Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

COVID-Associated Myocardial Injury: Crossing the Threshold for Mechanical Circulatory Support

Myocardial injury, or a troponin elevation above the 99th percentile,[1] is common in hospitalized patients with coronavirus disease 2019 (COVID-19). In one large New York City cohort of 2,736 COVID patients, 36% had evidence of myocardial injury.[2] In this cohort, even minimal troponin I elevations (from >0.03 to 0.09 ng/mL) were associated significantly with death (hazard ratio [HR] 1.75; 95% CI: 1.37-2.24); while troponin I > 0.09 ng/mL had an even higher risk of mortality (HR 3.03; 95% CI 2.42-3.80).[2] Nevertheless, myocardial injury is merely one complication of COVID-related illness. Other mechanisms of cardiac dysfunction include type 1 myocardial infarction, type 2 myocardial infarction, vascular endothelial injury, embolic disease, and a systemic hyperinflammatory syndrome.[3] Although optimal short-term management strategies for COVID-associated myocardial injury remain unclear, experience can be drawn from other infections and prior pandemics, such as influenza. The influenza virus illness, like COVID-19, is associated with elevated cardiac biomarkers, pericarditis, myocarditis, arrhythmias, and higher mortality.[4] In one influenza A (H1N1) cohort of critically ill patients, troponin I was four times higher in patients who also developed acute respiratory distress syndrome.[5] Furthermore, influenza-related myocarditis has been reported in 0.4% to 13% of patients, while autopsy data have demonstrated evidence of myocyte inflammation in necrosis in 30% to 50% of patients.[6]

In this month's *Journal of Cardiothoracic and Vascular Anesthesia*, Qian et al. retrospectively reviewed early experience in one intensive care unit (ICU) in Wuhan, China.[7] The authors highlighted the incidence of myocardial injury and its association with increased cardiovascular complications in the ICU, higher Acute Physiology and Chronic Health Evaluation II scores, and overall mortality. The authors noted a 28-day mortality increase in patients with myocardial injury (HR 2.2, 95% CI 1.29-3.74; p = 0.004). Myocardial injury in the setting of infection is not unique to COVID and has been studied in many systemic illnesses.[8] Elevated troponin occurred frequently in critically ill patients with influenza (H1N1) and resulted in longer ICU stay and higher mortality.[9] In starting to appreciate now that there is cardiac involvement in COVID-19 patients, Qian et al. have started the early process of studying myocardial markers. The pathobiologic mechanism of COVID-19 cardiac failure is not understood fully but certainly everything from stress-induced catecholamine cardiomyopathy to cytokine storm are being considered. Future studies likely will focus on understanding the most likely molecular mechanisms leading to cardiac decline to start to understand possible future therapeutics. With the push forward focusing on vaccine development and possible therapeutics, there is the ability to use support strategies, such as extracorporeal membrane oxygenation (ECMO) and other advanced mechanical support devices, for these critically ill patients.

The authors highlighted the need for venovenous (VV) ECMO in five of their ICU patients (two with myocardial injury). The details surrounding decision making for VV ECMO in this study are lacking. Additionally, venoarterial (VA) ECMO strategies also were not included in this study. Although VA ECMO outcome data in COVID-19 are still emerging, it is an important strategy in COVID-related myocardial injury and shock. Information can be learned from the H1N1 experience. In one Australian and New Zealand cohort of critically ill H1N1 patients with ARDS, 68 patients were placed on VV ECMO and 71% survived to ICU discharge.[10] In another review of 184 patients with influenza-associated myocarditis, 48 required mechanical circulatory support (21 VA ECMO) and had a mortality rate of 33%.[11] Multiple other small case series have demonstrated success with VA ECMO utilization in the setting of fulminant myocarditis associated with influenza. Similarly, VA ECMO has been used intermittently with COVID. Data from the Extracorporeal Life Support Organization Registry recently identified 1,035 COVID patients who required ECMO, of whom 40 (4%) patients received VA ECMO support.[12] Among the patients who required VA ECMO support, 22 had clinical evidence of myocarditis. Although data still are being analyzed for the Extracorporeal Life Support Organization cohort, about 40% of the entire ECMO cohort has been discharged alive.[12]

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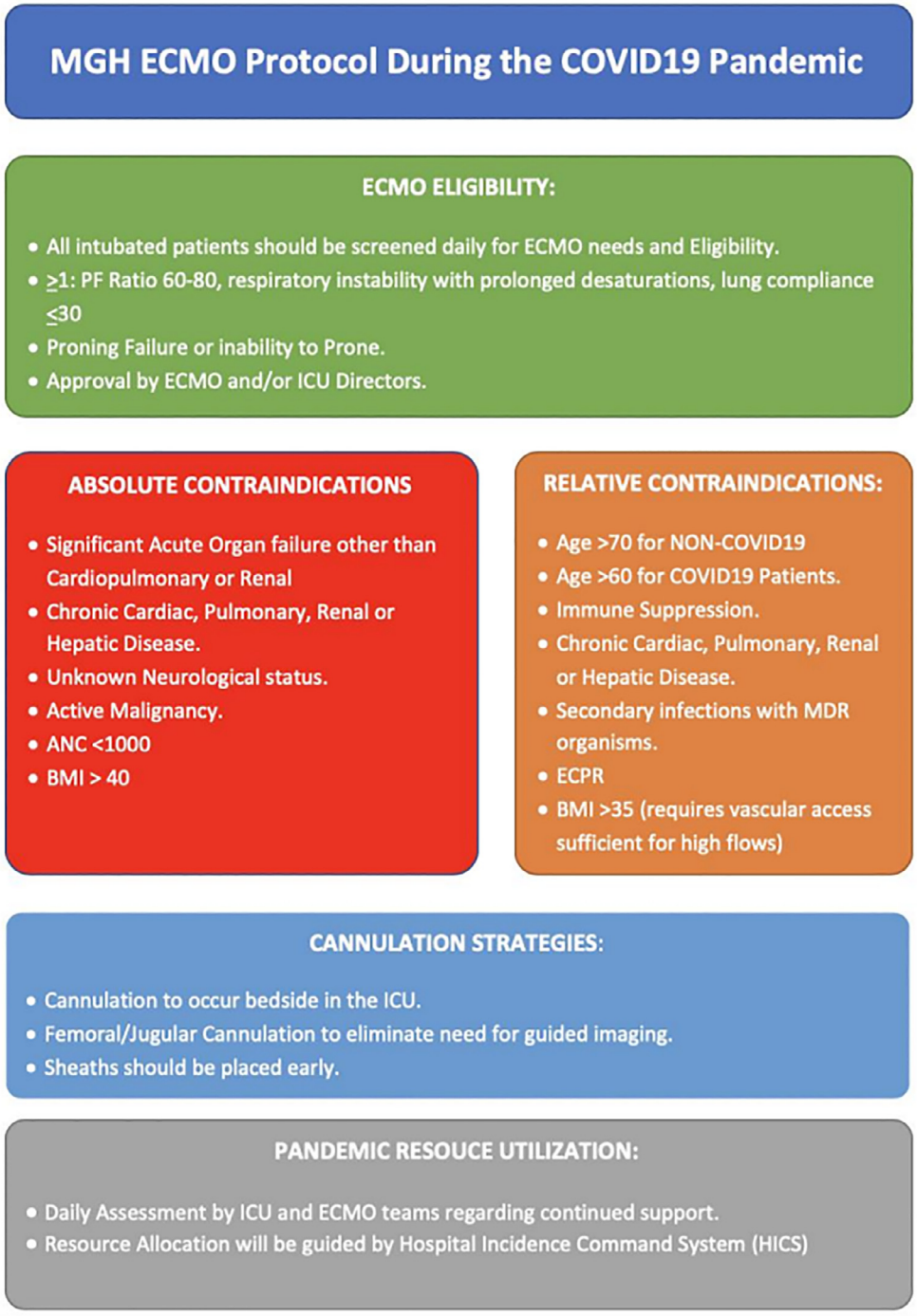

Fig 1. MGH ECMO protocol. ANC, absolute neutrophil count; BMI, body mass index; COVID-19, coronavirus diesase 2019; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; ICU, intensive care unit; MDR, multiple drug resistance; MGH, Massachusetts General Hospital; PF ratio, arterial PO_2 divided by fraction of inspired oxygen.

In the authors' experience VA ECMO is an important tool available for severe COVID-associated myocardial dysfunction and shock. VA ECMO may be considered for patients with refractory cardiogenic shock despite optimal medical therapies. Absolute contraindications include active malignancy, body mass index > 40, unknown neurologic status, significant organ failure besides cardiopulmonary or renal, and severe chronic medical illnesses. Although COVID forced the authors' hospital and many others to be more conscious of distribution of resources, VA ECMO is and should be reserved for appropriate indications (Fig 1). Although ECMO currently is not thought of as a therapeutic, it does provide the

hemodynamic and gas exchange capability to support end-organ function. In circumstances in which patients improve with critical care and/or options exist in the form of durable mechanical devices (left ventricular assist devices) or possibly transplantation, ECMO provides the time and the physiologic bridge necessary to achieve these goals. As discussed in recent reviews, the current pandemic now has proven that respiratory failure is just part of multiorgan failure in COVID-19. The ability as anesthesiologists and critical care physicians to manage a second surge of COVID-19 critical illness will depend heavily on the ability to understand the molecular mechanisms of multiorgan failure. Successful treatment also will rely on fundamental critical care knowledge and available support strategies like ECMO.[13]

Early identification of myocardial injury among COVID patients is critical, as many are at risk for further cardiovascular compromise and collapse. Qian et al. successfully illustrated the high prevalence of myocardial injury in a Wuhan cohort, many of whom developed severe cardiac complications. Mechanical circulatory support, in particular VA ECMO, is an important strategy to consider in the management of COVID patients with severe cardiac dysfunction.[14] The use and success of VA and VV ECMO in COVID-19 patients will depend most likely on the preparedness of the healthcare system, as well as the ability for clinicians to identify patients who may require ECMO support for rapid assessment by a multidisciplinary ECMO team and possible transfer to specialized ECMO centers.[14] Lastly, although ECMO complications have been well- studied, the profession is just starting to understand the thromboembolic and hemostatic complications associated with COVID-19 ECMO patients compared to the incidence previously reported in non−COVID-19 ECMO patients.[15] This further highlights the importance of a dedicated cross-specialty and multidisciplinary critical care team to weigh the risks and benefits of ECMO on a case-by-case basis to ensure optimal patient care.

In conclusion, the pathophysiology of COVID-19 extends beyond the pulmonary system and can lead to significant myocardial injury. It can cause significant cardiovascular compromise, warranting consideration for advanced therapies, such as VA ECMO, in a subset of affected patients. Early identification of COVID patients in cardiopulmonary distress and a multidisciplinary critical care team to assess patients who have failed traditional medical therapy are crucial to ensure optimal care of the most critically ill COVID-19 patients.

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Conflicts of interest

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References

1 Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. Circulation 2018;138:e618–51.
2 Lala A, Johnson KW, Januzzi JL, et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. J Am Coll Cardiol 2020;76:533–46.
3 Mitrani RD, Dabas N, Goldberger JJ. COVID-19 cardiac injury: Implications for long-term surveillance and outcomes in survivors. Heart Rhythm 2020;17:1984–90.
4 Estabragh ZR, Mamas MA. The cardiovascular manifestations of influenza: A systematic review. Int J Cardiol 2013;167:2397–403.
5 Brown SM, Pittman J, Miller RR III, et al. Right and left heart failure in severe H1N1 influenza A infection. Eur Respir J 2011;37:112–8.
6 Sarda C, Palma P, Rello J. Severe influenza: Overview in critically ill patients. Curr Opin Crit Care 2019;25:449–57.
7 Qian H, Gao P, Tian R, et al. Myocardial injury on admission as a risk in critically ill COVID-19 patients: A retrospective in-ICU study. J Cardiothorac Vasc Anesth 2021;35:846–53.
8 Olejniczak M, Schwartz M, Webber E, et al. Viral myocarditis−Incidence, diagnosis and management. J Cardiothorac Vasc Anesth 2020;34:1591–601.
9 Ni Z, Guo Z, Chen X, et al. Cardiac injury in patients with pandemic 2009 influenza A (H1N1) infection. Acta Cardiol 2011;66:427–32.
10 Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators, Davies A, et al. Extracorporeal membrane oxygenation for 2009 influenza A(H1N1) acute respiratory distress syndrome. JAMA 2009;302:1888–95.
11 Hekimian G, Jovanovic T, Brechot N, et al. When the heart gets the flu: Fulminant influenza B myocarditis: A case-series report and review of the literature. J Crit Care 2018;47:61–4.
12 Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation support in COVID-19: An international cohort study of the Extracorporeal Life Support Organization registry. Lancet 2020;396:1071–8.
13 Shelton KT, Wiener-Kronish JP. Evolving role of anesthesiology intensivists in cardiothoracic critical care. Anesthesiology 2020;133:1120–6.
14 Alom S, Haiduc AA, Melamed N, et al. Use of ECMO in patients with coronavirus disease 2019: Does the evidence suffice? [e-pub ahead of print]. J Cardiothorac Vasc Anesth 2020 Jul 30. https://doi.org/10.1053/j.jvca.2020.07.070.
15 Usman AA, Han J, Acker A, et al. A case series of devastating intracranial hemorrhage during venovenous extracorporeal membrane oxygenation for COVID-19. J Cardiothorac Vasc Anesth 2020;34:3006–12.