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Case Reports

Recovery of Lung Function After 149 Days on Extracorporeal Membrane Oxygenation for COVID-19

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Abstract

This report highlights survival and the patient's perspective after prolonged venovenous extracorporeal membrane oxygenation (ECMO) for COVID-19–related respiratory failure.

A 36-year-old man with COVID-19 presented with fever, anosmia, and hypoxia. After respiratory deterioration necessitating intubation and lung-protective ventilation, he was referred for ECMO. After 3 days of conventional venovenous ECMO, he required multiple creative cannulation configurations. Adequate sedation and recurrent bradycardia were persistent challenges. After 149 consecutive days of ECMO, he recovered native lung function and was weaned from mechanical ventilation.

This represents the longest-duration ECMO support in a survivor of COVID-19 yet reported. Necessary strategies included unconventional cannulation and flexible anticoagulation.

Keywords: Case reports; extracorporeal membrane oxygenation; COVID-19; severe acute respiratory syndrome; survival

Case Report

The emergence of COVID-19–related acute respiratory distress syndrome (ARDS) highlighted the importance of venovenous extracorporeal membrane oxygenation (VV-ECMO) as rescue therapy for refractory hypoxemia. According to the July 2023 update by the international Extracorporeal Life Support Organization Registry, ECMO has been used nearly 17,000 times in patients with COVID-19 worldwide.[1] Both ECMO duration and mortality on ECMO increased over the course of the pandemic.[2]

Various case reports and series have described the success of prolonged ECMO (ie, ECMO lasting longer than 14 days) for patients with COVID-19.[3] This report highlights a patient with COVID-19–related ARDS who underwent 149 consecutive days of VV-ECMO. This patient achieved native lung recovery, was successfully decannulated and weaned off mechanical ventilation, and was discharged home. The patient's perspective is included, with instructive lessons for health care teams. The patient provided informed consent to publish this case report.

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Presentation and Physical Examination

A 36-year-old, unvaccinated man (height, 178 cm; weight, 99 kg) was referred to a cardiovascular center for possible escalation to ECMO, having spent 5 days at another hospital and intensive care unit. At the center, transthoracic echocardiography showed depressed left ventricular systolic function (30%), normal right ventricular function, no valvular abnormalities, and estimated pulmonary artery systolic pressure of 20 mm Hg. Right and left cardiac catheterization with right ventricular biopsy were performed because of concerns for myocarditis (final pathology negative), and the patient was placed on VV-ECMO via left-femoral-to-left-axillary cannulation (25F inflow, 19F outflow) (Bio-Medicus NextGen; Medtronic), with simultaneous placement of a right femoral intra-aortic balloon pump. Intravenous immunoglobulin and inhaled epoprostenol were initiated.

Medical History

The patient had presented at an outside facility in July 2021 with fever, cough, dyspnea on exertion, and anosmia. His medical history included having asthma and being a former smoker. His nasopharyngeal polymerase chain reaction test was positive for SARS-CoV-2. The initial examination and chest radiograph were unremarkable, and he was discharged home. He returned 3 days later with worsening cough and hypoxemia; chest radiography showed extensive bilateral ground-glass opacities (Fig. 1A). He was admitted and started on methylprednisolone, remdesivir, tocilizumab, supplemental oxygen, and empiric antimicrobial therapy with azithromycin and ceftriaxone. His transthoracic echocardiography results showed normal biventricular function.

Deteriorating respiratory status necessitated the patient's transfer to the intensive care unit, use of high-flow nasal cannulation at 60 L/min with 100% fraction of inspired oxygen, noninvasive bilevel positive airway pressure ventilation, and intermittent awake proning. He was intubated on hospital day 4 and started on lung-protective ventilation with neuromuscular blockade and daily proning. His ARDS progression is shown in Figure 1 and Figure 2. He was transferred to this report's institution on day 5; his ECMO course is outlined in Figure 3.

Key Points

- In patients with COVID-19–related ARDS and single-organ system failure, very prolonged (>120 days) use of VV-ECMO is a viable option as a bridge to recovery or lung transplantation.
- In patients with COVID-19–related ARDS and near-absent native lung function, VV-ECMO may require unconventional cannulation strategies, including the use of multiple circuits, because of the higher flow required to address hypoxemia.
- Discussions regarding the futility of prolonged VV-ECMO support can be difficult, especially during periods of clinical stagnation. Open, transparent communication with the patient's loved ones, including regular progress reports, is paramount. Upon restoration of normal cognition, the patient's perspective should be sought to ensure that patient desires are respected and that the goals of care remain appropriate.

Abbreviations and Acronyms

ARDS	acute respiratory distress syndrome
ECMO	extracorporeal membrane oxygenation
VV	venovenous

Technique

Anticoagulation, Hemorrhage, Hemolysis

Throughout ECMO therapy (Fig. 4A), the circuit was closely monitored for clot burden, and laboratory results were evaluated for evidence of hemolysis. Anticoagulation treatment switched from unfractionated heparin (partial thromboplastin time goal, 60-80 seconds) to bivalirudin after thrombocytopenia developed. Despite a negative heparin antibody test, bivalirudin was continued during the entire ECMO run except for a 2-week pause because of recurrent tracheostomy-site bleeding.

ECMO Circuit Exchanges

On overall hospital day 8, repeat transthoracic echocardiography showed left ventricular functional recovery, and the balloon pump was removed. Refractory hypoxemia, however, persisted despite a flow rate of more than 4 L/min and neuromuscular blockade, and on hospital day 10, a second VV-ECMO circuit was added via cannulation of the right femoral vein (21F inflow) and the right axillary vein (17F outflow) (Bio-Medicus NextGen, Medtronic), with atrial septostomy to decrease pulmonary hypertension (pulmonary artery systolic pressure of 45 mm Hg). Satisfactory oxygenation was achieved by increasing the total VV-VV-ECMO flow to more than 6 L/min; tracheostomy (8-0 Shiley XLT; Medtronic) was performed on day 14 (Fig. 4B).

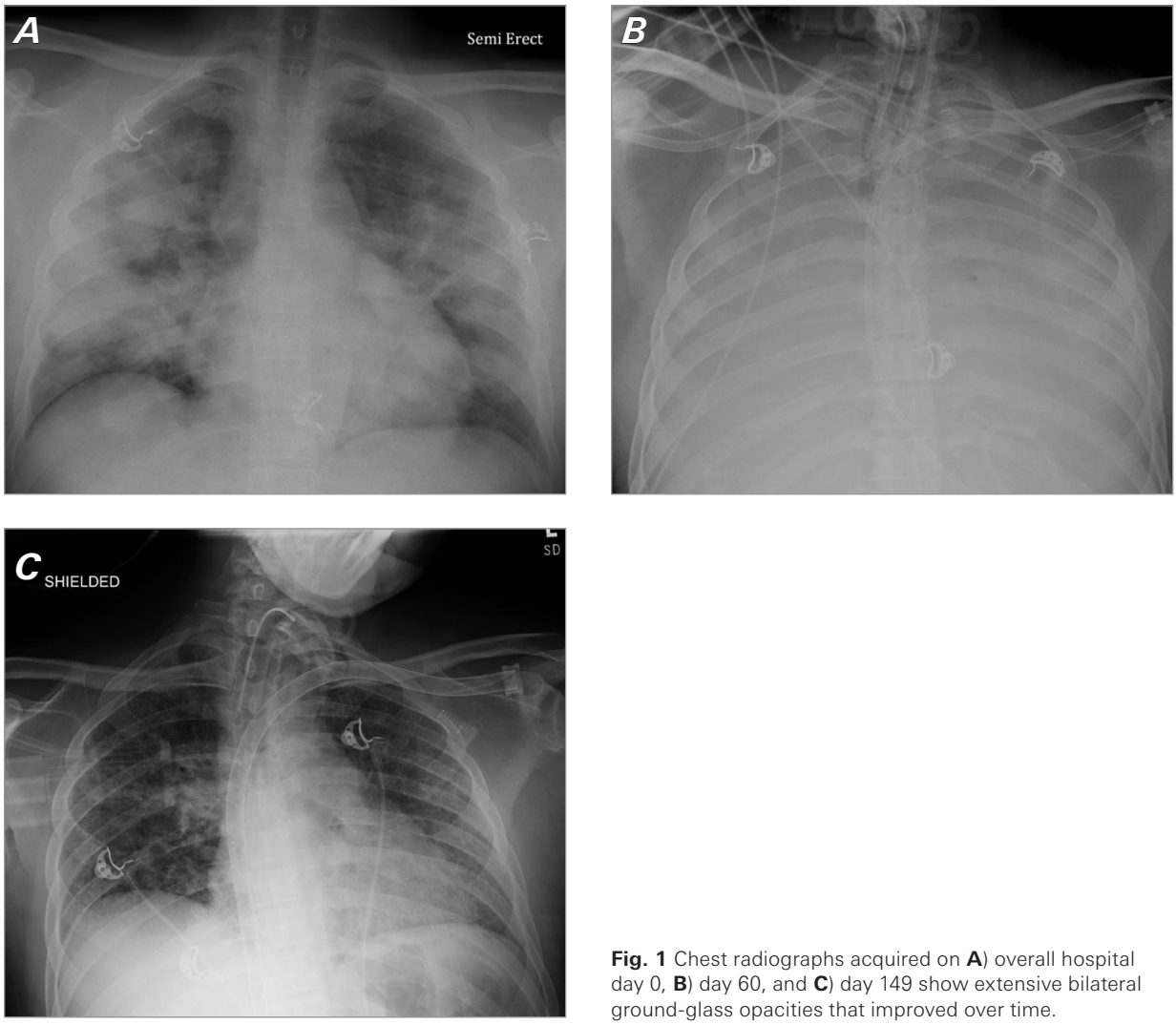

Fig. 1 Chest radiographs acquired on **A**) overall hospital day 0, **B**) day 60, and **C**) day 149 show extensive bilateral ground-glass opacities that improved over time.

On hospital day 17, the patient was transitioned to single-circuit veno-VV-ECMO with left femoral inflow and bilateral subclavian outflow with a Y connection to reduce recirculation (Fig. 4C). The circuit was exchanged on hospital day 47 because of oxygenator thrombosis, laboratory evidence of hemolysis (anemia with increased lactate dehydrogenase levels), and increased sweep requirement. On day 115, the subclavian and femoral cannulas were exchanged for a single dual-lumen cannula (Medtronic) in the left subclavian vein (Fig. 4D).

Severe Bradycardia

Approximately 2 weeks into VV-ECMO support, the patient began having recurrent episodes of severe bradycardia that persisted for most of the ECMO run despite discontinuation of dexmedetomidine and intermittent administration of dopamine and epinephrine. The bradycardia was eventually attributed to vasovagal response; counterintuitively, low-dose β-blocker therapy resolved the episodes.

Sedation Management

Initially, deep sedation was accomplished with hydromorphone, propofol, dexmedetomidine, and ketamine; however, the need to assess neurological function required that sedation be diminished. Subsequent agitation, ventilator dys-synchrony, and profound hemodynamic lability caused periodic drops in ECMO flow. Hypertriglyceridemia on hospital day 19 prompted the weaning of propofol and compensatory administration of oral benzodiazepines, selective serotonin reuptake inhibitors, and quetiapine. Slow daily weaning from sedative infusions continued until the patient awoke on hospital day 98. He remained hemodynamically stable, with preserved ECMO flows. He exhibited substantial muscle weakness but no neurological deficits.

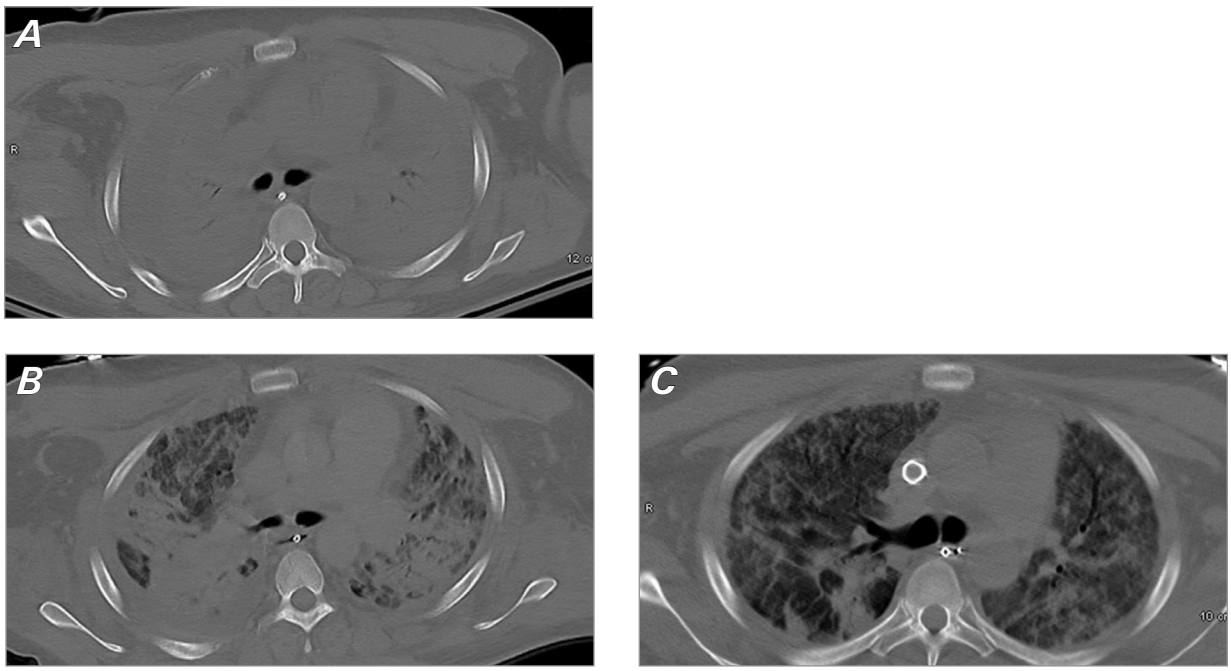

Fig. 2 Computed tomography imaging shows the severity of acute respiratory distress syndrome and improvement on **A**) overall hospital day 0, **B**) day 60, and **C**) day 149.

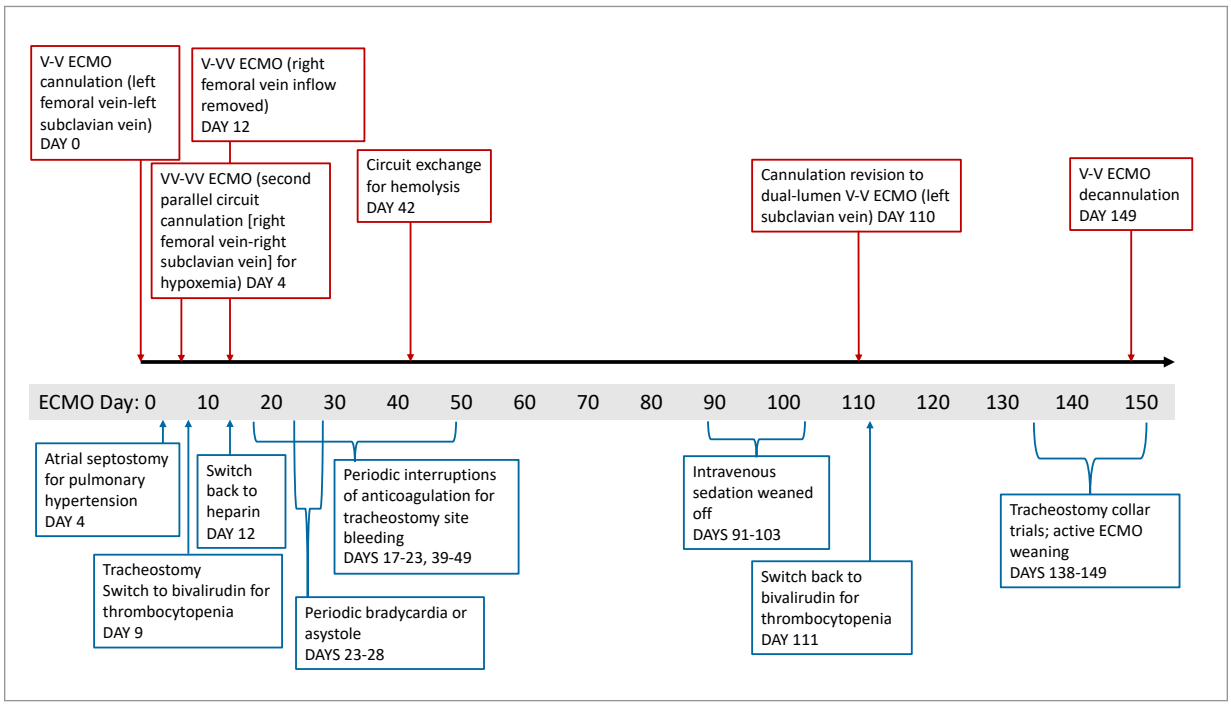

Fig. 3 Timeline of patient's 149-day ECMO course, with highlights of major events.

ECMO, extracorporeal membrane oxygenation; V-VV, veno-venovenous; VV-VV, venovenous-venovenous.

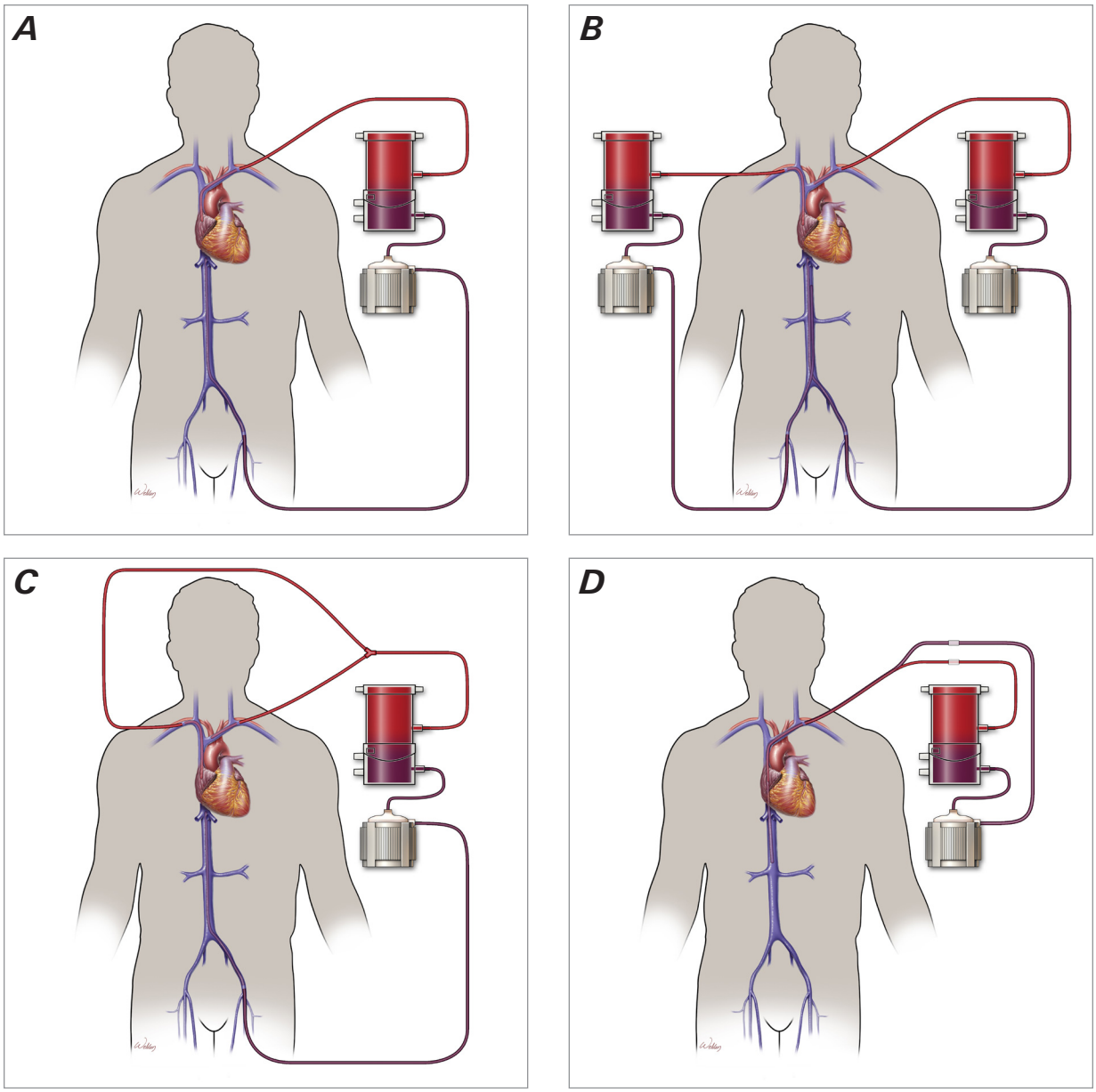

Fig. 4 Depiction of different cannulation configurations used through ECMO course shows **A**) the initial VV-ECMO configuration using the left femoral and internal jugular veins, which then was converted to **B**) a dual-circuit VV-VV configuration with the addition of right femoral and axillary vein cannulas. This was then transitioned to **C**) a V-VV configuration with a femoral venous inflow cannula and bilateral subclavian veins outflow cannulas. Finally, the patient was transitioned to **D**) a left subclavian dual-lumen cannula.

ECMO, extracorporeal membrane oxygenation; V-VV, veno-venovenous; VV-VV, venovenous-venovenous.

Outcome

Progressive recovery of lung function and mobilization were noted once the patient awoke and could actively participate in physical therapy and daily spontaneous-breathing trials. Overall improvement is shown in Figure 1 and Figure 2. The patient was progressively weaned from ECMO support, and after 149 consecutive days, he was successfully decannulated. The patient was thereafter weaned from ventilation over a 2-week period and discharged home.

Fig. 5 Photograph of the patient (center) after recovery (used with patient permission).

Latest Follow-Up

The patient was alive and physically well at home 6 months after discharge, but his mental health has been in ongoing recovery. As the patient recalls, his most vivid memories of these 149 days were of being confined to the bed while conscious on ECMO. He states, "It was fear of the unknown, worrying about my family, and questioning if I could make it through this" (Fig. 5). These intrusive thoughts nearly paralyzed him into depression. Prolonged stays in the intensive care unit can induce psychological distress in patients, with reports of fear, anxiety, depression, and the development of posttraumatic stress disorder.[4] He credits his wife and family and the dedicated nursing staff and health care teams for encouraging him and motivating him to survive. "Everyone taking care of me helped me get over the feeling that I couldn't do it." The patient focused on ambulation as a challenge to overcome his condition. He was especially fearful at the time of ECMO decannulation that he would not survive, but apprehension soon became joy after he was successfully decannulated.

Discussion

Traditionally, VV-ECMO is reserved for patients with severe oxygenation or ventilation impairment—for example, in patients with ARDS as a bridge to lung transplantation as well as after lung transplantation in patients with primary graft dysfunction—and when all available conventional mechanical ventilation methods have failed.[5] A systematic review and meta-analysis of 2 randomized controlled trials and 3 observational studies before the COVID-19 pandemic found reduced 60-day mortality rates with a moderate risk for increased bleeding in patients with severe ARDS who were treated with VV-ECMO.[6]

Evaluation for VV-ECMO candidacy at this center involves a multidisciplinary review of objective patient data (including patient age, severity and length of illness, and comorbidities) led by the ECMO intensivist. One measure frequently employed is the Respiratory ECMO Survival Prediction score, developed initially from retrospective data and subsequently validated in a prospective trial.[7,8]

The arrival of the COVID-19 pandemic required judicious ECMO criteria to be established, given the limited ECMO resources available at most health care institutions.[9,10] Results from the international Extracorporeal Life Support Organization showed that for patients on ECMO with COVID-19, ARDS-related mortality rates worsened when patients were treated after 2020, from less than a 40% mortality rate before May 2020 to a more than 50% mortality rate from May 2020 onward.[2] This may result from changes in the therapies available for managing COVID-19, the increasing number of centers with ECMO availability, or changes in physician-determined appropriateness for ECMO. A constant throughout the evolving COVID-19 pandemic, however, has been the direct relationship between more days spent on ECMO and greater mortality risk.[2] Indeed, case reports identified differences in ventilation parameters and systemic interleukins between ARDS from COVID-19 and non–COVID-19 causes.[11]

The case presented here highlights several lessons to be learned from the COVID-19 ECMO experience. First, the use of unconventional cannulation strategies to achieve adequate oxygenation requires creativity and multispecialty collaboration.[12] Second, sedation protocols in refractory respiratory failure with long ECMO runs need to be investigated. Sedation management and weaning proved difficult for this patient because of hypoxemia and because bradycardia from vasovagal response produced brief episodes of asystole. Third, anticoagulation strategies may require adjustment. For this patient, achieving adequate anticoagulation was hindered by recurrent instances of airway bleeding and

ongoing hemolysis and thrombus formation, necessitating multiple circuit and oxygenator exchanges.

Notably, the ECMO multidisciplinary care team at this center, which includes palliative care specialists, conducts weekly videoconferences with patients' families. On more than 1 occasion, the seeming futility of this case and consideration of palliative withdrawal were discussed with the patient's family as there were no meaningful signs of improvement. The family wished to continue care unless the patient developed an irreversible complication. Fortunately, he did not. The patient's experience and his specific fears, moreover, have been instructive for treatment teams as they care for patients on ECMO going forward.

The center's experience with this patient and others requiring ECMO for COVID-19 respiratory failure confirms the importance of persisting with prolonged ECMO support—as a bridge either to lung transplantation or to native lung recovery—in selected patients with single-organ failure to maximize survival.

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