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Extracorporeal Membrane Oxygenation in Severe Acute Respiratory Distress Syndrome: Possible Late Indication for Coronavirus Disease 2019?

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Background: There is now substantial evidence to support venovenous extracorporeal membrane oxygenation efficacy and safety for patients with severe acute respiratory distress syndrome. However, recent guidelines recommend against the initiation of extracorporeal membrane oxygenation in patients with mechanical ventilation for coronavirus disease 2019 severe acute respiratory distress syndrome for greater than 7–10 days.

Case Summary: We report the case of a patient with coronavirus disease 2019 severe acute respiratory distress syndrome with successful late venovenous extracorporeal membrane oxygenation initiation after 20 days of mechanical ventilation. Respiratory compliance, arterial blood gases, and radiological lesions improved progressively under venovenous extracorporeal membrane oxygenation and ultraprotective ventilation. The patient was discharged from ICU.

Conclusions: As coronavirus disease 2019 is a new and incompletely understood entity, we believe that late extracorporeal membrane oxygenation may be considered in selected patients as a bridge to recovery. Further prospective studies are, however, needed.

Key Words: acute respiratory distress syndrome; coronavirus disease 2019; extracorporeal membrane oxygenation; severe acute respiratory syndrome coronavirus 2

Venovenous extracorporeal membrane oxygenation (VV-ECMO) can support gas exchange and there is now substantial evidence to support its efficacy and safety for patients with severe acute respiratory distress syndrome (ARDS) (1, 2). Recent reports have suggested that ECMO might be an effective salvage treatment for patients with coronavirus disease 2019 (COVID-19) severe acute respiratory distress syndrome (ARDS), but data are conflicting (3–5). In addition, the timing of ECMO initiation is still debated but early initiation is associated with improved outcomes in non-COVID-19 severe ARDS (6). In line with this, recent guidelines for pandemic ECMO usage recommend against the initiation of ECMO in patients with mechanical ventilation for COVID-19 severe ARDS for greater than 7–10 days (7, 8).

We, therefore, aim to report a case of COVID-19 severe ARDS with successful late VV-ECMO initiation.

CASE SUMMARY

The 54 year-old male had a past medical history of acute myeloid leukemia for which he received allo-hematopoietic stem cell transplantation after conditioning regimen including busulfan and fludarabine in August 2019. A treatment including steroids at 5 mg per day and tacrolimus was continued for cutaneous graft-versus-host disease.

He presented to the emergency department in March 2020 with asthenia, fever, and cough for 6 days. Vital signs on presentation were significant for an elevated temperature (39°C), heart rate 100/min, blood pressure 123/65, and 93% oxygen saturation on 4 L of oxygen. Physical examination was notable for bibasilar crackles

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but otherwise unremarkable. Initial laboratory work demonstrated lymphopenia and high fibrinogen and C-reactive protein levels (**Fig. 1**). CT chest demonstrated diffuse ground-glass opacities in the periphery of both lungs and was suggestive of COVID-19 (**Fig. 2**). Furthermore, a nasopharyngeal swab for severe acute respiratory syndrome coronavirus 2 was found positive, confirming COVID-19.

He progressively worsened and was admitted to the ICU department 6 days after hospital admission. A treatment including hydroxychloroquine, azithromycin, and tazobactam-piperacillin was given for 5 days. In addition, invasive mechanical ventilation and neuromuscular blockers were started. No nosocomial infection was identified.

Despite optimal ARDS therapy, including eight prone-positioning sessions, respiratory gas exchange and respiratory compliance progressively worsened. Steroids at 1 mg/kg per day were, therefore, initiated. After 20 days of invasive mechanical ventilation, VV-ECMO was required because of arterial blood pH less than 7.24 with a $Paco_2$ at 69 mm Hg for greater than 6 hours (with respiratory rate increased to 35/min), whereas Pplat was in the 30-cm H_2O range (1, 9). In addition, the patient experienced severe hypoxemia (Pao_2/Fio_2 at 98 mm Hg) and very low respiratory system compliance (17.5 mL/cm H_2O). VV-ECMO was performed percutaneously at bedside by cannulating the right femoral vein for the drainage of the blood and the right internal jugular vein for venous return. Placement was facilitated by using transesophageal echocardiography. CardioHelp device with HLS Set Advanced 5.0 circuit was used (Maquet Getinge, Hirrlingen, Germany). Anticoagulation was achieved with unfractionated heparin that was adjusted to a target antiXa activity between 0.3 and 0.5 international units per milliliter. In addition to ECMO, ultraprotective ventilation (tidal volume at 3 mL/kg) was initiated.

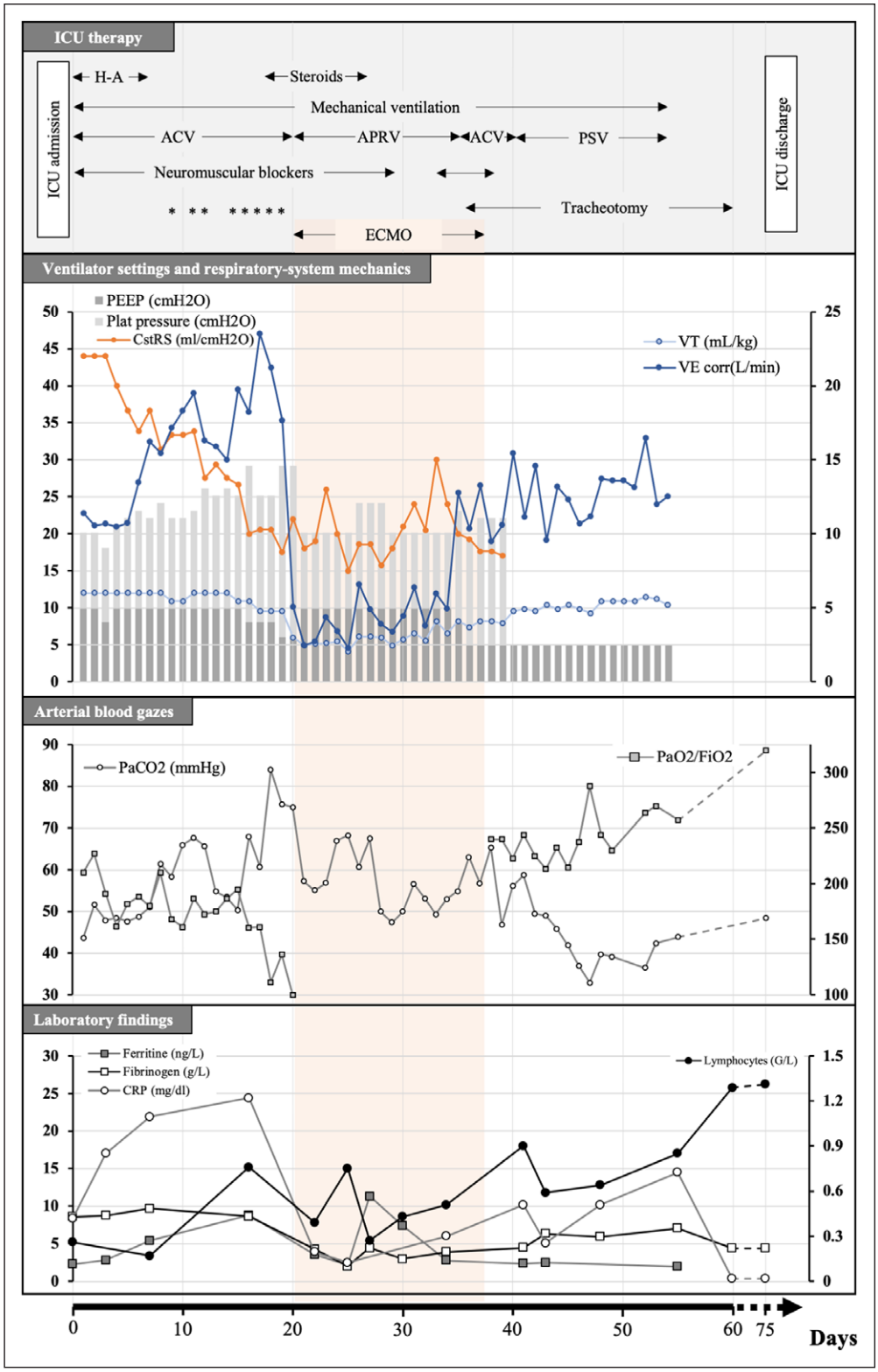

Figure 1. Time-course of respiratory system mechanics, ventilator setting, blood gazes, and laboratory findings during ICU hospitalization. Day 1 represents the onset of COVID-19 symptoms. *Asterisk* indicates prone positioning session. ACV = assisted controlled ventilation, APRV = airway pressure release ventilation, CRP = C-reactive protein, CstRS = static compliance of the respiratory system, ECMO = extracorporeal membrane oxygenation, H-A = hydroxychloroquine + azythromycine, PEEP = positive end-expiratory pressure, PSV = pressure support ventilation.

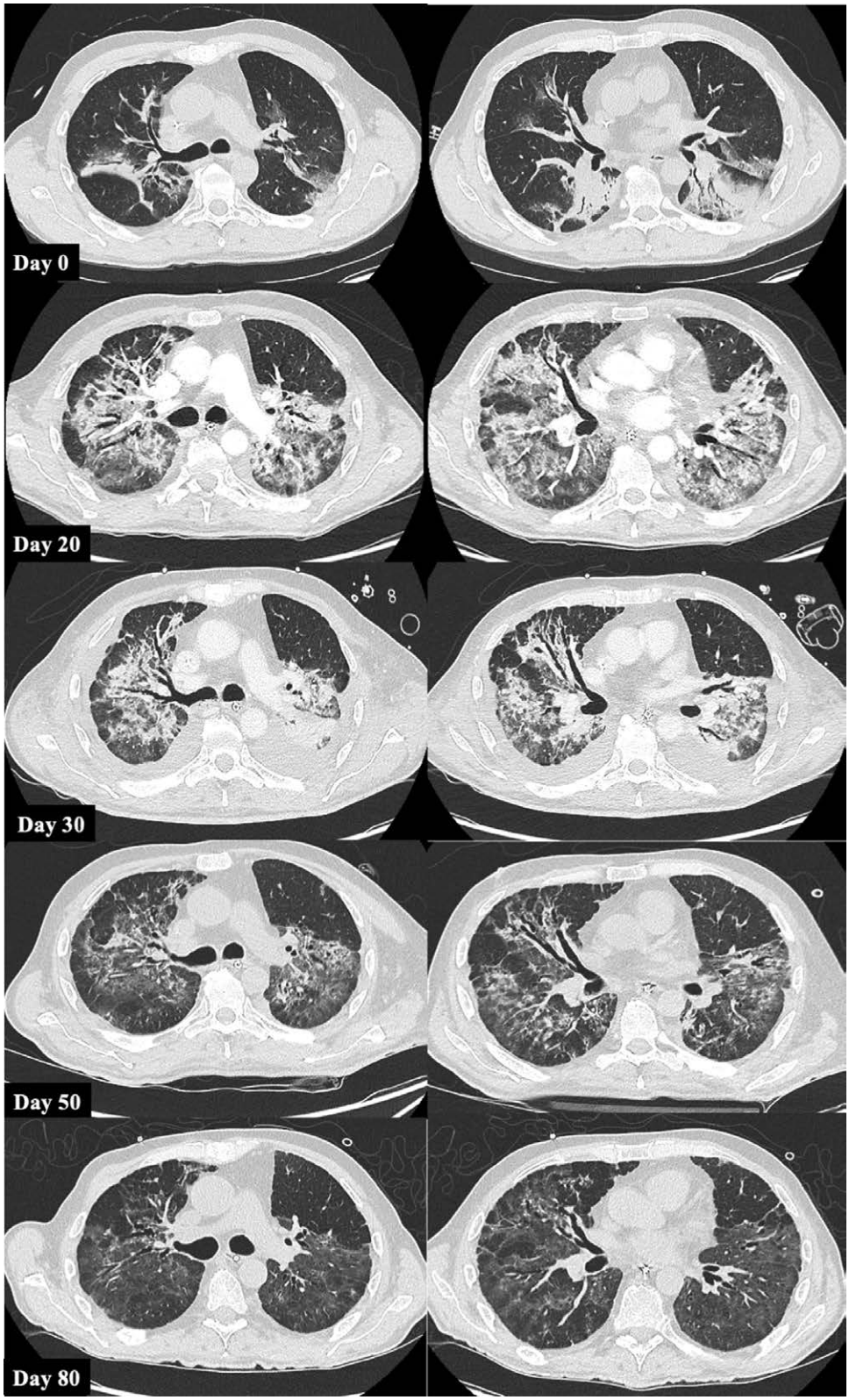

Figure 2. Time-course of chest CT from ICU admission to hospital discharge.

Respiratory compliance and arterial blood gases improved progressively under VV-ECMO and ultraprotective ventilation (Fig. 1). The patient was tracheotomized and was weaned from VV-ECMO after 17 days of ECMO. No complication of ECMO was noticed (infection, severe hemorrhagic complications, cannula thrombosis, and intravascular hemolysis) except need for red cell transfusion (2 units). In addition, mechanical ventilation was stopped at day 54 and tracheotomy was removed at day 60. The patient was discharged from ICU at day 60 and from hospital at day 90 after post-ICU rehabilitation (performance status 1, no need for oxygen supply).

Regarding radiological evolution, ground glass opacities progressively resolved (Fig. 2) but slight fibrotic appeared over time. In addition, quantitative radiological assessment showed progressive pulmonary improvement (**Fig. 3**).

DISCUSSION

Recent studies have reported that mortality in patients requiring ECMO for COVID-19 severe ARDS ranged from 40% to 60% (3–5, 10, 11). This mortality is somewhat higher than that in non-COVID-19 ARDS patients including bacterial pneumonia and severe influenza A (H1N1) ARDS (1, 12, 13). This higher mortality rate should, however, be interpreted with caution as large studies are lacking.

In reported cases of COVID-19, the time between the onset of symptoms and cannulation was of approximately 10–17 days (3, 10, 14). In addition, all reported cases of COVID-19 had a duration from invasive mechanical ventilation to ECMO of less than 7 days (3, 10, 14). Furthermore, Yang et al (3) suggested that in the setting of COVID-19, earlier initiation of ECMO (evaluated by the length of mechanical ventilation

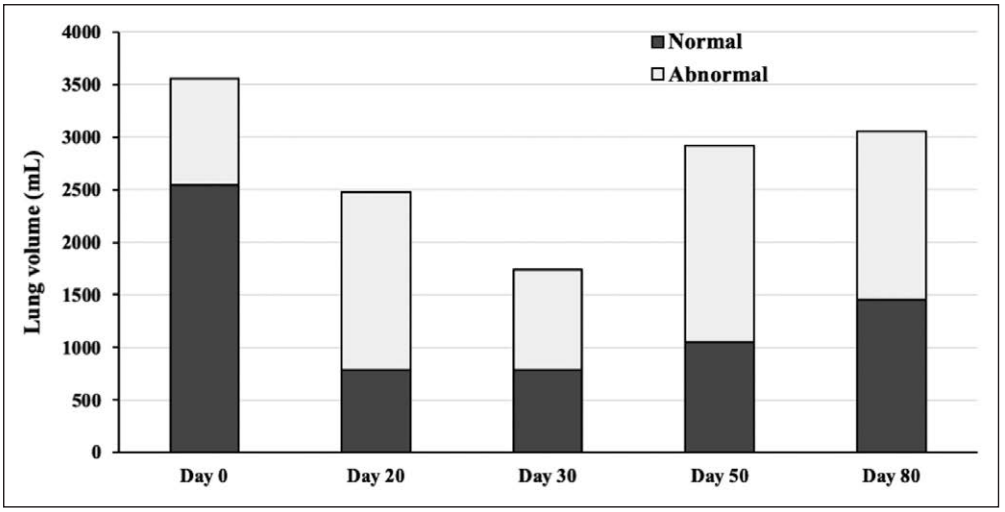

Figure 3. Quantitative assessment of chest CT. Pulmonary analysis was done on a dedicated spectral imaging postprocessing software (Thoracic VCAR, Advantage Workstation platform, Version 3.2 Ext 3.3, GE Healthcare, Milwaukee, WI). Initial post-treatment was lung segmentation, excluding small pulmonary vessels, and airways. The lung parenchyma was divided into two volumes thanks to maps based on HU values as follows: normal = (−1024 HU; −730 HU) and hyperdense lung (i.e., abnormal) = (−729 HU; +1024 HU).

before ECMO initiation) might be associated with improved outcomes. In that view, our case is of interest, as it highlights that late initiation of ECMO may be considered in severe COVID-19. Careful patient selection for late initiation of ECMO is needed, because patient age and comorbidities appear to influence outcomes in critically ill patients with COVID-19. Patients with younger age (< 65 years old) and few comorbidities might be potential candidates for late ECMO implantation.

When combined with lower tidal volumes and airway pressures (i.e., ultraprotective ventilation), ECMO may help to minimize ventilator-induced lung injury, which is a key contributor to the morbidity and mortality of the ARDS (2). We, therefore, postulate that support with VV-ECMO and ultraprotective mechanical ventilation provided time for our patient to enhance lung recovery.

In addition, recent data have suggested that ultraprotective ventilation may reduce biotrauma in patients with non-COVID 19 ARDS and in experimental models (15, 16). Furthermore, as cytokine release syndrome appears to be an emerging component of severe COVID-19, some authors have speculated that targeting hyperinflammation in severe COVID-19 combined with VV-ECMO might be considered (17). In line with this, our patient might have benefit from both steroids by abrogating hyperinflammation and VV-ECMO to enhance lung recovery.

Finally, it is still unclear whether pulmonary fibrosis associated with COVID-19 is reversible (18). Therefore, VV ECMO could be seen as a bridge to recovery by giving time for pulmonary improvement.

CONCLUSIONS

As COVID-19 is a new and incompletely understood entity, we believe that late ECMO may be considered in selected patients. The applicability of our single-patient experience must be, however, cautioned. In addition, as many resources may be limited in the setting of COVID-19 pandemic, strict adherence to standard intensive care management practices and infection control protocols should be among the primary goals of care. Further prospective studies, such as the extracorporeal membrane oxygenation for 2019 novel coronavirus acute respiratory disease study, are needed.

Informed consent has been obtained from the patient.

The authors have disclosed that they do not have any potential conflicts of interest.

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