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A care pathway for the cardiovascular complications of COVID-19: Insights from an institutional response

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The infection caused by severe acute respiratory syndrome coronavirus-2, or COVID-19, can result in myocardial injury, heart failure, and arrhythmias. In addition to the viral infection itself, investigational therapies for the infection can interact with the cardiovascular system. As cardiologists and cardiovascular service lines will be heavily involved in the care of patients with COVID-19, our division organized an approach to manage these complications, attempting to balance resource utilization and risk to personnel with optimal cardiovascular care. The model presented can provide a framework for other institutions to organize their own approaches and can be adapted to local constraints, resource availability, and emerging knowledge. (Am Heart J 2020;225:3-9.)

The infection caused by severe acute respiratory syndrome coronavirus-2, or COVID-19, interacts with the cardiovascular system in numerous ways. Patients with a history of cardiovascular disease more commonly suffer critical illness following infection,[1,2] COVID-19 can directly cause cardiac complications (including myocardial injury, heart failure [HF], and arrhythmias),[3,4] and potential therapies for COVID-19 can have adverse cardiac effects.[5] To date, the overall case fatality rate for patients with COVID-19 has exhibited variation, perhaps related in part to utilization and rates of testing, testing operating characteristics, availability of health care resources, and/or clinical characteristics of the population.[6-8] Regardless of the causes for the heterogeneity, mortality rates appear to be higher among those with cardiovascular disease.[3,7]

As COVID-19 cases began to accelerate in the United States, it was clear to our institution, and more specifically our cardiology division, that (1) cardiologists would be playing an important role in the care of affected patients and (2) preparations at a health system level were necessary to organize our response. Thus, to streamline care, limit risk to personnel, ensure provision of limited resources (including diagnostics, invasive procedures, and service lines), and align clinical care across multiple divisions, we felt it necessary to develop a clinical care pathway at our institution (Figure 1) to organize our approach to these cardiovascular problems and complications. This pathway is (1) based on available evidence (which we present in the following) and expert opinion, (2) continuously being iterated by our division, and (3) not an authoritative document but rather may serve as a guide for other institutions from which to help organize their responses.

Myocardial injury

Troponin elevations may be present in anywhere from 7% to 28% of all patients who are hospitalized with COVID-19 but appear to be more common in patients with critical illness and serve as an independent risk factor for mortality.[2-4,9-12] Two recent reports from Wuhan (one with 187 and another with 415 patients) found *myocardial injury* (defined as high-sensitivity troponin elevations greater than the 99th percentile of upper reference limit) to be present in 27.8% and 19.7% of patients, respectively.[3,10] Patients with myocardial injury were older, had higher rates of comorbid conditions (including hypertension, coronary artery disease, history of cardiomyopathy, and chronic obstructive pulmonary disease), and had higher serum concentrations of N-terminal pro–B-type natriuretic peptide (NT-pBNP) compared with those without myocardial injury.[3,10] Notably,

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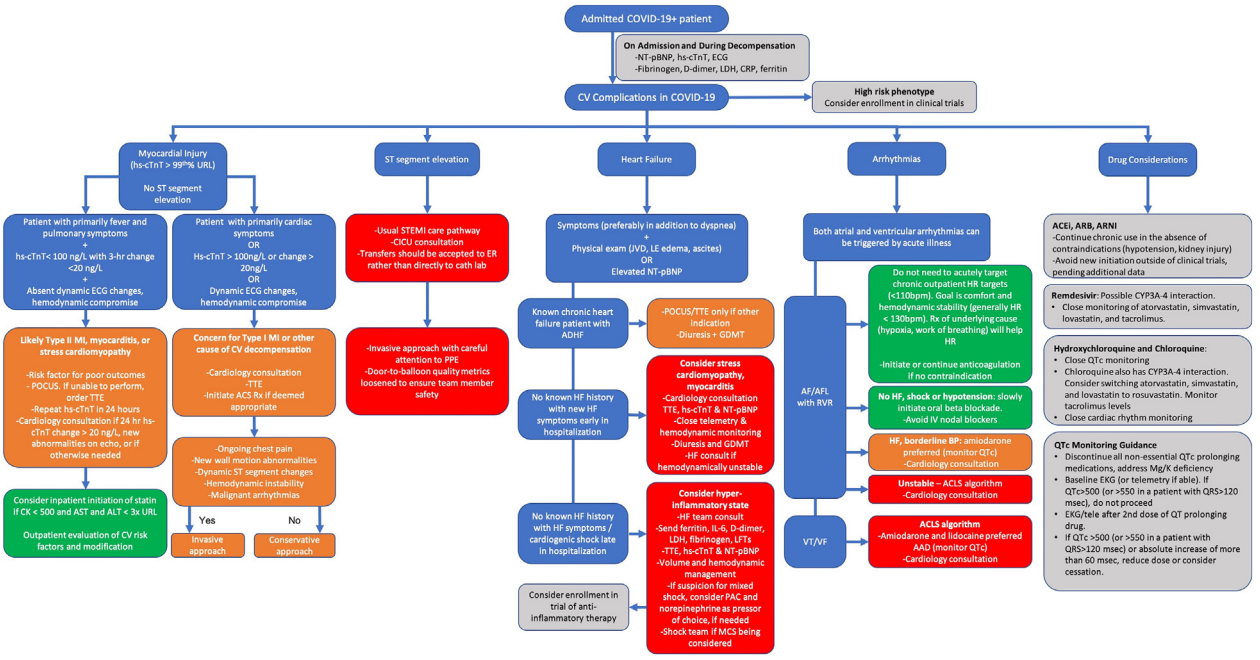
Figure 1



A framework for addressing cardiovascular complications associated with COVID-19. Infection with SARS-CoV-2 can result in myocardial injury, HF, and arrhythmias, and putative treatments can have interactions with the cardiovascular system. A framework for approaching these complications is presented.*AAD*, antiarrhythmic drug; *ACLS*, advanced cardiac life support; *ACEi*, angiotensin-converting enzyme inhibitor; *ACS*, acute coronary syndrome; *ADHF*, acute decompensated heart failure; *AF*, atrial fibrillation; *AFL*, atrial flutter; *ALT*, alanine aminotransferase; *ARB*, angiotensin receptor blocker; *ARNI*, angiotensin receptor-neprilysin inhibitor; *AST*, aspartate aminotransferase; *BP*, blood pressure; *bpm*, beats per minute; *CICU*, cardiac intensive care unit; *CK*, creatinine kinase; *COVID-19*, coronary virus disease 2019; *CRP*, C-reactive protein; *CV*, cardiovascular; *CYP*, cytochrome P450; *ECG*, electrocardiogram; *ER*, emergency room; *GDMT*, guideline-directed medical therapy; *HF*, heart failure; *HR*, heart rate; *hs-cTnT*, high-sensitivity cardiac troponin T; *IL-6*, interleukin-6; *IV*, intravenous; *JVD*, jugular venous distension; *K*, potassium; *LDH*, lactate dehydrogenase; *LE*, lower extremity; *LFT*, liver function test; *MCS*, mechanical circulatory support; *Mg*, magnesium; *MI*, myocardial infarction; *NT-pBNP*, N-terminal pro–B-type natriuretic peptide; *PPE*, personal protective equipment; *PAC*, pulmonary artery catheter; *POCUS*, point-of-care ultrasound; *QTc*, corrected QT interval; *RVR*, rapid ventricular response; *Rx*, treatment; *STEMI*, ST-segment elevation myocardial infarction; *TTE*, transthoracic echocardiogram; *URL*, upper reference limit; *VF*, ventricular fibrillation; *VT*, ventricular tachycardia.

only 13.4% of patients with myocardial injury presented with chest pain (compared with 0.9% in those without).[10] Most importantly, patients with myocardial injury had significantly worse outcomes in these studies: they more commonly developed acute respiratory distress syndrome (58%/59% vs 12%/15%), more frequently had ventricular tachycardia (VT) or ventricular fibrillation (VF) (17% vs 2%), and had much higher mortality (60%/51% vs 9%/5%) compared with those without.[3,10] Myocardial injury was an independent risk factor for mortality after multivariable adjustment,[10] and, in patients with both myocardial injury and underlying cardiovascular disease, in-hospital mortality was staggering at 69.4%.[3]

Initial reports suggest at least 2 possible patterns of myocardial injury.[13,14] The first is an early presentation with primary cardiovascular symptoms along with echocardiographic and electrocardiographic changes.[15-19] These "early presenters" may have stress cardiomyopathy, supply-demand mismatch (type II myocardial infarction), or myocarditis, sometimes mimicking ST-segment elevation myocardial infarction (STEMI).[16-18] In one case report of fulminant myocarditis, a patient was successfully treated with methylprednisolone (200 mg/d) and immunoglobulin (20 g/d) for 4 days along with standard management for cardiogenic shock with subsequent recovery of systolic function.[15] However, the presence of COVID-19 does not obviate the risk many of our patients face for plaque-rupture–mediated (type I) myocardial infarction (MI) and may even serve as an exacerbating factor (as has been seen in influenza).[20] A separate rise in troponin has been observed later in the disease course (between day 7 and 14 of illness) concurrently with other markers of systemic inflammation (interleukin-6, ferritin, C-reactive protein) and may represent cytokine-mediated myocardial dysfunction[4,14,21] or possibly right ventricular strain in the setting of severe pulmonary dysfunction.

Our algorithm (Figure 1) recommends evaluation of cardiac biomarkers of all confirmed COVID-19 patients requiring admission to the hospital for prognostication and during any acute decompensation to screen for cardiac dysfunction. Although our recommendation is different than a recent report by the American College of Cardiology,[22] where the only recommended testing of cardiac troponin is in cases of suspected acute MI, we do not interpret every rise in cardiac troponin as indicative of a type I MI and atherosclerotic plaque rupture. As outlined on the left side of Figure 1, if patients have (1) primarily pulmonary symptoms and fever, (2) low-level elevation of high-sensitivity cardiac troponin T (hs-cTnT) with minimal 3-hour change, and (3) no other high-risk features (dynamic electrocardiographic [ECG] changes, hemodynamic compromise), we temporarily categorize these people as having myocardial injury likely due to supply-demand mismatch, myocarditis, or stress cardiomyopathy.

Point-of-care ultrasound (POCUS) to assess left ventricular ejection fraction by capable frontline providers is ideal to prevent additional resource utilization. To limit staff exposure and reduce the chance that echocardiography machines serve as vectors for disease transmission, we have stationed artificial intelligence–enabled POCUS devices on dedicated COVID-19 wards to assist providers with image acquisitions, which can then be read remotely by trained staff. However, limited echocardiograms can be ordered if POCUS is not available or if there is insufficient training/expertise in this modality. Following baseline evaluation, we recommend repeat assessment of cardiac biomarkers in 24 hours to ensure that there is no significant rise. If troponin levels are stable or decreasing and echocardiogram is unremarkable, we do not recommend routine cardiology consultation unless otherwise indicated. Repeat troponin assessments at routine intervals (every 24 to 72 hours) may be considered for ongoing prognostication or early detection of deterioration. Inpatient initiation of statin therapy may be considered in patients with risk factors for atherosclerotic disease (if no significant liver or muscle injury), although no strong data yet exist for initiation specifically for COVID-19. We recommend that this group of patients have outpatient evaluation for risk factor assessment and modification.

On the other hand, if patients present with primarily cardiac symptoms, significantly elevated or rapidly changing hs-cTnT, dynamic ECG changes, or hemodynamic compromise, these patients are high risk and warrant echocardiogram and urgent cardiology consultation for assessment of type I MI or other acute cardiovascular complications (eg, fulminant myocarditis, cardiac tamponade). If type I MI is suspected, acute coronary syndrome therapies should be initiated. Ongoing chest pain, new wall motion abnormalities, dynamic ECG changes, and hemodynamic or electrical instability should prompt consideration of an early invasive approach, as resources are available, whereas low-risk non-STEMI may be treated conservatively to minimize personnel exposure.[23] In conjunction with echocardiographic assessment of ventricular function, we are also exploring the role of coronary computed tomography angiography to further risk stratify patients in this population.[24]

Of note, the troponin values we have chosen (baseline hs-cTnT >100 ng/L, change of 20 ng/L) are higher than the usual values used at our institution (upper reference limit 19 ng/L, change of 7 ng/L) to establish a diagnosis of acute cardiac injury but reflect our best attempt to balance the use of limited resources while still capturing patients who may benefit from cardiology input. These specific cutoffs (1) are based on expert opinion, (2) are dynamic and still a subject of ongoing discussion in our division, and (3) will be continuously revisited and updated as both evidence and our experience with COVID-19 grow.

Patients presenting with ST-segment elevation on ECG should prompt an institution's usual STEMI care pathway. If these are known or suspected COVID-19 patients presenting from outside institutions, they should be directed to the dedicated staging areas in the emergency department rather than directly to the cardiac catheterization laboratory, allowing more preparation time to comply with enhanced infection control measures. Despite case reports of patients with COVID-19 presenting with a clinical picture mimicking STEMI without findings of obstructive coronary disease on coronary angiography,[16,17,25] our protocol currently recommends an invasive approach to rule out this this life-threatening diagnosis,[23] with meticulous attention to team member safety and use of personal protective equipment. Standard quality metrics (door-to-balloon time) should be eased or suspended during this period to prevent penalization of safety initiatives.[26] Currently, our institution does not anticipate being strained to the point of needing fibrinolytic therapy rather than an early invasive strategy for STEMI, but this has been done in other countries where health care systems exceeded local patient care capacity.[27] Overall, our recommendations are consistent with a recent consensus statement by the Society for Cardiovascular Angiography and Interventions, American College of Cardiology, and American College of Emergency Physicians.[28] Providers caring for patients with COVID-19 and STEMI should consider enrollment in an ongoing registry sponsored by the Society for Cardiovascular Angiography and Interventions and the Canadian Association of Interventional Cardiology, the North American COVID-19 ST-Segment Elevation Myocardial Infarction Registry, to improve our understanding of this condition.

Heart failure

Heart failure has been reported to complicate approximately 23% of admissions in a cohort from China and was more commonly seen among intensive care unit patients (52%).[4] However, prior series have limited granular

cardiovascular phenotyping, leaving it unclear whether reported cases represented exacerbations of existing HF or new-onset cardiomyopathy.[5] Currently, there are several postulated phenotypes of HF in COVID patients[29]:

1. Patients with pre-existing HF with diastolic dysfunction or chronically elevated end-diastolic pressures who develop capillary leak, or develop exacerbation of HF in the setting of higher sympathetic drive or fluid administration.[17,29]
2. An early presentation with new systolic dysfunction (with associated early troponin elevation) possibly related to myocarditis[15-19] or stress cardiomyopathy.
3. A later decompensation that accompanies systemic inflammation from a cytokine storm-like syndrome.[14,17,21,29,30]

For patients with chronic HF who have an exacerbation in the context of COVID-19 infection, our algorithm (Figure 1) encourages management with diuresis and guideline-directed therapy, including continuing use of previously prescribed angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), and angiotensin receptor-neprilysin inhibitors (ARNI) in the absence of acute contraindications (hypotension, acute kidney injury). Although it has been hypothesized that angiotensin pathway inhibitors may increase viral cell entry, it has also been postulated that these agents may mitigate potential deleterious increases in angiotensin II activity with severe acute respiratory syndrome coronavirus-2 infection.[31-33] Until additional evidence is available, we advise continuation of these agents, in line with recommendations from major cardiovascular societies.[34,35] Routine echocardiography is not encouraged in the absence of other indications (eg, new murmur, hemodynamic instability) to limit personnel exposure.

Patients presenting with new systolic dysfunction (eg, stress cardiomyopathy, myocarditis) warrant cardiology consultation, echocardiography, and assessment of cardiac biomarkers. If these patients are hemodynamically stable, we recommend close monitoring of hemodynamics and telemetry, diuresis (as needed), and guideline-directed therapy, except for new initiation of ACEi, ARB, or ARNI outside of clinical trials. Once patients are recovering, these agents can be initiated toward the end of hospitalization with close monitoring or during early outpatient follow-up. If patients are hemodynamically unstable (eg, fulminant myocarditis), an advanced HF team should be consulted for recommendations on hemodynamic management including consideration of mechanical support. Given the lack of clear benefit, immunomodulatory therapy (eg, steroids) is not universally recommended but can be considered on a case-by-case basis.

Patients presenting with HF symptoms or cardiogenic shock later in their hospitalization, generally around the time of development of progressive hypoxia and acute respiratory distress syndrome, may have myocardial dysfunction due to a hyperinflammatory state.[14,17,21,29,30] We recommend consulting the advanced HF team, obtaining an echocardiogram, and assessing biomarkers of inflammation (interleukin-6, lactate dehydrogenase, liver function tests, fibrinogen, D-dimer) and of myocardial stress and injury (hs-cTnT and NT-pBNP). Management of hemodynamics and achievement of euvolemia are pillars of treatment. If patients are critically ill with undifferentiated shock, we recommend tailoring therapy with pulmonary artery catheter guidance and using norepinephrine as the initial vasoactive agent.[36] Mechanical circulatory support can be considered, although data are very limited.[17,37,38]

Arrhythmias

Arrhythmias have been reported in 17% of those infected in a small series from Wuhan, with higher prevalence (44%) in the intensive care unit,[12] but remain poorly characterized. Atrial fibrillation seems to be a common comorbidity among patients who are at risk for poor outcomes,[6] can certainly be triggered by severe respiratory infections, and is a well-recognized complication of sepsis.[39] A separate series of 187 patients from Wuhan reported a 5.9% incidence of ventricular arrhythmias (VT/VF), occurring primarily among patients with elevated cardiac troponin.[3] As with HF, arrhythmias in the setting of COVID-19 infection can arise through several mechanisms, including, but not limited to, exacerbation of prior known (or previously subclinical) arrhythmias, de novo arrhythmia from myocardial inflammation or injury, drug therapy, or any combination of these factors.

For the time being, there are no special considerations or treatment algorithms specifically for arrhythmias related to COVID-19. Our algorithm provides basic guidance to frontline care providers who may be unfamiliar with managing arrhythmias. The first principle for atrial arrhythmias presenting with rapid ventricular response (RVR) in the setting of COVID-19 is that there is no need to acutely lower heart rates in these patients if they are hemodynamically stable. Easing their respiratory distress with oxygen and treating their fever may decrease some of their drive for RVR. Furthermore, we recommend that patients be initiated on appropriate anticoagulation in the absence of coagulopathy, bleeding, or other contraindications. As we learn more about potential prothrombotic complications of COVID-19, we anticipate that anticoagulation maybe indicated in additional specific subgroups (those at risk for venous thromboembolism), but data are currently limited.

To avoid iatrogenic hypotension, bradycardia, or decompensation of systolic HF, we recommend avoidance of intravenous calcium channel blockers. If patients are hemodynamically stable and without evidence of HF,

oral β-blockers can be slowly introduced. If there is concern for acute HF, hypotension, or other hemodynamic derangements, amiodarone is our antiarrhythmic of choice. To date, we are unaware of any specific interaction between amiodarone and COVID-19 that could result in any higher incidence or severity of amiodarone-mediated pulmonary disease, although data are limited. Patients presenting with unstable atrial arrhythmias or malignant ventricular arrhythmias should be treated per advanced cardiac life support guidelines with immediate cardiology consultation.

Therapeutics

The mainstay of treatment for COVID-19 infection remains supportive therapy, but clinical trials have proliferated in response to this pandemic. Patients with COVID-19 who suffer a cardiovascular complication are high-risk patients and should be screened for enrollment in clinical trials. In our "Drug Considerations" heading, we provide some guidance around possible cardiovascular interactions with these therapeutic agents, focusing on those that are most likely to be used at our institution.

There are several trials of the antiviral remdesivir in patients across the spectrum of disease severity (NCT04280705, NCT04292730, NCT04292899). Remdesivir interacts with cytochrome P450 (CYP)-3A4, but it is unclear if this results in clinically meaningful drug interactions.[40] We currently recommend close monitoring for drug interactions in patients taking other CYP3A4 substrates, including atorvastatin, simvastatin, lovastatin, and tacrolimus.

There are several phase III trials assessing efficacy of the antimalarial agents chloroquine and hydroxychloroquine for treatment of COVID-19 (NCT04321278, NCT04321993, NCT04316377, NCT04322123). These agents are well known to cause QT prolongation[5]; thus, our algorithm offers simplified guidance to frontline providers for monitoring the QT interval in patients being treated with these agents, either in randomized trials or in an off-label manner.

Finally, various anti-inflammatory agents, including interleukin-6 inhibitors (NCT04310228), colchicine (NCT04322682), and steroids (NCT04323592), are currently under investigation and should be considered for any patient suffering from the severe inflammatory phenotype that can be seen in later stages of disease. Data on novel treatment strategies, such as convalescent plasma,[41] continue to emerge and can be iterated into the framework as appropriate.

Conclusions

The spread of COVID-19 in a community can overwhelm health systems. To prepare for a possible surge in COVID-related hospitalizations, our division first implemented primarily telehealth visits and triaged procedures for the cardiac catheterization and electrophysiology laboratories. However, as it became clear that cardiovascular complications may be common among the sickest patients with COVD-19, we felt it necessary to develop a clinical approach to treating these patients, balancing team safety and resource utilization with optimal patient care. We present here a consensus framework based on available evidence and expert opinion. It has helped organize our internal discussions around management of cardiovascular complications and provides clear guidance to providers on the frontlines who may be less familiar with the care of cardiovascular patients. As with much of our knowledge surrounding COVID-19, this model continues to evolve and can be adapted to emerging evidence but is presented here to serve as a scaffold that can be used and modified by other institutions depending on local resources, constraints, and treatment preferences.

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References

1. Chen C, Chen C, Yan JT, et al. Analysis of myocardial injury in patients with COVID-19 and association between concomitant cardiovascular diseases and severity of COVID-19. Zhonghua Xin Xue Guan Bing Za Zhi 2020;48, E008.

2. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol 2020;109(5):531-8.
3. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020, https://doi.org/10.1001/jamacardio.2020.1017.
4. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054-62.
5. 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 2020;27204.
6. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA 2020;323(18):1775-6.
7. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020;323(13):1239-42, https://doi.org/10.1001/jama.2020.2648.
8. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized With COVID-19 in the New York City Area. JAMA 2020, https://doi.org/10.1001/jama.2020.6775.
9. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): evidence from a meta-analysis. Prog Cardiovasc Dis 2020, https://doi.org/10.1016/j.pcad.2020.03.001.
10. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020, https://doi.org/10.1001/jamacardio.2020.0950.
11. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497-506.
12. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323(11):1061-9.
13. Bonow RO, Fonarow GC, O'Gara PT, et al. Association of coronavirus disease 2019 (COVID-19) with myocardial injury and mortality. JAMA Cardiol 2020, https://doi.org/10.1001/jamacardio.2020.1105.
14. Clerkin KJ, Fried JA, Raikhelkar J, et al. Coronavirus disease 2019 (COVID-19) and cardiovascular disease. Circulation 2020, https://doi.org/10.1161/CIRCULATIONAHA.120.046941.
15. Hu H, Ma F, Wei X, et al. Coronavirus fulminant myocarditis saved with glucocorticoid and human immunoglobulin. Eur Heart J 2020, https://doi.org/10.1093/eurheartj/ehaa190.
16. 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.
17. Fried JA, Ramasubbu K, Bhatt R, et al. The variety of cardiovascular presentations of COVID-19. Circulation 2020, https://doi.org/10.1161/CIRCULATIONAHA.120.047164.
18. Sala S, Peretto G, Gramegna M, et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. Eur Heart J 2020, https://doi.org/10.1093/eurheartj/ehaa286.
19. Zeng J-H, Liu Y-X, Yuan J, et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. Infection 2020, https://doi.org/10.1007/s15010-020-01424-5.
20. Kwong JC, Schwartz KL, Campitelli MA, et al. Acute myocardial infarction after laboratory-confirmed influenza infection. N Engl J Med 2018;378(4):345-53.
21. Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: a clinical-therapeutic staging proposal. J Heart Lung Transplant 2020;39(5):P405-7, https://doi.org/10.1016/j.healun.2020.03.012.
22. Januzzi J. *Troponin and BNP use in COVID-19*. Cardiology Magazine, ACC. 2020.
23. Welt FGP, Shah PB, Aronow HD, et al. Catheterization laboratory considerations during the coronavirus (COVID-19) pandemic: from ACC's Interventional Council and SCAI. J Am Coll Cardiol 2020;75(18), https://doi.org/10.1016/j.jacc.2020.03.021.
24. Linde JJ, Kelbaek H, Hansen TF, et al. Coronary CT angiography in patients with non–ST-segment elevation acute coronary syndrome. J Am Coll Cardiol 2020;75(5):453-63.
25. Bangalore S, Sharma A, Slotwiner A, et al. ST-segment elevation in patients with COVID-19—a case series. New England Journal of Medicine 2020, https://doi.org/10.1056/NEJMc2009020.
26. Tam CF, Cheung KS, Lam S, et al. Impact of coronavirus disease 2019 (COVID-19) outbreak on ST-segment-elevation myocardial infarction care in Hong Kong. China Circ Cardiovasc Qual Outcomes 2020;13(4), e006631.
27. Zeng J, Huang J, Pan L. How to balance acute myocardial infarction and COVID-19: the protocols from Sichuan Provincial People's Hospital. Intensive Care Med 2020, https://doi.org/10.1007/s00134-020-05993-9.
28. Mahmud E, Dauerman HL, Welt FG, et al. Management of acute myocardial infarction during the COVID-19 pandemic. J Am Coll Cardiol 2020;27295.
29. Mehra MR, Ruschitzka F. COVID-19 illness and heart failure. JACC: Heart Failure 2020;1248.
30. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395(10229):1033-4.
31. Bavishi C, Maddox TM, Messerli FH. Coronavirus disease 2019 (COVID-19) infection and renin angiotensin system blockers. JAMA Cardiol 2020, https://doi.org/10.1001/jamacardio.2020.1282.
32. Vaduganathan M, Vardeny O, Michel T, et al. Renin-angiotensin-aldosterone system inhibitors in patients with COVID-19. New England Journal of Medicine 2020;382(17):1653-9.
33. Zhang P, Zhu L, Cai J, et al. Association of inpatient use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. Circ Res 2020, https://doi.org/10.1161/CIRCRESAHA.120.317134.
34. Peng YD, Meng K, Guan HQ, et al. Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV. Zhonghua Xin Xue Guan Bing Za Zhi 2020;48, E004.
35. Patel AB, Verma A. *COVID-19 and angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: what is the evidence? JAMA*. 2020.
36. Poston JT, Patel BK, Davis AM. Management of critically ill adults with COVID-19. JAMA 2020;323(18):1839-41, https://doi.org/10.1001/jama.2020.4914.
37. MacLaren G, Fisher D, Brodie D. Preparing for the most critically ill patients with COVID-19: the potential role of extracorporeal membrane oxygenation. JAMA 2020;323(13):1245-6, https://doi.org/10.1001/jama.2020.2342.

38. Ramanathan K, Antognini 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 Respir Med 2020;8(5):518-26, https://doi.org/10.1016/S2213-2600(20)30121-1.
39. Walkey AJ, Wiener RS, Ghobrial JM, et al. Incident stroke and mortality associated with new-onset atrial fibrillation in patients hospitalized with severe sepsis. JAMA 2011;306(20):2248-54.
40. McCreary EK, Pogue JM, Pharmacists obotSoID. *COVID-19 treatment: a review of early and emerging options.* Open Forum Infectious Diseases. 2020.
41. Shen C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA 2020;323(16):1582-9, https://doi.org/10.1001/jama.2020.4783.