Successful management of COVID-19 and associated coagulopathy in a patient with durable left ventricular assist device

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Abstract
Patients with durable left ventricular assist devices pose special problems for management in the setting of COVID-19 infection. We describe the successful management of a 44-year-old man with severe COVID-19 infection and HeartMate 3 left ventricular assist device. His course was complicated by cytokine storm and COVID-19-associated coagulopathy. We describe our institutional protocol for managing COVID-19 infection in patients on mechanical circulatory support, focusing on the need for a thoughtful, multidisciplinary approach.

KEYWORDS
cardiovascular pathology, coronary artery disease

1 | INTRODUCTION
Patients with durable left ventricular devices (LVADs) pose special problems for management in the setting of COVID-19 infection. Among these is balancing the risk of bleeding and thrombosis in the setting of COVID-19 associated coagulopathy, which is a well-described complication of COVID-19 infection. We present the case of a patient with ischemic cardiomyopathy supported by durable LVAD who developed severe COVID-19 infection with acute respiratory distress syndrome complicated by coagulopathy. We focus on the interdisciplinary approach used to successfully manage this complex patient.

2 | CASE REPORT
A 44-year-old man with a HeartMate 3 (Abbott Laboratories, Chicago, IL) left ventricular assist device implanted in June 2019 as destination therapy for end-stage ischemic cardiomyopathy presented to an outside hospital with flu-like symptoms, intermittent fevers and worsening dyspnea on exertion. Upon admission, he was diagnosed with COVID-19, started on ceftriaxone and hydroxychloroquine and transferred to our institution for further management.

On arrival, the patient was hemodynamically stable with LVAD support (RPM 5400, Flow: 4.5 liters per minute, pulsatility index: 2.6, and pump power: 4.1 W) and in moderate respiratory distress on high flow nasal cannula. His heart failure regimen included carvedilol, lisinopril, spironolactone, and furosemide. Inflammatory markers were elevated (C-reactive protein: 20.9 mg/dL, ferritin: 958 ng/mL, lactate dehydrogenase (LDH): 414 U/L, fibrinogen: 812 mg/dL, D-dimer: 670 ng/mL FEU, and procalcitonin: 0.11 ng/mL). Initial chest radiograph showed bilateral patchy airspace opacities consistent with COVID-19 pneumonia (Figure 1). On hospital day 2, the patient developed progressively worsening oxygen requirement necessitating endotracheal intubation and initiation of norepinephrine for hemodynamic support. He was intermittently febrile and developed leukocytosis (WBC = 17 k/μL). He was empirically treated with intravenous piperacillin-tazobactam and vancomycin, and given a dose of tocilizumab for cytokine reduction. Hydroxychloroquine was discontinued due to QT prolongation and an episode of torsade de pointes. On hospital day 3 the patient’s International normalized ratio (INR) became supratherapeutic (INR: 5.2) and was corrected...
with vitamin K. Thereafter, therapeutic anticoagulation was main-
tained with heparin infusion. Antiplatelet therapy was maintained
with aspirin (81 mg daily).

On hospital day 10, the patient was noted to have mottling of the
left foot and loss of left pedal arterial Doppler signals, associated with
an elevation in D-dimer to 4230 ng/mL (Figure 2). Left femoral arterial
Doppler signals were preserved. In the subsequent days, there was a
precipitous decrease in platelet count and fibrinogen (Figure 2). Ultra-
sound evaluation of lower limbs was negative for deep vein thrombosis.
After consultation with vascular surgery, it was deemed that the risk for
surgical intervention was prohibitive. Lower extremity warming was
initiated along with continued therapeutic anticoagulation. The patient’s
lower extremity exam improved over the course of 2 weeks with re-
established pedal Doppler signals.

During this period, the patient had nasopharyngeal bleeding, gross
hematuria, and retroperitoneal hematoma requiring transfusion. Antico-
augulation was held for 6 days in the setting of retroperitoneal hema-
toma without active reversal (hospital day 18-24). The patient did not
develop signs of recurrent arterial thrombosis in the absence of ther-
apeutic anticoagulation.

The patient was extubated after 11 days of mechanical ventila-
tion (hospital days 2-13) and noted to have negative COVID testing
on hospital day 19 and 23. The patient continued to improve and was
discharged home on hospital day 31.

3 | COMMENT

Management of COVID-19 infection in the context of durable LVAD
support requires careful institutional planning and a multidisciplinary
approach. We recommend that such patients be managed at in-
tstitutions with robust surgical and medical heart failure programs, as
well as expertise in infectious disease and an array of subspecialty
services. We also recognize the challenges in transferring patients
with COVID-19. Therefore, our recommendations is that LVAD pa-
tients with COVID-19 be treated at the nearest center with appro-
priate resources and expertise.

Likewise, management of COVID-19-infected LVAD patients
requires a careful balance between isolation precautions and avail-
ability of expert clinicians. Our institution has designated an 18-bed
cardiothoracic intensive care unit as an isolation unit for COVID-19-
infected patients who require mechanical circulatory support. Here,
board-certified cardiothoracic intensive care physicians lead virtual
multidisciplinary rounds with medical and surgical heart failure spe-
cialists via teleconference on mobile workstations at the bedside.
This allows our heart failure specialists to jointly manage these pa-
tients while maintaining strict isolation to safeguard other patients,
including heart and lung transplant recipients.

COVID-19 is often complicated by the development of coagu-
lopathy, characterized by inappropriate activation and consumption
of coagulation factors, thrombocytopenia, elevated D-dimer, and
prolonged prothrombin time. Elevated D-dimer (> 1 µg/mL) has been
reported to be a strong, predictor of death in these patients.5 Unlike
with disseminated intravascular coagulation in sepsis or trauma,
thrombocytopenia is often mild and is not considered a predictor of
mortality.5,6 Based on these observations, the International Society
on Thrombosis and Haemostasis (ISTH) recommends frequent

![Figure 1](image1.png)

**Figure 1** Chest radiograph demonstrating bilateral interstitial
pulmonary opacities consistent with COVID-19 pneumonia. Also in
picture are sternal wires from previous sternotomy, implantable
cardioverter-defibrillator (ICD), and HeartMate 3 left ventricular
devices

![Figure 2](image2.png)

**Figure 2** Trends in D-dimer, fibrinogen, and platelets during the first 22 days of hospitalization. A sharp rise in D-dimer was noticed at the
time of left foot ischemia from presumed intravascular thrombosis (black arrows). In the subsequent days, there was a sharp decline in platelets
and fibrinogen
measurement of D-dimer, prothrombin time, and platelet counts in all hospitalized patients being treated for COVID-19.\textsuperscript{4,5}

These findings have prompted interest in the use of anticoagulation for management and prophylaxis in COVID-19 patients. In particular, low molecular weight heparin may have benefit due to its anticoagulant and anti-inflammatory properties.\textsuperscript{4} ISTH guidelines state that prophylactic low molecular weight heparin should be considered in all patients admitted for management for COVID-19, including noncritically ill patients.\textsuperscript{4}

Even in the absence of COVID-19 infection, management of anticoagulation for patients with durable LVADs requires a careful balance between potential complications of thrombosis and bleeding. COVID-19-associated coagulopathy complicates this balance by alterations in normal coagulation that are only partially understood. In our case, the use of parenteral anticoagulation with heparin allowed for rapid titration in response to life-threatening thrombotic and bleeding events over the patient’s hospital course. Anticoagulation may be especially important in the setting of acute cytokine-inflammatory storm but requires vigilance for signs of serious bleeding.

There is emerging evidence that a cytokine storm-driven in part by IL-6 may play an important role in the pathogenesis of severe COVID-19 infection. Tocilizumab is an IL-6 inhibitor that has generated attention as a potential therapy in this patient group.\textsuperscript{7} We utilized this agent empirically in our patient in an effort to limit the severity of cytokine storm. Whether this or other cytokine modulators prove effective in large series is the subject of ongoing investigations that will more clearly define the importance of cytokine storm in the pathogenesis of severe COVID-19 infection.

CONFLICT OF INTERESTS
Dr Hodges discloses a financial relationship with Atricure, Dr Estep with Abbott and Medtronic, Dr Tong with Abbott and Abiomed, Dr Soltesz with Abbott, Atricure, Edwards, and Abiomed. The other authors have nothing to disclose.

ETHICS STATEMENT
According to the Cleveland Clinic Institutional Review Board: a case report for 1 to 3 patient(s) is considered a non-research activity because it is not a systematic investigation designed to contribute to generalizable knowledge. Therefore, CCF IRB approval is not required however; the ethical principle of obtaining consent is relevant whether or not the case report meets the formal definition of human subject research. Accordingly, this case report was discussed with the patient and verbal consent was obtained for publication and witnessed by two Cleveland Clinic employees.

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