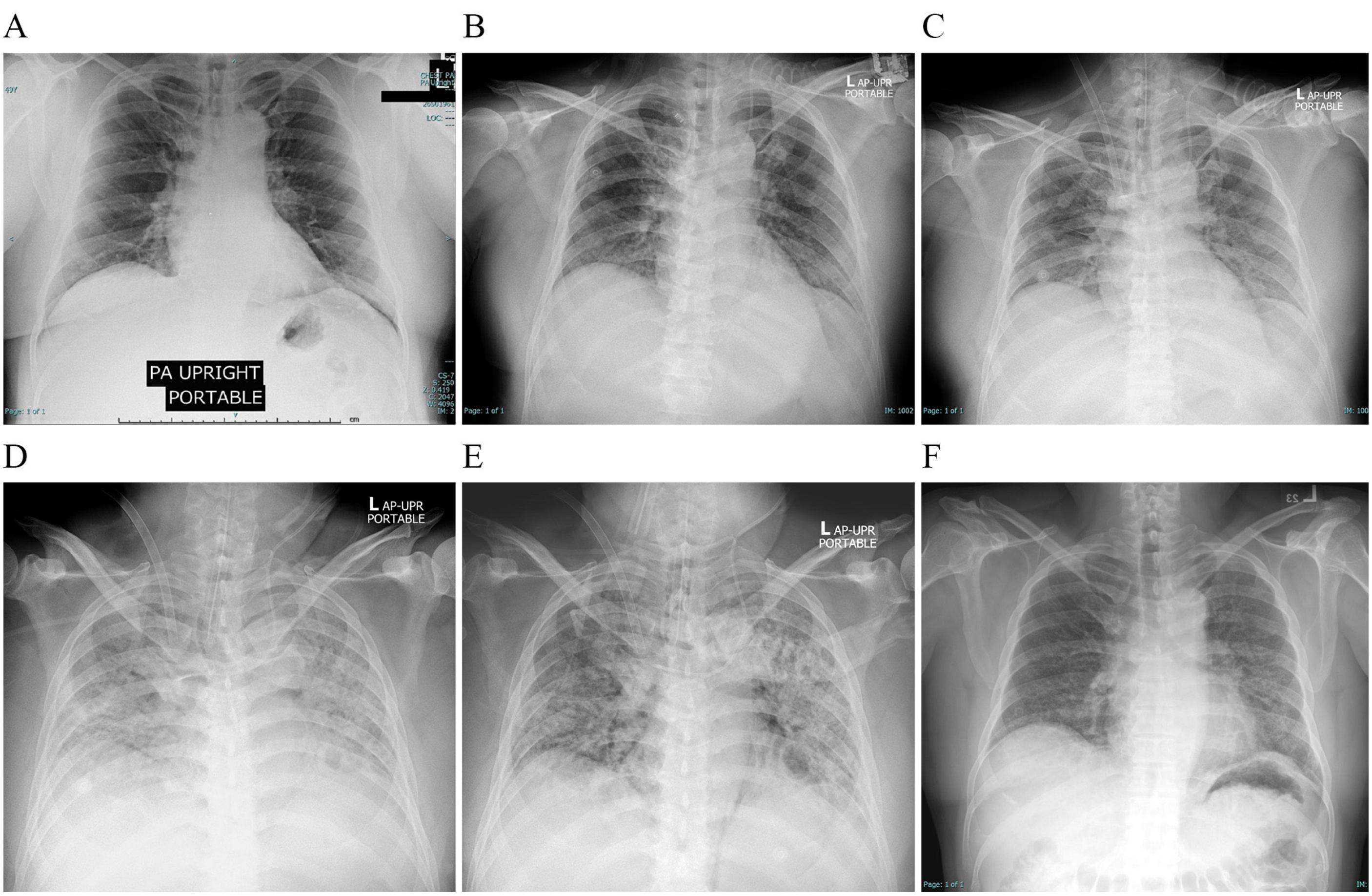

Figure 1. Chest radiographs of the patient **(A)** upon admission to another hospital at the onset of his symptoms; **(B)** upon admission to our intensive care unit; **(C)** after cannulation of V-V ECMO; **(D)** after 44 days of V-V ECMO, before prone positioning; **(E)** after 51 days of V-V ECMO, after five sessions of prone positioning; **(F)** at the follow-up visit one year after hospital discharge

Table 1. Mechanical ventilation, ECMO settings and arterial blood gas before and after prone positioning

Parameter	Prior to prone positioning	4 hour after 1st prone positioning	After 5 sessions of prone positioning
Mechanical ventilation and lung mechanics			
Mode	PC-AC	PC-AC	PC-AC
Inspire pressure, cmH_2O	24	24	22
Respiratory rate, min^{-1}	16	16	16
Tidal volume, mL	240	410	400
PEEP, cmH_2O	8	8	8
FiO_2	0.6	0.6	0.45
Respiratory system compliance, ml/cmH_2O	14.7	26.2	27.9
ECMO settings			
Pump speed, RPM	4300	4200	4200
ECMO flow, LPM	3.4	2.3	2.6
Sweep gas flow, LPM	6.0	6.0	5.0
FiO_2	1.0	1.0	1.0
Arterial blood gas			
pH	7.36	7.40	7.38
PaO_2/FiO_2	111	141	264
PaO_2, mmHg	66.6	84.8	119
$PaCO_2$, mmHg	51.4	35.8	50
SaO_2, %	90	93	98

Discussion

Prone positioning in patients with acute respiratory distress syndrome

Prone positioning is recommended as a standard treatment in patients with ARDS who have PaO_2/FiO_2 less than 150 mmHg (1). This is consistent with the inclusion criteria of the PROSEVA study which demonstrated the reduction in 28-day mortality among those underwent prone positioning (5). Since the study specifically enrolled patients who were ventilated for less than 36 hours, most recommendations also specify that prone positioning should be done early in the course of ARDS (6). However, the optimal timing of prone positioning is not well-established, and satisfactory response in patients who are ventilated for a longer period, as is the case of our patient, could not be ruled out.

Theoretically, the lungs in the early phase of ARDS are more likely to respond favorably to prone positioning (6). In the first few days, the lungs are marked by diffuse exudation due to disrupted alveolar membrane (7). The resulting increased lung weight causes extensive collapse of the lungs in dependent part – which is the dorsal part in supine position (8). By placing the patient into prone position, the local pleural pressure of these dorsal part is reduced, leading to increase in transpulmonary pressure and lung recruitment. Consequently, gas exchange and lung mechanics improve. In contrast, as the lungs progressively develop fibrosis, patients later in the course of ARDS become resistant to recruitment by prone positioning (6).

In patients with COVID-19 pneumonia and ARDS, a recent study reported greater improvement in oxygenation with patients who underwent prone positioning within 24 hours after intubation, along with better survival than those who were treated later (9). In contrast, another study showed that in patients with COVID-19 pneumonia who were ventilated for 3 weeks, prone positioning resulted in even worse oxygenation (10). The CT scan analyses of these patients showed consolidation predominating in the dorsal parts of the lungs. The lesions were not amendable with positive pressure, resulting in limited dorsal lung recruitment in prone position (10).

These data support the idea that prone positioning should be performed early, and later use may not be beneficial or even harmful to the patients. To our knowledge, successful use of prone positioning in patients after several weeks of mechanical ventilation, in addition to V-V ECMO use, has not been reported before.

Prone positioning in patients undergoing veno-venous extracorporeal membrane oxygenation

Veno-venous ECMO is a life support currently provided to patients with ARDS who are severely hypoxemic or who cannot be safely ventilated with other less invasive therapies (1). The treatment is also widely utilized in patients who suffered ARDS after SARS-CoV2 infection (11). As patients who are treated with V-V ECMO are likely severely hypoxemic, prone positioning could also be used to improve gas exchange and outcome in these patients (3, 4).

Recently, two propensity-score matched retrospective cohorts from ECMO centers with conflicting results regarding the benefits of prone positioning in patients receiving V-V ECMO were published. One was from a single center registry where 24.1% of ECMO patients were placed in prone (12). Analysis of resultant 38 score-matched pairs showed no difference in successful ECMO weaning (47.4 vs 44.7%, p=0.818) and hospital survival (36.8 vs 36.8%, p=1.0). On the other hand, in another multicenter retrospective cohort study, 66 pairs were analyzed and lower hospital mortality was demonstrated in those receiving prone positioning (30.3 vs 52.5%, p=0.0241) (13).

Although results were conflicting regarding the clinical benefits, both cohorts performed prone positioning early after starting V-V ECMO support; 1.7 (interquartile range [IQR], 0.5-5.0) days in the former cohort (12) and 4 (IQR, 2-7) days in the latter (13). Remarkably, in the first study, early use of prone positioning within 17 hours after ECMO was also an independent predictor of survival (12).

The late use of prone positioning – after weeks of V-V ECMO use – has not been comprehensively reported. The EOLIA study, though failed to demonstrate mortality reduction with early V-V ECMO in very severe ARDS, was notable in that 54% of patients in ECMO group received prone positioning during their ECMO runs (14, 15). As one of the indications to perform prone positioning was failure to wean ECMO support after 10 days, some of these patients would have undergone prone positioning later than those reported in the aforementioned cohorts. Unfortunately, the outcome of this subgroup of patients were not provided.

To conclude, similarly to those not receiving V-V ECMO, data concerning the optimal timing of prone positioning in patients with ARDS treated with V-V ECMO use are limited to the early use within days after the support. We therefore report this case to illustrate that prone positioning could also be performed later with acceptable outcomes.

Successful use of prone positioning in our patient

The patient in our report underwent the first prone position in the same day of intubation, with unsatisfactory results. He was subsequently placed on V-V ECMO as the treatment for life-threatening hypoxemia. He later developed hospital-acquired pneumonia and lower gastrointestinal bleeding, which were associated with frequent decline in the native lung function and precluded weaning of V-V ECMO. Another prone positioning was done on day 44 of V-V ECMO use (that is, on day 45 of mechanical ventilation), which was rather late in the ECMO run even in our center experience (16). Nevertheless, the procedure resulted in substantial improvement in blood gases and lung mechanics. Chest radiographs also demonstrated better aeration to most parts of the lungs. The patient continued to improve and could eventually be liberated from the V-V ECMO support.

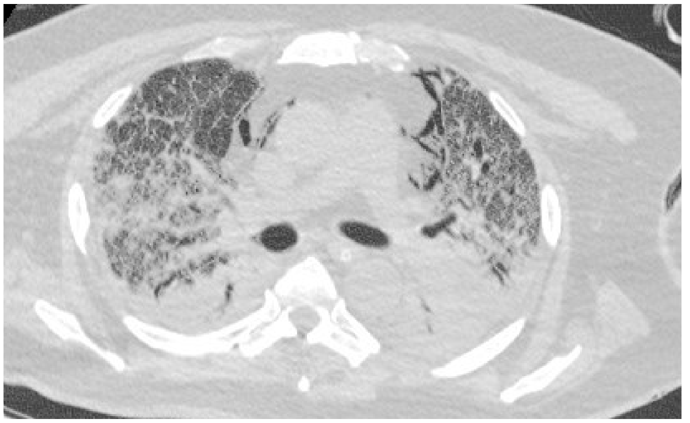

Figure 2. Computerized chest tomography after 40 days of V-V ECMO

This unusually favorable response could be explained by multiple episodes of lung injuries the patient sustained. We hypothesized that because his in-hospital complications – namely, infection and transfusion-related lung injury – were staggered, different parts of his lungs were injured at different time in the course of ICU admission. Hence, parts where the insults were recent may still be in the exudative phase, rather than fibrotic, at the time of prone positioning. In other words, even after several weeks of mechanical ventilation and V-V ECMO use, recent insults causing further lung injury may still be amendable with prone positioning. This was also corroborated by his computerized tomography which showed active ground-glass opacities bilaterally, with minimal degree of fibrosis (Figure 2). Therefore, the response to prone positioning in this patient was satisfactory.

Conclusion

Prone positioning serves as a potential treatment in patients receiving V-V ECMO, even in those who have been treated with ECMO for longer periods. Hence, timing should not be solely used as contraindication of prone positioning in these patients.

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AUTHOR CONTRIBUTIONS:

Concept: ST; **Supervision:** ST; **Materials:** SB, NW; **Data Collection and/or Processing:** SB, NW; **Analysis and/or Interpretation**: SB, NW, ST; **Literature Search:** SB, NW; **Writing Manuscript**: SB, NW; **Critical Review:** ST.

Informed Consent: The patient has provided written informed consent to share his medical data as an anonymized case report. The consent was also cosigned by his wife.

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors have no conflicts of interest to declare.

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