Circulation: Arrhythmia and Electrophysiology

SPECIAL REPORT

Cardiac Arrhythmias in COVID-19 Infection

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Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the virus that causes COVID-19, has affected >1 million people worldwide.[1] As of this writing, >60 000 people have died as a result of this virus in the United States alone,[2] and New York City has over 167 000 confirmed coronavirus disease 2019 (COVID-19) cases, the highest number of any city in the United States. New York City is now considered a COVID-19 epicenter. While this disease predominantly affects the lungs, often leading to pneumonia and acute respiratory distress syndrome, adverse effects on the heart have also been described.[3] Electrophysiological issues are increasingly recognized as a disease manifestation, with one study reporting arrhythmias in 44% of individuals with severe illness.[4] Sudden cardiac death has also been described anecdotally.[5] However, the type and severity of arrhythmias associated with COVID-19 have not been described. In this article, we present 4 cases that highlight the spectrum of arrhythmias observed in patients with COVID-19 infection. New York-Presbyterian/Columbia University Irving Medical Center is located in the New York City COVID-19 epicenter and herein, we describe the clinical presentations we have seen and discuss decision-making regarding therapeutic options, acknowledging difficulties pertaining to resource conservation and healthcare worker safety.

This study was approved by the Columbia University Institutional Review Board, and procedures followed were in accordance with institutional guidelines. Due to the nature of the study, written informed consent was not required. The authors declare that all supporting data are available within the article.

CASE 1: HIGH-GRADE ATRIOVENTRICULAR BLOCK

A 76-year-old man with a history of diabetes mellitus type II and hypertension presented with progressive dyspnea, weakness, and myalgias for 6 days. On admission, vital signs were remarkable for a blood pressure of 130/61 mm Hg, heart rate of 44 bpm, and oxygen saturation at 76% on room air, which improved to 93% with a nonrebreather mask. Chest radiography (CXR) demonstrated multifocal pneumonia and an enlarged cardiac silhouette (Figure 1A). Transthoracic echocardiography showed normal left ventricle ejection fraction (LVEF), and initial ECG demonstrated sinus bradycardia with high-grade atrioventricular block with likely atrioventricular Wenckebach and a right bundle branch block (Figure 1B). Admission labs were notable for high-sensitivity troponin T (hs-TropT) of 36 ng/L, creatinine of 1.5 mg/dL, venous lactate of 2.0 mmol/L, normal electrolyte levels, and elevated inflammatory markers (ferritin 1091 ng/mL, CRP [C-reactive protein] 69 ng/L). SARS-CoV-2 testing was positive. Continuous intravenous dopamine infusion was initiated, and the patient's heart rate improved with resolution of the complete heart block. He was found to have a deep vein thrombosis and started on systemic anticoagulation. He developed progressive hypoxemia, requiring intubation and intensive care unit admission, where he ultimately expired.

This patient presented with hypoxemic respiratory failure and atrioventricular block complicated by renal and hepatic dysfunction, which improved with dopamine infusion. Temporary venous pacing was not chosen as first-line therapy due to constraints regarding need for an

Key Words: atrial fibrillation ■ cardiac arrhythmias ■ COVID-19 ■ heart block ■ heart rate ■ pulseless electrical activity ■ Sars-CoV-2 ■ torsades de pointes

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This manuscript was sent to N.A. Mark Estes III, MD, Senior Guest Editor, for review by expert referees, editorial decision, and final disposition.

For Sources of Funding and Disclosures, see page 584.

Circulation: Arrhythmia and Electrophysiology is available at www.ahajournals.org/journal/circep

Nonstandard Abbreviations and Acronyms

AF	atrial fibrillation
COVID-19	coronavirus disease 2019
CRP	C-reactive protein
CXR	chest radiography
hs-TropT	high-sensitivity troponin T
LVEF	left ventricle ejection fraction
NT-pro BNP	N-terminal pro-B-type natriuretic peptide
SARS-CoV-2	severe acute respiratory syndrome coronavirus-2

intensive care unit bed for monitoring and personal protective equipment for an invasive procedure. Dopamine was chosen instead of isoproterenol to avoid inadvertent β-2 receptor agonism.[6,7] The mechanism underlying the atrioventricular block, in the absence of metabolic disarray, is uncertain but suggests diffuse conduction system involvement in the atrioventricular node, His bundle, and Purkinje system. Myocarditis due to COVID-19 has been reported,[8] and elevation in cardiac and inflammatory markers may reflect a direct effect of the virus on the cardiac conduction system, although one report on cardiac biopsy of a patient with COVID-19 myocarditis, showed absence of the SARS-CoV-2 genome within the myocardium.[9] Hypoxia may lead to conduction defects, potentially mediated via endogenous adenosine[10]; however, treatment of the patient's hypoxia did not resolve the atrioventricular block as would have been expected if poor oxygenation were the driving cause.[11] This case highlights atrioventricular block as a potential manifestation of COVID-19, and despite successful amelioration of the bradycardia with dopamine infusion without transvenous pacing; the pulmonary process independently deteriorated. We have had at our center, at least one patient, an 82 year old man with COVID infection who was found during his sixth day of hospitalization to have symptomatic bradycardia and high degree atrioventricular block that eventually required permanent pacemaker implantation on hospital day 9.

CASE 2: ATRIAL FIBRILLATION

A 56-year-old with no past medical history presented with 2 days of fever and dyspnea was found be hypoxic with oxygen saturation of 89% on room air. CXR showed bilateral lower lobe opacities (Figure 2A) and ECG demonstrated normal sinus rhythm. He tested positive for SARS-CoV-2. Labs were notable for a ferritin of 8000 ng/mL and CRP 84 ng/L. He was given hydroxychloroquine and azithromycin for 4 days, but his respiratory status rapidly declined, and he required intubation and intensive care unit admission. Intravenous tocilizumab, intravenous immunoglobulin 400 mg/kg×5 doses, and compassionate use of Remedesivir were administered. He was maintained on low dose phenylephrine for blood pressure support. On hospital day 4, he developed frequent premature atrial beats, and subsequently developed new onset paroxysmal atrial fibrillation (AF) on day 7. Transthoracic echocardiography showed normal LVEF, normal atrial size, and negative hs-TropT. On intensive care unit day 10, he developed hemodynamically unstable AF with rapid ventricular rates refractory to intravenous amiodarone and intravenous metoprolol (Figure 2B). Systemic anticoagulation was initiated with intravenous heparin before emergent cardioversion. He converted to normal sinus rhythm, however, LVEF decreased from 60% to 45% and respiratory failure worsened prompting cannulation for veno-venous extracorporeal membrane oxygenation. Course was further complicated by gram-negative bacteremia secondary to acute cholecystitis

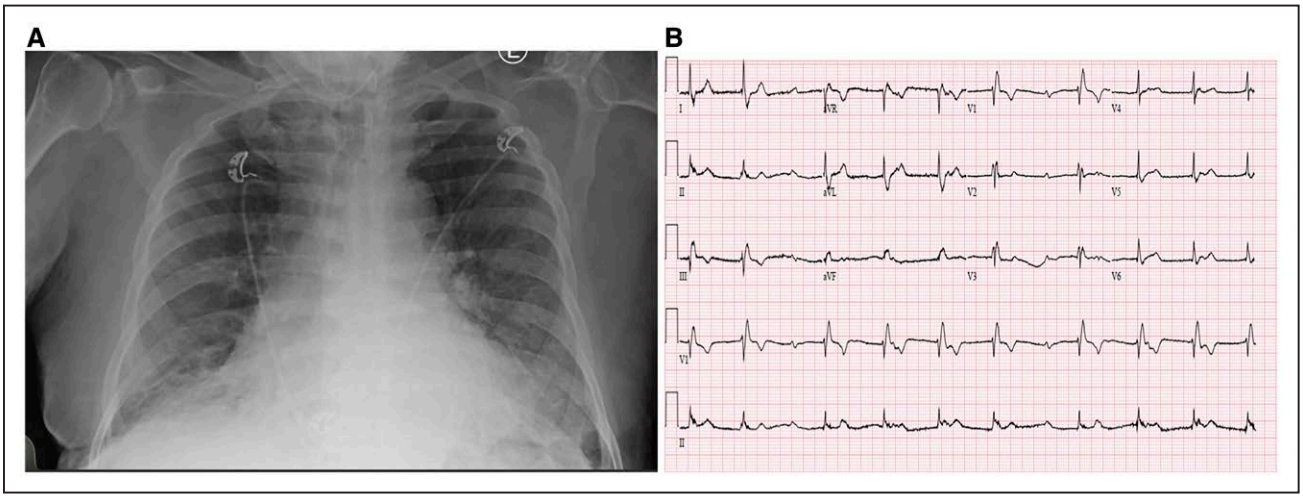

Figure 1. Atrioventricular block.
A, Chest radiography demonstrating multifocal pneumonia and cardiomegaly; (**B**) ECG demonstrating atrioventricular dissociation, high-grade heart block, with an unstable junctional escape rhythm.

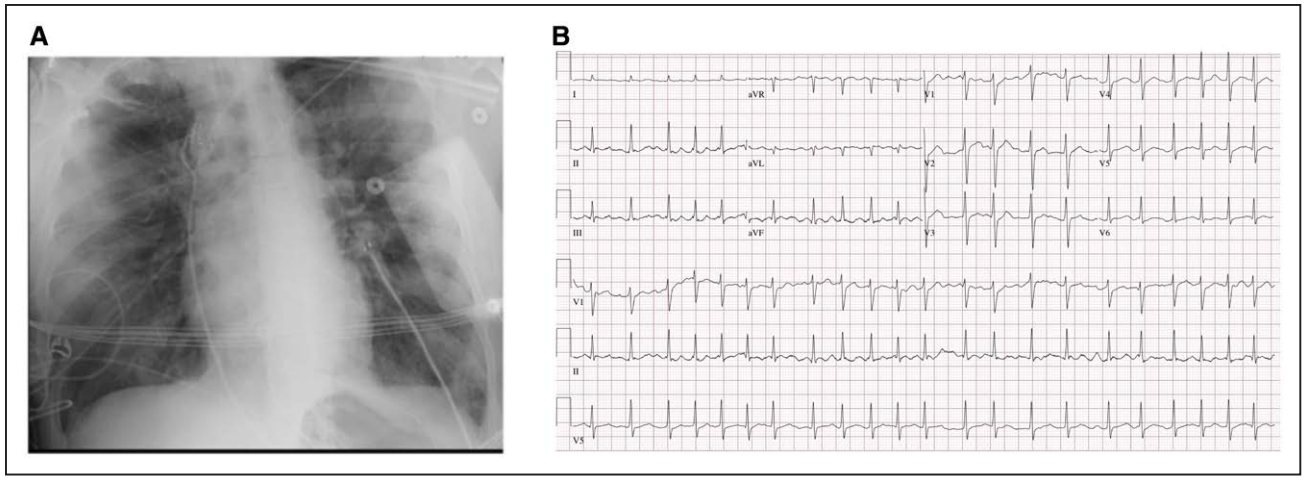

Figure 2. Atrial fibrillation.
A, Chest radiography demonstrating bilateral lower lobe opacities; (**B**) ECG demonstrating atrial fibrillation with rapid ventricular rate.

requiring percutaneous cholecystostomy and acute renal failure necessitating dialysis. Nearly 20 days after symptom onset, nasopharyngeal swab repeat testing for COVID-19 was negative. He is as of this writing, 30 days into his hospitalization, extubated, off all vasopressors, decannulated from extracorporeal membrane oxygenation, no longer on dialysis and in normal sinus rhythm.

This case highlights several challenges regarding ideal AF therapies and safety of cardioversion in patients with COVID-19. The preferred rate control agent is unknown, but it is reasonable to be cautious with β-blocker use due to risk of bronchospasm. There have been previous reports that amiodarone in vitro alters late compartments of the endocytic pathway and inhibits SARS-CoV-1 by acting after the transit of the virus through endosomes, but its utility in treating AF in patients with COVID-19 is unclear.[12] The potential for QT prolongation with amiodarone use, particularly if used in conjunction with hydroxychloroquine and azithromycin, must also be considered.

During the COVID-19 pandemic, both transthoracic and transesophageal echocardiography have been used sparingly to minimize exposure of healthcare workers, particularly given the risk of aerosolization with the latter. The logistics of transportation for cardiac computed tomography to rule out left atrial clot is difficult in the setting of limited staff and personal protective equipment, and hemodynamic instability of patients who are intubated.

Fortunately, this patient was cardioverted without incident. Our patient had a CHA_2DS_2-VASc score of 0. Notably, patients with COVID-19 may be prone to increased thromboembolic risk given elevated D-dimer levels, and this should be considered in decision-making regarding anticoagulation initiation for AF, even in the presence of a low CHA_2DS_2-VASc score.[4,13]

While little is known about incidence of new onset AF in patients with COVID-19, it has been associated with poor outcomes in critically ill patients.[14,15] As inflammation and its associated immune response are involved in the initiation and maintenance of AF, it is possible that anti-inflammatory therapies may be therapeutic, though this requires further study.

CASE 3: POLYMORPHIC VENTRICULAR TACHYCARDIA

A 64-year-old woman with a remote history of nonischemic cardiomyopathy recovered LVEF of 55% to 60%, paroxysmal AF, and diabetes mellitus type II presented with 2 days of cough and shortness of breath and was diagnosed with SARS-CoV-2. On admission, she was tachypneic with an oxygen saturation of 86% on room air. Initial ECG demonstrated normal sinus rhythm with premature atrial and ventricular complexes and a prolonged QTc of 528 ms. ECGs from prior admissions demonstrated QTc 500 ms. CXR showed bilateral patchy opacities (Figure 3A). Initial laboratory analysis was notable for white blood cell count of 6000 per microliter, creatinine 1.1 mg/d, ferritin of 639 µg/L, CRP of 20 ng/mL, hs-TropT 42 ng/mL, and NT-pro BNP (N-terminal pro-B-type natriuretic peptide) 6137 pg/mL. She had no significant bradycardia and was treated empirically with broad-spectrum antibiotics including intravenous azithromycin. She did not receive hydroxychloroquine due to prolonged QTc. She developed refractory hypoxemia requiring intubation and mechanical ventilation on hospital day 2. She developed transient hypotension briefly requiring vasopressor and inotropic support. A premature ventricular complex caused a classic long-short sequence followed by polymorphic ventricular tachycardia requiring multiple defibrillation attempts (Figure 3B). ECG demonstrated marked QTc prolongation of 581 ms and marked T wave inversion (Figure 3C). Repeat laboratory analysis was notable for serum potassium of 4.2 mmol/L and magnesium 1.4 mg/dL. She was treated with intravenous magnesium, and azithromycin was

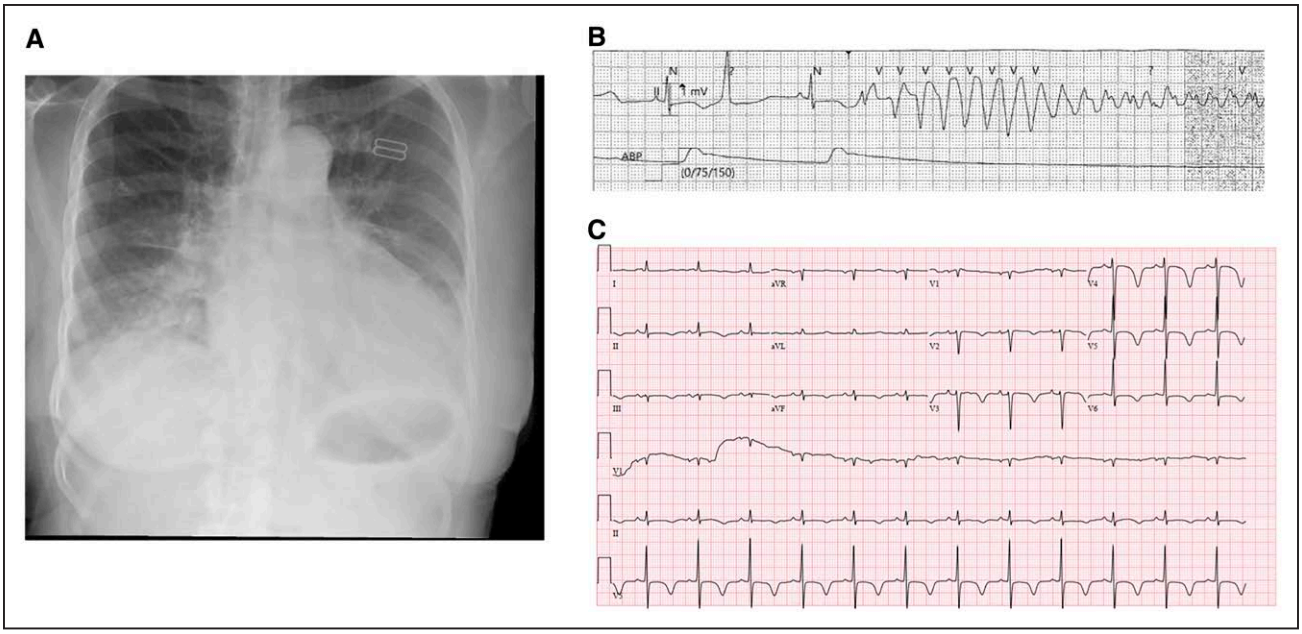

Figure 3. Polymorphic ventricular tachycardia.
A, Chest radiography demonstrating bilateral patchy opacities; (**B**) telemetry strip demonstrating torsades de pointes; (**C**) ECG demonstrating marked T wave inversions and QT prolongation.

discontinued with subsequent shortening of QTc duration and no further ventricular arrhythmias. At the time of publication, she remains mechanically ventilated after 20 days of hospitalization.

In this case, we highlight the arrhythmic risk faced among critically ill patients treated with potential COVID therapeutics which have QTc prolonging effects. The patient developed torsades de pointes, likely precipitated by azithromycin in the setting of a baseline prolonged QT interval, which may have been related to previous cardiomyopathy, inherited ion-channel disorders, or possibly the effects of SARS-CoV-2 infection on the heart. Although there are no Food and Drug Administration-approved therapies for SARS-CoV-2 infection, the treatment regimen of hydroxychloroquine and azithromycin has been widely adopted for all patients with moderate to severe pneumonia with oxygen saturation <90% on room air, based on early limited studies suggesting improved clinical outcomes and viral clearance.[16–18] Both of these medications are known to prolong the QT interval, and there is concern regarding an elevated risk of arrhythmia, particularly torsades de pointes, with combined therapy. In patients with baseline prolonged QTc intervals, particularly >500 ms, the risks of therapy may outweigh the benefits and should be considered on an individual basis.[19] However, this patient did not receive hydroxychloroquine, and the QTc prolongation may have been due to azithromycin in a patient with low repolarization reserve.

Should a patient develop torsades de pointes, as in the above case, we recommend electrical defibrillation as necessary, electrolyte repletion, cessation of offending medications, consideration of lidocaine use. Overdrive pacing to decrease QTc may be considered if the patient has a preexisting permanent pacemaker or defibrillator. Notably, secondary prevention implantable cardioverter-defibrillator therapy may not be indicated in the presence of a clear reversible precipitant; however, studies are needed to determine if after recovery from COVID-19 with arrhythmic complications, one is still at increased risk for ventricular arrhythmias. Although not described here, we have seen other ventricular arrhythmias in COVID+ patients such as accelerated idioventricular rhythm.

Health care workers must don appropriate personal protective equipment in emergent situations such as defibrillation and provision of advanced life support.[5] The rapidity in which these patients can decline can make it quite challenging for health care workers to prepare themselves with sufficient personal protective equipment before rushing to the bedside.

CASE 4: CARDIOGENIC SHOCK AND PULSELESS ELECTRICAL ACTIVITY ARREST

A 70-year-old man with hypertension, hyperlipidemia, diabetes mellitus type II, and ischemic cardiomyopathy with known LVEF 35% to 40%, presented with one day of cough, shortness of breath, and chest pain. He was afebrile with a blood pressure of 108/82 mm Hg, heart rate of 80 bpm, and oxygen saturation of 100% on room air. SARS-CoV2 testing was positive. Cardiac biomarkers included hs-TropT 43 ng/mL and NT-pro BNP 8077 pg/mL. CXR demonstrated pulmonary vascular congestion

(Figure 4A). Initial ECG to the intensive care unit demonstrated sinus tachycardia with left bundle branch block, PR 188 ms, QRS 138 ms, and QTc 479 ms (Figure 4B). He was briefly treated with azithromycin and hydroxychloroquine, but therapy was stopped due to QTc prolongation. On hospital day 3, his LVEF decreased to 10% to 15% with global hypokinesis. Treatment with intravenous dobutamine and furosemide was initiated; however, he developed progressive hypoxemia requiring intubation. Laboratory analyses revealed hs-TropT of 281 ng/mL, NT-pro BNP of 31 518 pg/mL, D-dimer 4.55 ug/mL, CRP 96 mg/L, interleukin-6 30 pg/mL, and ferritin 11 160 ng/mL. On hospital day 5, the patient was noted to be hypotensive requiring vasopressor support. Approximately 30 minutes later, he acutely went into complete heart block with no escape rhythm (Figure 4C), and advanced cardiac life support was initiated. He regained a normal rhythm but then developed pulseless electrical activity. He was subsequently defibrillated for ventricular fibrillation but suffered a second pulseless electrical activity arrest and expired despite all efforts.

This case demonstrates rapid hemodynamic decline in the setting of COVID-19 infection, likely due to fulminant myocarditis and a proinflammatory state, complicated by sudden atrioventricular block without an escape rhythm. Possible mechanisms of cardiac failure include global cardiomyocyte injury, and cytokine storm, leading to inflammation-mediated conduction disturbance.[20] Histopathologic analysis will be key in further eliciting these mechanisms on a cellular level. Serious consideration should be given to the early administration of immunomodulatory therapy, which may prevent the development of multi-organ failure and potentially fatal conduction disease.

CONCLUSIONS

In this article, we illustrate various cardiac arrhythmias associated with COVID-19 infection and treatment (Figure 5) that do not correlate with severity of lung injury on CXR. In patients presenting with symptoms of COVID-19 infection, clinicians need to be wary of the potential for significant, often life-threatening arrhythmias, particularly if fulminant myocarditis is also suspected, and perform appropriate rhythm monitoring. Importantly, during this pandemic, it is crucial to conserve healthcare resources and minimize risks to clinical providers. Likewise, when making decisions regarding choice of antiarrhythmics, inotropes, and vasopressors, clinicians need to keep in mind potential proarrhythmic effects of antimalarial and antibiotic therapies currently being investigated as therapeutic agents against COVID-19. We have implemented a policy in which these therapies are withheld if the baseline QTc is >500 ms for QRS <120 ms, or if QTc is >550 ms for QRS >120 ms. Usage of QT prolonging drugs are reconsidered if the QTc prolongs by 60 ms or more. Our institution has not discontinued angiotensin converting enzyme inhibitor or angiotensin receptor blocker usage. Additionally, management of new onset AF requires a discussion of whether anticoagulation is warranted, even in the absence of classic risk factors for stroke given the prothrombotic potential of COVID-19, and duration of anticoagulation following recovery. Future studies are needed to better understand the mechanisms underlying the effects of COVID-19 on

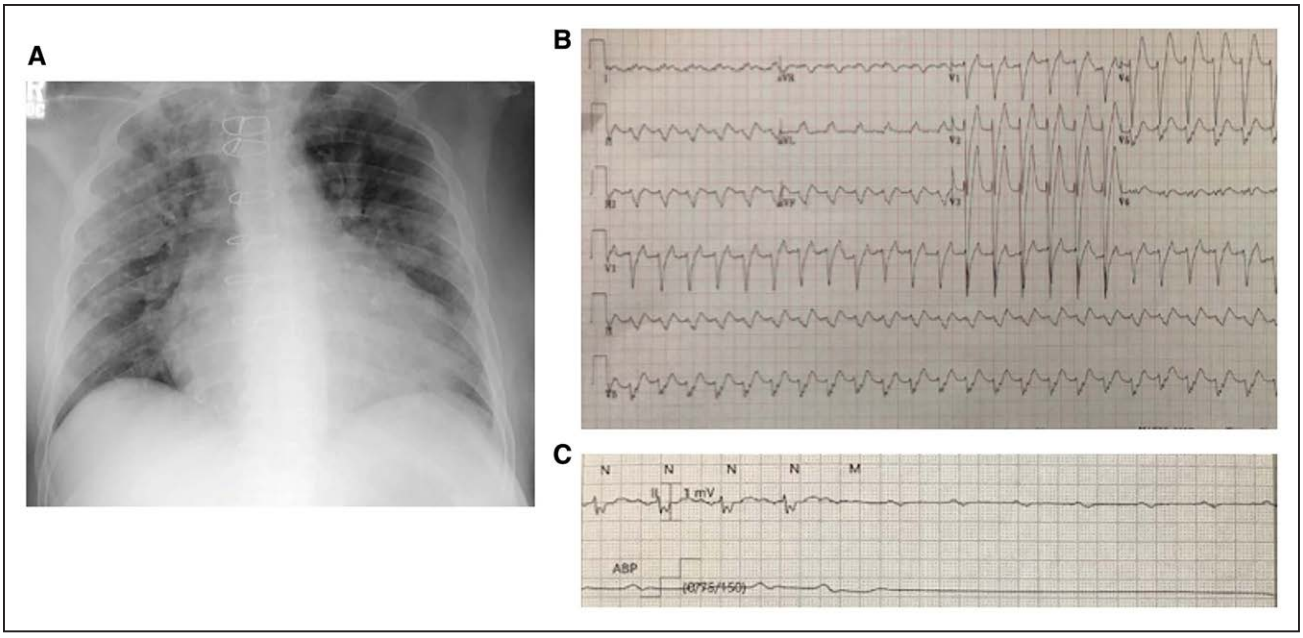

Figure 4. Cardiogenic shock and pulseless electrical activity arrest.
A, Portable chest radiography demonstrating patchy bilateral opacities; (**B**) ECG upon presentation showing sinus tachycardia with left bundle branch block; (**C**) telemetry strip demonstrating sudden heart block without escape rhythm.

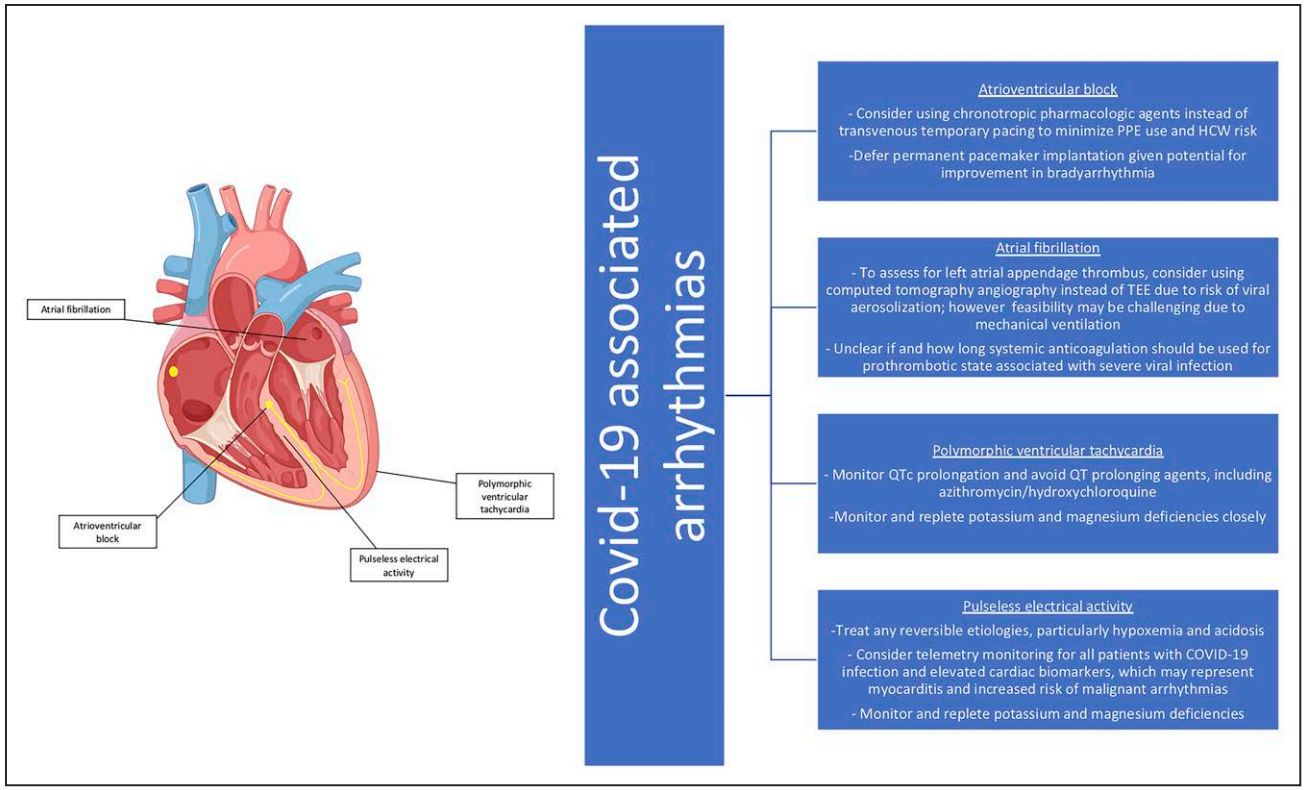

Figure 5. Spectrum of cardiac arrhythmias associated with coronavirus disease 2019 (COVID-19) infection.
Spectrum of cardiac arrhythmias associated with COVID-19 infection (**A**) relative to disease onset and (**B**) special management considerations. CTA indicates computed tomography angiography; HCW, healthcare workers; PPE, personal protective equipment; and TEE, transesophageal echocardiography.

the heart as well as how best to treat arrhythmias associated with viral infection and treatment.

ARTICLE INFORMATION

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Sources of Funding

Dr Kochav is supported by the National Institutes of Health (NIH)/National Heart, Lung, and Blood Institute to Columbia University Irving Medical Center (T32HL007343). Dr Gupta is supported by NIH training grant T32 HL007854. Dr Wan is supported by NIH K08HL122526, NIH R01HL152236, and NIH R03HL146881; the Louis V. Gerstner, Jr Scholars Program; Lewis Katz Prize; the Esther Aboodi Endowed Professorship at Columbia University; the M. Iréne Ferrer Scholar Award from the Foundation of Gender Specific Medicine; and a gift from Howard and Patricia Johnson.

Disclosures

None.

REFERENCES

1. World Health Organization. Coronavirus Disease (COVID-19) Situation Reports. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200404-sitrep-75-covid-19.pdf?sfvrsn=99251b2b_2. Accessed April 5, 2020
2. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19): Cases in the U.S. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-in-us.html. Accessed April 5, 2020
3. Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E, Rabbani L, Brodie D, Jain SS, Kirtane A, et al. The variety of cardiovascular presentations of COVID-19. *Circulation.* 2020;141:1930–1936. doi: 10.1161/CIRCULATIONAHA.120.047164
4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020;323:1061–1069. doi: 10.1001/jama.2020.1585
5. Lakkireddy DR, Chung MK, Gopinathannair R, Patton KK, Gluckman TJ, Turagam M, Cheung J, Patel P, Sotomonte J, Lampert R, et al. Guidance for cardiac electrophysiology during the COVID-19 pandemic from the Heart Rhythm Society COVID-19 Task Force; Electrophysiology Section of the American College of Cardiology; and the Electrocardiography and Arrhythmias Committee of the Council on Clinical Cardiology, American Heart Association. *Circulation.* 2020;141:e823–e831. doi: 10.1161/CIRCULATIONAHA.120.047063
6. Tattersfield AE, McNicol MW. Salbutamol and isoproterenol. A double-blind trial to compare bronchodilator and cardiovascular activity. *N Engl J Med.* 1969;281:1323–1326. doi: 10.1056/NEJM196912112812402
7. Paterson JW, Conolly ME, Davies DS, Dollery CT. Isoprenaline resistance and the use of pressurised aerosols in asthma. *Lancet.* 1968;2:426–429. doi: 10.1016/s0140-6736(68)90467-4
8. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, Brown TS, Der Nigoghossian C, Zidar DA, Haythe J, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 Pandemic. *J Am Coll Cardiol.* 2020;75:2352–2371. doi: 10.1016/j.jacc.2020.03.031
9. Sala S, Peretto G, Gramegna M, Palmisano A, Villatore A, Vignale D, De Cobelli F, Tresoldi M, Cappelletti AM, Basso C, et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. *Eur Heart J.* 2020;41:1861–1862. doi: 10.1093/eurheartj/ehaa286

10. Belardinelli L, Belloni FL, Rubio R, Berne RM. Atrioventricular conduction disturbances during hypoxia. Possible role of adenosine in rabbit and guinea pig heart. *Circ Res.* 1980;47:684–691. doi: 10.1161/01.res.47.5.684
11. Clark RE, Christlieb I, Sanmarco M, Diaz-Perez R, Dammann JF, Zipser ME. Relationship of hypoxia to arrhythmia and cardiac conduction hemorrhage. *Circulation.* 1963;27:742–747.
12. Stadler K, Ha HR, Ciminale V, Spirli C, Saletti G, Schiavon M, Bruttomesso D, Bigler L, Follath F, Pettenazzo A, et al. Amiodarone alters late endosomes and inhibits SARS coronavirus infection at a post-endosomal level. *Am J Respir Cell Mol Biol.* 2008;39:142–149. doi: 10.1165/rcmb.2007-0217OC
13. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China [published online March 13, 2020]. *JAMA Intern Med.* doi: 10.1001/jamainternmed.2020.0994. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2763184.
14. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA.* 2020;323:1775–1776. doi: 10.1001/jama.2020.4683
15. Fernando SM, Mathew R, Hibbert B, Rochwerg B, Munshi L, Walkey AJ, Møller MH, Simard T, Di Santo P, Ramirez FD. New-onset atrial fibrillation and associated outcomes and resource use among critically ill adults-a multicenter retrospective cohort study. *Crit Care.* 2020;24:15. doi: 10.1186/s13054-020-2730-0
16. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends.* 2020;14:72–73. doi: 10.5582/bst.2020.01047
17. Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents.* 2020;55:105932. doi: 10.1016/j.ijantimicag.2020.105932
18. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, Doudier B, Courjon J, Giordanengo V, Vieira VE, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial [published online March 20, 2020]. *Int J Antimicrob Agents.* doi: 10.1016/j.ijantimicag.2020.105949. https://www.sciencedirect.com/science/article/pii/S0924857920300996?via%3Dihub.
19. Giudicessi JR, Noseworthy PA, Friedman PA, Ackerman MJ. Urgent guidance for navigating and circumventing the QTc-prolonging and torsadogenic potential of possible pharmacotherapies for Coronavirus Disease 19 (COVID-19). *Mayo Clin Proc.* 2020;95:1213–1221. doi: 10.1016/j.mayocp.2020.03.024
20. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Ze. Cardiovascular implications of fatal outcomes of patients with Coronavirus Disease 2019 (COVID-19) [published online March 27, 2020]. *JAMA Cardiol.* doi: 10.1001/jamacardio.2020.1017. https://jamanetwork.com/journals/jamacardiology/fullarticle/2763845