

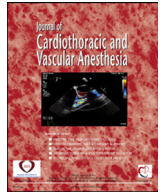


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## Case Report

# Uninterrupted Continuation of VV-ECMO Without Anticoagulation for 44 Days in COVID-19 ARDS: A Precarious Quandary

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Venovenous extracorporeal membrane oxygenation (VV-ECMO) has become a mainstay treatment modality for a select patient population who do not respond to conventional medical therapy suffering from severe acute respiratory distress syndrome (ARDS) due to COVID-19. This therapy necessitates the utilization of anticoagulation, whether unfractionated heparin or bivalirudin, to prevent thrombotic complications. Scarce are reports of VV-ECMO implementation leading to acute hemorrhage mandating cessation of anticoagulation in a patient suffering from COVID-19 ARDS. Herein, the authors report a case of a successful outcome in a COVID-19 ARDS patient who suffered an acute hemorrhagic complication leading to pre-emptive termination of systemic anticoagulation. The authors believe this to be one of the first such cases in the literature.

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**Key Words:** extracorporeal membrane oxygenation; COVID-19; acute respiratory distress syndrome; thrombotic complications; hemorrhage; anticoagulation; survival

HEAVILY RE-INSTITUTED during the H1N1 flu epidemic, venovenous extracorporeal membrane oxygenation (VV-ECMO) has remained a revolutionary treatment option for adult patients with severe acute respiratory distress syndrome providing pulmonary support as either a bridge to lung transplantation or a path to recovery. When severe acute respiratory distress syndrome (ARDS) from COVID-19 can no longer be managed with mechanical ventilatory support alone, a collaborative decision is made to determine candidacy for VV-ECMO support. As intensivists become tasked with managing large volumes of critically ill patients, the advent of systematic

protocolized approaches at many institutions has led to efficacious initiation, maintenance, and weaning of VV-ECMO.

The majority of ECMO protocols involve systemic anticoagulation with very adherent monitoring of activated clotting time, anti-Xa, or activated partial thromboplastin time to ensure minimizing thromboembolic complications.<sup>1</sup> Nonetheless, systemic anticoagulation also comes with a complication rate which cannot be ignored. Hemorrhagic complications from ECMO can be life-threatening if left unnoticed.<sup>2</sup> Timely recognition of hemorrhage along with prompt cessation of anticoagulants is crucial; nonetheless, locating the source for hemorrhage is also paramount. Upon identification of hemorrhage, there is no setpoint in time for how long one should hold off on anticoagulation. Bleeding severity, location, and overall clinical status of each individualized patient all play a

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key role in guiding the decision of an ECMO team to withhold or cautiously continue with anticoagulation. This decision can be overwhelming for a physician alone, thus input from a multi-disciplinary ECMO team is necessary.

The authors highlight a patient who encountered an intra-abdominal hemorrhage likely secondary to systemic anticoagulation in conjunction with VV-ECMO initiated owing to COVID-19 ARDS. This report serves to illustrate the complexity in proceeding with VV-ECMO management in a patient suffering from severe COVID-19 ARDS with minimal use of systemic anticoagulation.

### Case Report

A 43-year-old man with no significant medical history, unvaccinated against SARS-CoV-2, presented to the authors' institution reporting an 8-day history of cough, myalgias, sore throat, and dyspnea (height: 165 cm; weight: 106 kg; body mass index: 33.8 kg/m<sup>2</sup>).

On arrival at the hospital, viral Polymerase Chain Reaction testing (PCR) confirmed positivity for SARS-CoV-2 infection, and the patient was noted to be tachypneic with a respiratory rate varying from 25 to 40 breaths/min and hypoxic with initial oxygen saturation (as measured by pulse oximetry) of 82% on room air improving to 95% with placement of non-rebreather mask. An arterial blood gas (ABG) was obtained unveiling a pH of 7.40, PaCO<sub>2</sub> of 37.8 mmHg, and PaO<sub>2</sub> of 56.3 mmHg with a PaO<sub>2</sub>:FiO<sub>2</sub> ratio of 128 indicating moderate ARDS and he was admitted to the intensive care unit (ICU). His oxygenation was supported with noninvasive positive pressure ventilation, but after persistent tachypnea and labored breathing, the patient agreed to mechanical ventilatory support and was intubated. Throughout his initial course, the patient underwent fine ventilatory adjustments to target optimal settings in accordance with his lung mechanics to no avail. Serial ABGs revealed worsening of hypoxic respiratory failure in conjunction with hypercapnic respiratory failure, with ABG 4 days after placement on ventilatory support revealing pH of 7.40, PaCO<sub>2</sub> of 79 mmHg, PaO<sub>2</sub> of 72 mmHg, and a PaO<sub>2</sub>:FiO<sub>2</sub> ratio of 79. At this time, a multidisciplinary team collaborated

and decided to implement VV-ECMO in response to the patient's worsening respiratory failure.

The patient was transferred to the neighboring campus, where the ECMO team was consulted. He was brought directly to the ECMO ICU and cardiothoracic surgery was notified of his arrival. ECMO cannulation proceeded in the ICU, and the patient was prepped appropriately and sterilely draped. Access was obtained in the right internal jugular vein with serial dilation under fluoroscopic guidance up to a 22Fr return cannula inserted in the jugular venous tract, with the tip terminating near the junction of the superior vena cava and the right atrium. Subsequent access was obtained in the right femoral vein, with dilation up to a 25Fr drainage cannula, confirmed just below the level of the diaphragm with fluoroscopy. The ECMO circuit was initiated thereafter without complications, and the patient's oxygen saturation (as measured by pulse oximetry) rose to >90% immediately. The sweep was titrated gradually to 6 L/min, pump speed of 3,500 rotations/min generating a flow of 4.5 L/min, and the patient remained under concomitant mechanical ventilatory support. He also was placed on a bivalirudin infusion to maintain oxygenation circuit permeability and prevent thrombosis as part of the authors' VV-ECMO anticoagulation protocol.

The next day after ECMO cannulation, the patient's hemoglobin dropped from 12.9 to 9.7 g/dL and noncontrast chest abdomen and pelvis computed tomography was performed (Fig. 1). As expected, the patient had severe diffuse consolidations throughout bilateral lung fields; however, he inadvertently also had developed a large 7.3 × 6.3 cm circumferential hematoma in the left rectus sheath with no evidence of an active bleed. This posed a therapeutic challenge given urgency to continue uninterrupted anticoagulation in the setting of VV-ECMO. Given expansion of hematoma over the course of several hours off anticoagulation with down-trending hemoglobin to 8.2 the next day, the decision was made to withhold systemic anticoagulation temporarily and observe the left groin site. To complicate matters further, point-of-care doppler ultrasound of the left lower extremity revealed a nonobstructive deep vein thrombus in the popliteal and peroneal veins posing a threat to early mobilization as well. The patient was placed

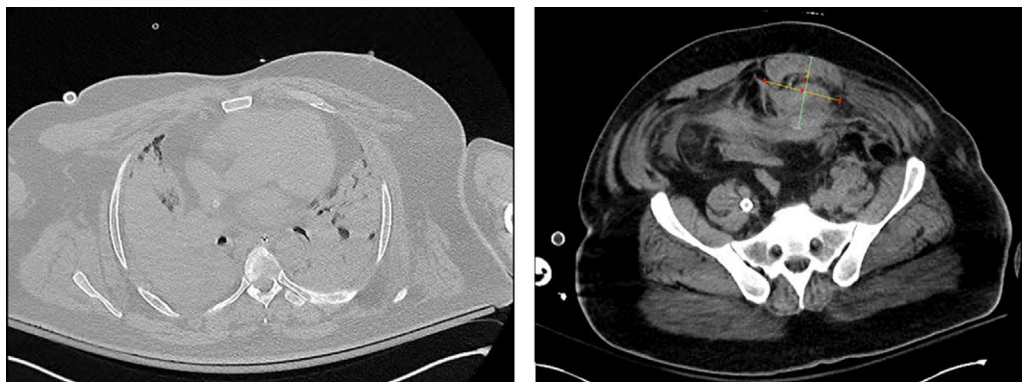


Figure 1. Diffuse bilateral lung consolidations consistent with severe COVID-19 ARDS (left); large 7 × 6 cm left rectus sheath hematoma as seen on CT Abdomen/Pelvis (right).

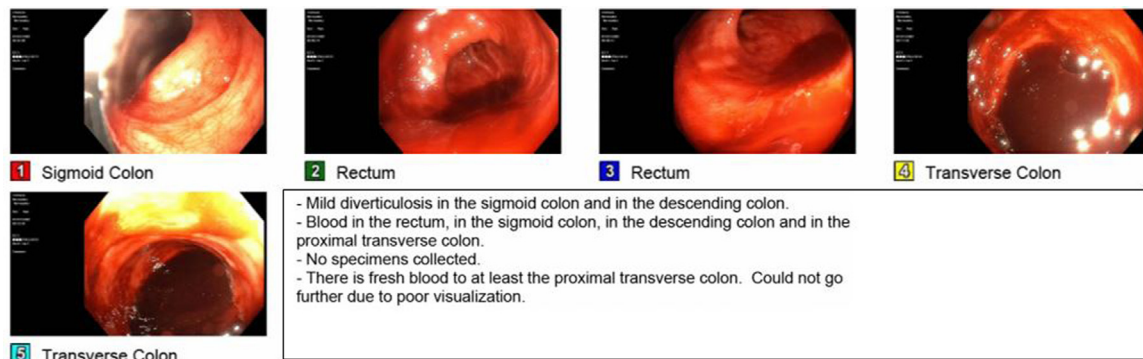


Figure 2.

judiciously back on anticoagulation, after receiving 2 packed red blood cell transfusions due to worsening anemia, and after 2 weeks of intermittent bivalirudin infusion at suboptimal dosing with increased monitoring to achieve an activated partial thromboplastin time of 40 to 60 seconds, joint decision was made to withhold anticoagulation indefinitely. Because the patient was 2 weeks into the VV-ECMO course, it also was decided to pursue tracheostomy and transition from dual cannula system to the Medtronic Crescent dual-lumen single cannula apparatus.

The patient was brought from the COVID ECMO ICU to the cardiovascular operating room and the existing ECMO support was maintained at a rate of 3.5 L/min. Left subclavian access was obtained for preparation of insertion of the Crescent cannula, which subsequently was inserted to the level of the inferior vena cava under fluoroscopic guidance. Tubing was deaired and attached to a new ECMO circuit with removal of the femoral and right subclavian cannulas, and appropriate hemostasis of both previous insertion sites was obtained. Transesophageal echocardiography and fluoroscopy confirmed location of the Crescent cannula revealing cannulas in the superior vena cava and inferior vena cava with appropriate jet crossing the tricuspid valve. The patient's vital signs and hemodynamics remained stable throughout the ECMO cannula exchange, and he underwent concomitant tracheostomy as well. He was then brought to the cardiovascular ICU, where management of all mechanical circulatory support patients occurs, because he needed to be at least 20 days after COVID-PCR (polymerase chain reaction testing) positivity before allowing transfer per the authors' protocol. The day after exchange and tracheostomy, significant bleeding was noticed around the tracheostomy site and the flank hematoma remained a concern on follow-up abdominal computed tomography scans, thus decision was made to cease systemic anticoagulation indefinitely only 2 weeks into his VV-ECMO course. Through the transition from dual cannula apparatus to the single cannula dual-lumen Crescent cannula, the patient gradually was weaned off intravenous sedatives and able to participate in aggressive rehabilitation with physical therapy and move out of bed to the chair.

Even while off systemic anticoagulation with receipt of only subcutaneous prophylactic heparin, the patient suffered a

massive lower gastrointestinal hemorrhage 1 month into his VV-ECMO course. He was noted to have dark, maroon bowel movements and his hemoglobin rapidly dropped from 10.3 g/dL to 6.9 g/dL. He was transfused multiple units of packed red blood cells, fresh frozen plasma, and packed platelets as well as initiated on phenylephrine infusion. The source for the bleed remained unclear, so after equivocal sigmoidoscopy (Fig. 2), the patient was brought down to interventional radiology suite and underwent mesenteric angiography. This revealed a pseudoaneurysm from the left anterior branch of the superior rectal artery believed to be the source of spontaneous hemorrhage, for which coil embolization was performed without complication. The patient's hemoglobin subsequently remained stable and continuous weaning of sweep ensued. The day after coil embolization, the patient's oxygenator began clotting, and sweep was weaned over a 48-hour period from 4 L/min to 2 L/min to 0 L/min, where it remained 24 hours thereafter. Decision was made to pursue decannulation after 59 days on VV-ECMO support (44 of which were without systemic anticoagulation), as the patient's native lung mechanics appeared to be improving based on ABGs and observed compliance. He underwent removal of the Crescent cannula at the bedside without complication after ECMO circuit was no longer circulating and continued on mechanical ventilatory support alone. He was able to wean off the ventilator and transfer to the medical floor, where he eventually was discharged home on 2 L nasal cannula and doing very well.

## Discussion

There have been numerous reports in the literature regarding the implementation of VV-ECMO without concurrent systemic anticoagulation in patients with very high risk for life-threatening hemorrhage and anticoagulation-induced thrombocytopenia.<sup>3,4</sup> In the setting of VV-ECMO, the rate of thromboembolic complications off anticoagulation has been shown to be far less than the complication rate off anticoagulation in VA-ECMO, given that VV-ECMO presumes biventricular functional preservation and blood is recirculated into the venous system.<sup>5</sup> The feasibility of VV-ECMO without anticoagulation has even been examined through large retrospective analysis, concluding safe administration of VV-ECMO

without systemic anticoagulation can be performed in patients with reduced bleeding diathesis and need for transfusions.<sup>6</sup> Nonetheless, almost 2 years into the COVID-19 pandemic, to the authors' knowledge there is not yet a report of VV-ECMO pursued without systemic anticoagulation.

SARS-CoV-2 infection has been shown to independently increase the rate of thrombosis in hospitalized patients through a multifactorial etiopathogenetic modality. This is believed to occur through prominent cytokine upregulation leading to activation of proinflammatory mediators precipitating thrombosis.<sup>7</sup> Therefore, several studies have demonstrated the potential benefit of therapeutic anticoagulation in patients with COVID-19 with the primary endpoint being decrease in mortality.<sup>8</sup> The risk, nonetheless, of maintaining patients with severe COVID-19 on anticoagulation involves potentially fatal hemorrhagic complications and heparin-induced thrombocytopenia (if a heparin product is used). These same risks apply when deciding to implement systemic anticoagulation for patients necessitating VV-ECMO. The authors' patient had 2 potentially distinct indications for requirement of therapeutic anticoagulation: a deep vein thrombus in the left popliteal and peroneal vein and placement on VV-ECMO. This posed a therapeutic dilemma once encountering the large rectus sheath hematoma followed by temporary trial on and off anticoagulation until decision was made to merely hold it indefinitely. As highlighted, even without therapeutic anticoagulation, the patient still suffered a significant gastrointestinal hemorrhage, and it is unfathomable what may have happened had he been continued on systemic anticoagulation given his propensity to bleed. Nonetheless, pre-emptive cessation of anticoagulation also posed risk of oxygenator malfunction hence the quandary amongst the care team.

## Conclusion

Herein, the authors showcased the first presumed case in the literature of a COVID-19 ARDS patient necessitating VV-

ECMO with minimal use of systemic anticoagulation successfully being weaned off and decannulated without major complications. This report serves to showcase the challenging dilemma posed by withholding anticoagulation in the setting of a prothrombotic viral infection in conjunction with VV-ECMO.

## Conflict of Interest

None.

## References

- 1 Delmas C, Jacquemin A, Vardon-Bouines F, et al. Anticoagulation monitoring under ECMO support: A comparative study between the activated coagulation time and the anti-XA activity assay. *J Intensive Care Med* 2020;35:679–86.
- 2 Thomas J, Kostousov V, Teruya J. Bleeding and thrombotic complications in the use of extracorporeal membrane oxygenation. *Semin Thromb Hemost* 2018;44:20–9.
- 3 Herbert DG, Buscher H, Nair P. Prolonged venovenous extracorporeal membrane oxygenation without anti-coagulation: A case of Goodpasture syndrome-related pulmonary haemorrhage. *Crit Care Resusc* 2014;16:69–72.
- 4 Wen PH, Chan WH, Chen YC, et al. Non-heparinized ECMO serves a rescue method in a multitrauma patient combining pulmonary contusion and nonoperative internal bleeding: A case report and literature review. *World J Emerg Surg* 2015;10:15.
- 5 Choi JH, Luc JGY, Weber MP, et al. Heparin-induced thrombocytopenia during extracorporeal life support: Incidence, management and outcomes. *Ann Cardiothorac Surg* 2019;8:19–31.
- 6 Kurihara C, Walter JM, Karim A, et al. Feasibility of venovenous extracorporeal membrane oxygenation without systemic anticoagulation. *Ann Thorac Surg* 2020;110:1209–15.
- 7 Hanff TC, Mohareb AM, Giri J, Cohen JB, Chirinos JA. Thrombosis in COVID-19. *Am J Hematol* 2020;95:1578–89.
- 8 Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost* 2020;18:1094–9.