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

Cardiovascular Consequences and Considerations of Coronavirus Infection – Perspectives for the Cardiothoracic Anesthesiologist and Intensivist During the Coronavirus Crisis

THE CURRENT pandemic owing to coronavirus disease 2019 (COVID-19) has been associated in about 10% to 15% of cases with severe clinical presentations that require admission to hospital.[1-4] In the cohort of patients with severe COVID-19, the risks of admission to an intensive care unit are high owing to critical conditions such as acute respiratory distress syndrome, cardiovascular collapse, and acute renal failure.[1-4] The unique considerations of this important infection significantly affect the management approaches to these patients by cardiothoracic anesthesiologists and intensivists with respect to airway management, echocardiography, anesthetic care, and extracorporeal membrane oxygenation.[5-11]

The purpose of this freestanding editorial is to highlight the considerations in patients who present with cardiovascular collapse in the setting of severe COVID-19. This clinical perspective will focus on the mechanisms and management of cardiovascular compromise in these challenging patients. The emphasis will relate to the best evidence and consensus in an effort to disseminate the highest standards for care during this crisis. The provided references serve as a guide to further details for healthcare teams as they navigate the cardiovascular demands of the pandemic at their respective institutions.

Myopericarditis as an Etiology for Cardiovascular Collapse

Patients with severe COVID-19 may present with cardiogenic shock.[12,13] The coronavirus can cause myocarditis and/or pericarditis that may or may not be associated with pneumonia.[14,15] This myocarditis may present clinically with heart failure accompanied by arrhythmias, diffuse ST-segment changes, and significant release of myocardial enzymes, such as natriuretic peptides and troponin.[15,16] The echocardiographic examination may reveal a diffuse echo-bright myocardial appearance with a pattern of hypokinesis that may or may not have a regional distribution.[14-16] There may be an associated pericardial effusion with or without clinical tamponade owing to associated pericarditis as part of the COVID-19 spectrum.[16,17] Specialized imaging with cardiac magnetic resonance and contrast enhancement can detect myocarditis owing to phenomena such as myocardial edema, necrosis, and scar.[17-19] In the appropriate clinical setting, these typical features of myocarditis detected by cardiac magnetic resonance may be diagnostic for myocarditis and are frequently equivalent to endomyocardial biopsy.[18,19]

The presentation of myocarditis can result in focal or global myocardial inflammation.[17] Focal myocarditis may present with acute chest pain and mimic an acute coronary syndrome, resulting in emergency coronary angiography.[17,18] There is typically no obstructive coronary artery disease in focal myocarditis.[17-19] In patients with COVID-19, there are unique considerations for the catheterization laboratory that have been fully discussed elsewhere.[20,21]

The pathogenesis of myocarditis associated with COVID-19 may be owing to direct viral involvement of the myocardium mediated by angiotensin converting enzyme 2.[22,23] Further mechanisms include a cytokine storm owing to dysregulated T-helper cells and/or myocardial apoptosis owing to excessive levels of intracellular calcium induced by hypoxia.[22] Additional research is required to define the relevance of these mechanisms in the pathogenesis of myocarditis associated with COVID-19.[22-24]

Vasoplegic Shock as an Etiology for Cardiovascular Collapse

Patients with severe COVID-19 also may develop vasoplegia and consequent distributive shock.[11,12] This vasoplegic shock may be secondary to sepsis and/or disordered function of the renin-angiotensin-aldosterone system.[11] In patients with severe COVID-19 who require intensive care, the prevalence of septic shock may be about 10% to 15%.[25] The management

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of septic shock in this setting should follow the current guidelines for sepsis, including the recommendations from the World Health Organization.[11-13]

Because pulmonary endothelial damage from adult respiratory distress syndrome is common in severe COVID-19, the function of angiotensin-converting enzyme is disrupted, given that it is located on the pulmonary endothelium.[24,25] This loss of functional angiotensin-converting enzyme interferes with the hydrolysis of angiotensin I to form angiotensin II.[25] The deficiency of angiotensin II leads to systemic vasodilation. Furthermore, the relative excess of angiotensin I also antagonizes vasoconstriction through multiple mechanisms including enhanced production of systemic vasodilators such as nitric oxide and bradykinin.[25]

The possibility therefore exists that patients with severe COVID-19 may have vasoplegic shock owing to sepsis and dysregulation of the renin-angiotensin-aldosterone system.[25,26] Furthermore, the coronavirus requires angiotensin-converting enzyme 2 for cell entry in the lung, leading to possible downregulation in this part of the renin-angiotensin-aldosterone system.[25,26] Future trials will explore in detail the effects of this viral process with respect to systemic vascular tone and therapy with inhibitors of the renin-angiotensin-aldosterone system.[25-27]

Acute Coronary Ischemia as an Etiology for Cardiovascular Collapse

There is currently no evidence to suggest that acute coronary arteritis is a clinical feature of COVID-19.[11,12] On the other hand, in older patients with COVID-19, coronary artery disease is likely and may predispose to acute coronary syndromes owing to the increased metabolic stress of severe infection.[24-26] Patients with atherosclerotic coronary artery disease may be at increased risk for plaque rupture secondary to systemic inflammation induced by viral infection, resulting in a type I myocardial infarction.[22,24,26] Patients with coronary stents may be at increased risk of stent thrombosis during COVID-19, as the resulting systemic inflammation induces a tendency to thrombosis.[26-28] Furthermore, in susceptible older patients with coronary artery disease, type 2 myocardial infarction may result from a supply-demand mismatch owing to precipitating factors such as tachycardia (increasing myocardial oxygen demand) and systemic hypotension from vasoplegia (decreasing oxygen supply).[12,22,24-26]

Patients with COVID-19 therefore may present with acute coronary syndromes owing to plaque rupture, stent thrombosis, and/or supply-demand mismatch.[12,22] These patients may require emergency coronary angiography for diagnosis and management.[20,21] The unique considerations related to coronavirus infection in this setting must be taken into consideration, as outlined by multiple professional societies.[29-31]

Right Ventricular Failure as an Etiology for Cardiovascular Collapse

Patients with severe COVID-19 are at high risk for adult respiratory distress syndrome.[31,32] Right ventricular dysfunction is common in this setting with an estimated prevalence of 25% to 50%.[33] Although the pathophysiology may be complex and multifactorial, the etiologies include hypoxia and increased afterload.[33] Furthermore, in patients with severe COVID-19, additional factors that may compromise right ventricular function include myocarditis, vasoplegic shock, and acute coronary syndromes as outlined above.[11,12,22,24,26]

An additional exacerbating factor may be decreased right ventricular functional reserve in older patients owing to comorbidities such as smoking, diabetes, coronary artery disease, and chronic lung disease.[34,35] Patients with severe COVID-19 also are at significant risk for deep venous thrombosis and acute pulmonary embolism as a result of factors such as immobility, systemic inflammation, and disseminated intravascular coagulation.[11-13] Owing to these multiple mechanisms that can challenge the right ventricle, echocardiography to assess right ventricular function and responses to therapy will facilitate a more individualized approach to resuscitation and management in patients with severe COVID-19.[36,37]

Medical and Mechanical Therapies for Cardiovascular Collapse

Patients with severe COVID-19 are at risk for cardiovascular collapse owing to multiple mechanisms that may be cardiogenic and/or noncardiogenic. The medical management of these shock states has been discussed extensively recently in the journal.[38-40] The role of angiotensin II may have particular therapeutic application in this setting.[25,26] Specific medical therapies for COVID-19 include antivirals, chloroquine, steroids, interferon, complement inhibitors, and interleukin blockers.[12-22,24] The antivirals under investigation include ribavirin, lopinavir/ritonavir, and remdesevir.[12,22] All these experimental therapies that target the infectious process may have multiple important medication interactions that must be taken into account during patient management.[12,22,24,26] The full details of these interactions are beyond the scope of this editorial but are covered extensively in the provided references.[12,22,24,26]

The mechanical support of the circulation in this challenging setting includes extracorporeal membrane oxygenation, especially in the setting of the adult respiratory distress syndrome.[8,9] In the setting of severe cardiovascular compromise, venoarterial extracorporeal membrane oxygenation is preferred for support of the failing heart as a bridge to clinical recovery.[41,42] The unique considerations for this important therapy during the coronavirus crisis must be taken into account and have been discussed in an earlier dedicated editorial.[8,9,43-46]

Conclusions

The clinical spectrum of severe COVID-19 includes cardiovascular collapse from multiple mechanisms. The mechanisms in this challenging setting include myocarditis, pericarditis, vasoplegia, right ventricular failure, and acute coronary syndromes. The therapeutic approaches for this life-threatening presentation include aggressive medical and mechanical options, including

extracorporeal membrane oxygenation. The management of circulatory shock in this pandemic must include a focus on infection control to prevent further transmission of coronavirus.

Conflict of Interes

The author has no conflict of interest.

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References

1 Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. https://doi.org/10.1056/NEJMoa2002032, Accessed March 28th 2020. [Epub ahead of print].
2 Huang C, Wang Y, Li X, et al. Clinical features of patients with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
3 Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. Lancet Respir Med. https://doi.org/10.1016/S2213-2600(20)30079-5, Accessed March 29th 2020. [Epub ahead of print].
4 Peng PWH, Ho PL, Hota SS. Outbreak of a new coronavirus: What anaesthetists should know. Brit J Anaesth. https://doi.org/10.1016/j.bja.2020.02.008, Accessed March 30th 2020. [Epub ahead of print].
5 He H, Zhao S, Han L, et al. Anesthetic management of patients undergoing aortic dissection repair with suspected severe acute respiratory syndrome coronavirus-2 infection. J Cardiothorac Vasc Anesth. https://doi.org/10.1053/j.jvca.2020.03.021, Accessed March 29th 2020. [Epub ahead of print].
6 Augoustides JG. Perioperative echocardiography: Key considerations during the coronavirus pandemic. J Cardiothorac Vasc Anesth. https://doi.org/10.1053/j.jvca.2020.03.046, Accessed March 29th 2020. [Epub ahead of print].
7 Pisano A, Landoni G, Zangrillo A. Protecting high-risk cardiac patients during the COVID-19 outbreak. J Cardiothorac Vasc Anesth. https://doi.org/10.1053/j.jvca.2020.03.043, Accessed March 29th 2020. [Epub ahead of print].
8 Augoustides JG. Extracorporeal membrane oxygenation – crucial considerations during the coronavirus crisis. J Cardiothorac Vasc Anesth 2020;34:1720–2.
9 The Extracorporeal Life Support Organization. Guidance document: Extracorporeal membrane oxygenation for COVID-19 patients with severe cardiopulmonary failure. Available at: http://covid19.elso.org. Accessed 29 March 2020.
10 Zhao S, Ling K, Yan H, et al. Anesthetic management of patients with suspected or confirmed 2019 novel coronavirus infection during emergency procedure. J Cardiothorac Vasc Anesth 2020. https://doi.org/10.1053/j.jvca.2020.02.039; Accessed March 30th 2020.
11 World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected - interim guidance. Available at: https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected. Accessed 29 March 2020.
12 Driggin E, Madhavan MV, Bikdeli B, et al. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. J Am Coll Cardiol. https://doi.org/10.1016/j.jacc.2020.03.031, Accessed March 29th 2020. [Epub ahead of print].
13 Greenland JR, Michelow MD, Wang L, et al. COVID-19 infection – implications for perioperative and critical care physicians. Anesthesiology. https://doi.org/10.1097/ALN.0000000000003303, Accessed March 29th 2020. [Epub ahead of print].
14 Lippi G, Lavie CI, Sanchus-Gomar F. Cardiac troponin 1in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Prog Cardiovasc Dis. https://doi.org/10.1016/j.pcad.2020.03.001, Accessed March 29th 2020. [Epub ahead of print].
15 Inciardi RM, Lupi L, Zaccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020. https://doi.org/10.1001/jamacardio.2020.1096; Accessed March 29th 2020. [Epub ahead of print].
16 Madjid M, Safavi-Naeini P, Solomon SD, et al. Potential effects of coronaviruses on the cardiovascular system: A review. JAMA Cardiol. https://doi.org/10.1001/jamacardio.2020.1286, Accessed March 29th 2020. [Epub ahead of print].
17 Olejniczak M, Schwartz M, Webber E., et al. Viral myocarditis – incidence, diagnosis and management. J Cardiothorac Vasc Anesth. https://doi.org/10.1053/j.jvca.2019.12.052, Accessed March 29th 2020. [Epub ahead of print].
18 Friedrich MG, Sechtrm U, Schulz-Menger J, et al. Cardiovascular magnetic resonance in myocarditis: A JACC white paper. J Am Coll Cardiol 2009;53:1475–87.
19 Fung G, Luo H, Qiu Y, et al. Myocarditis. Circ Res 2016;118:496–514.
20 Welt FGP, Shah PB, Aronow HD, et al. Catheterization laboratory considerations during the coronavirus-19 (COVID-19) pandemic: From ACC's Interventional Council and SCAI. J Am Coll Cardiol 2020.
21 Han Y, Zeng H, Jiang H, et al. CSC expert consensus on principles of clinical management of patients with severe emergent cardiovascular disease during the COVID-19 epidemic. Circulation. https://doi.org/10.1161/CIRCULATIONAHA.120.047011, Accessed March 28th 2020. [Epub ahead of print].
22 Clerkin KJ, Fried JA, Raihelkar J, et al. Coronavirus disease 2019 (COVID-19) and cardiovascular disease. Circulation. https://doi.org/10.1161/CIRCULATIONAHA.120.046941, Accessed March 28th 2020. [Epub ahead of print].
23 Oudit GY, Kassiri Z, Jiang C, et al. SARS –coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest 2009;39:618–25.
24 Zheng YY, Ma YT, Zhong JY, et al. COVID-19 and the cardiovascular system. Nat Rev Cardiol. https://doi.org/10.1038/s41569-020-0360-5, Accessed March 29th 2020. [Epub ahead of print].
25 Chow JH, Mazzeffi MA, McCurdy MT. Angiotensin II for the treatment of COVID-19-related vasodilatory shock. Anesth Analg. https://doi.org/10.1213/ANE.0000000000004825, Accessed March 29th 2020. [Epub ahead of print].
26 Xiong TY, Redwood S, Prendergast B, et al. Coronaviruses and the cardiovascular system: Acute and long-term implications. Eur Heart J. https://doi.org/10.1093/eurheartj/ehaa231, Accessed March 29th 2020. [Epub ahead of print].
27 Kuster GM, Pfister O, Burkhard T, et al. SARS-CoV2: Should inhibitors of the renin-angiotensin system be withdrawn in patients with COVID-19? Eur Heart J. https://doi.org/10.1093/eurheartj/ehaa235, Accessed March 29th 2020. [Epub ahead of print].
28 Libby P, Simon D. Inflammation and thrombosis: The clot thickens. Circulation 2001;103:1716–20.
29 Chen X, Liu Y, Gong Y, et al. Perioperative management of patients infected with the novel coronavirus: Recommendations from the joint task force of the Chinese Society of Anesthesiology and the Chinese Association of Anesthesiologists. Anesthesiology. https://doi.org/10.1097/ALN.0000000000003301, Accessed March 30th 2020. [Epub ahead of print].
30 Bowdle A, Munoz-Price LS. Preventing infection of patients and healthcare workers should be the new normal in the era of novel coronavirus epidemics. Anesthesiology. https://doi.org/10.1097/ALN.0000000000003295, Accessed March 30th 2020. [Epub ahead of print].
31 Meng L, Qui H, Wan L, et al. Intubation and ventilation amid the COVID-19 outbreak: Wuhan's experience. Anesthesiology. https://doi.org/10.1097/ALN.0000000000003296, Accessed March 30th 2020. [Epub ahead of print].
32 Ramanathan K, Antognimi D, Combes A, et al. Planning and provision of ECMO services for severe ARDS during the COVID-19 pandemic and other outbreaks of emerging infectious diseases. Lancet Resp Med. https://doi.org/10.1016/S2213-2600(20)30121-1, Accessed March 30th 2020. [Epub ahead of print].
33 Zochios V, Parhar K, Tunnicliffe W, et al. The right ventricle in ARDS. Chest 2017;152:181–93.

34 Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: A systematic review and meta-analysis. Int J Infect Dis. https://doi.org/10.1016/j.ijid.2020.03.017, Accessed March 30th 2020. [Epub ahead of print].
35 Guan WJ, Liang WH, Zhao YI, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A nationwide analysis. Eur Resp J. https://doi.org/10.1183/13993003.00547-2020, Accessed March 30th 2020. [Epub ahead of print].
36 Zochios V, Roscoe A. Echocardiography as an adjunct in venovenous extracorporeal membrane oxygenation. J Cardiothorac Vasc Anesth 2018;32:379–80.
37 Nasim R, Sukhal S, Ramakrishna H. Management strategies for severe and refractory acute respiratory distress syndrome: Where do we stand in 2018? J Cardiothorac Vasc Anesth 2019;33:2589–94.
38 Monaco F, Di Prima AL, Kim JH, et al. Management of challenging cardiopulmonary bypass separation. J Cardiothorac Vasc Anesth. https://doi.org/10.1053/j.jvca.2020.02.038, Accessed March 30th 2020. [Epub ahead of print].
39 Ortoleva J, Shapeton A, Vanneman M, et al. Vasoplegia during cardiopulmonary bypass: Current literature and rescue therapy options. J Cardiothorac Vasc Anesth. https://doi.org/10.1053/j.jvca.2019.12.013, Accessed March 30th 2020.
40 Shaefi S, Mittel A, Klick J, et al. Vasoplegia after cardiovascular procedures – pathophysiology and targeted therapy. J Cardiothorac Vasc Anesth 2018;32:1013–22.
41 Monaco F, Belletti A, Bove T, et al. Extracorporeal membrane oxygenation: Beyond cardiac surgery and the intensive care unit – unconventional uses and future perspectives. J Cardiothorac Vasc Anesth 2018;32:1955–70.
42 Alexis-Ruiz A, Ghadimi K, Raiten J, et al. Hypoxia and complications of oxygenation in extracorporeal membrane oxygenation. J Cardiothorac Vasc Anesth 2019;33:1375–81.
43 MacLaren G, Fisher D, Brodie D, et al. Preparing for the most critically ill patients with COVID 19: The potential role of extracorporeal membrane oxygenation. JAMA. https://doi.org/10.1001/jama.2020.2342, Accessed March 29th 2020.
44 Ronva C, Navalesi P, Vintcent JL. Coronavirus epidemic: Preparing for extracorporeal organ support in intensive care. Lancet Resp Med 2020;8:240–1.
45 Chopra V, Toner E, Waldhorn R, et al. How should US hospitals prepare for coronavirus disease 2019 (COVID-19)? Ann Int Med. https://doi.org/10.7326/M20-0907, Accessed March 29th 2020. [Epub ahead of print].
46 Swerdlow D, Finelli L. Preparation for possible sustained transmission of 2019 novel coronavirus: Lessons from previous epidemics. JAMA 2020;323:1129–30.