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Cardiac arrhythmias in COVID-19 patients: A combination of viral comorbidities and pro-arrhythmic drug interactions

Over the past year, substantial global efforts have been made to connect the signs, symptoms, and consequences of the SARS-CoV-2 virus (COVID-19). Among the associated sequel includes the noted higher incidence of cardiac arrhythmias [1]. A relationship is unfolding between this widespread virus, underlying cardiovascular disease (CVD) and new onset arrhythmias [1-3]. As these complications are associated with higher mortality rates and the number one cause of death in the US is CVD, it is crucial to develop proactive measures for at-risk patients [4].

The average incidence of atrial fibrillation (AF) in the US is around 2.3 million while supraventricular tachycardia is detected in 90,000 patients annually, while up to 80% of sudden cardiac death cases are associated with ventricular arrhythmias [5]. The pathophysiology of cardiac arrhythmias involves abnormalities in impulse formation or conduction. Electrolyte disturbance or structural disturbances can lead such disruptions in cardiac impulses. When considering the possible association of COVID-19 and cardiac arrhythmias, one must consider other contributing factors that may already be present in an infected patient. Hypertension, history of myocardial infarction, and diabetes are some of the more prevalent risk factors [4,5]. Several studies have reported the arrhythmia rates of the COVID-19 patients admitted to the hospital to be between 17 and 44%, with the higher rates related specifically to ICU patients [1]. Arrhythmias seen in COVID-19 patients may be due systemic inflammation, viral activity within the cardiac myocytes, cardiac comorbidities or drug interactions. Importantly, acute myocardial injury has been noted in 15–30% of COVID-19 patients, increasing their susceptibility of arrhythmic changes [1]. Of those with cardiac injury, one study found that more individuals were affected if they had comorbidities such as hypertension, diabetes, coronary heart disease or chronic heart failure [2].

COVID-19's influence on this pathophysiology may be centered on its interaction with Angiotensin-converting enzyme 2 (ACE2) [3]. The ACE2 enzyme is a membrane protein present in the kidneys, heart and lungs [3]. In the cardiovascular system, ACE2 works to lower the blood pressure by hydrolyzing angiotensin II, a vasoconstrictor, into angiotensin, a vasodilator [3]. SARS-CoV is a recognized cell receptor for ACE2 and, as COVID-19 is part of this viral family, it serves that it can also have the ability to bind to ACE2 receptors leading to membrane fusion and viral cell entry [3]. This eventually results in the downregulation of ACE2 and thus incurs a loss of ACE2-mediated cardio-protection.

Additionally, with the high expression of ACE2 in cardiac myocytes and coronary endothelial cells, there is more opportunity for the virus to infect cardiac tissue with ensuing myocardial damage. Disruption of these cells leaves the heart susceptible to adverse events such as cardiac arrhythmias.

In addition to the potential cardiac-damaging effects of the virus, the current treatment regimens have pro-arrhythmic side effects like QT prolongation. Chloroquine phosphate, hydroxychloroquine sulfate, azithromycin and other macrolides have been implicated in QT prolongation, progressing to torsade des pointes and even sudden cardiac death [1,2]. Implicated in QT prolongation, ritonavir and lopinavir anti-virals have also been shown to also cause PR prolongation and rarely second and third-degree heart AV block [1]. Patients with hypokalemia, hypomagnesaemia, bradycardia and class IA and class III anti-arrhythmics are at higher risk for QT prolongation with known risk factors such as these [1].

Using the known pathophysiology of cardiac arrhythmias and certain medications in COVID-19 patients as a guide, we suggest the following recommendations. First, the treatment regimen must be tailored to individual patients with particular regard for patients with known risk factors for arrhythmias and QT prolongation. As such, the combination use of more than one medication with a known risk for QT prolongation ought to be avoided. In patients with a known non-modifiable risk factors for QT prolongation, avoid the use of chloroquine, hydroxychloroquine, macrolides, ritonavir and lopinavir. These patients should also be placed on continuous telemetry for proactive monitoring. Electrolytes should be continually monitored, maintaining a potassium level of ≥ 4 mEq/L and a magnesium level of ≥ 2 mg/dL to avoid amassing risk factors. Additionally, all COVID-19 patients ought to be placed on proper anticoagulation for clot and thromboembolisms prevention. Regarding the use of ACE inhibitors/ARBs, there is preliminary evidence that it may be protective, however for now if patients were previously on an ACE inhibitor/ARB that should be continued rather than starting this as a new medication for other patients until further evidence is provided [2].

The COVID-19 infections increases the susceptibility of patients to life-threatening cardiac arrhythmias. This is not only due to the pathophysiology of the virus in cardiac myocytes but also the combination with cardiac comorbidities and pro-arrhythmic drug interactions. Appropriate precautions and measures must be executed in order to prevent adverse patient outcomes.

Conflicts of interests

Authors disclose no competing interest.

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References

- [1] Manolis AS, Manolis AA, Manolis TA, Apostolopoulos EJ, Papatheou D, Melita H. COVID-19 infection and cardiac arrhythmias. *Trends Cardiovasc Med.* 2020;30(8): 451–60. <https://doi.org/10.1016/j.tcm.2020.08.002>.
- [2] Kang Y, Chen T, Mui D, et al. Cardiovascular manifestations and treatment considerations in COVID-19. *Heart.* 2020;106(15):1132–41. <https://doi.org/10.1136/heartjnl-2020-317056>.
- [3] Lazaridis C, Vlachogiannis NI, Bakogiannis C, et al. Involvement of cardiovascular system as the critical point in coronavirus disease 2019 (COVID-19) prognosis and recovery [published online ahead of print, 2020 Jun 10]. *Hellenic J Cardiol.* 2020. <https://doi.org/10.1016/j.hjc.2020.05.004> S1109–9666(20)30093–2.
- [4] FastStats - Heart Disease. Centers for disease control and prevention <https://www.cdc.gov/nchs/fastats/heart-disease.htm>. Published October 30 ; 2020 (Accessed January 17, 2021).
- [5] Khurshid S, Choi SH, Weng LC, et al. Frequency of cardiac rhythm abnormalities in a half million adults. *Circ Arrhythm Electrophysiol.* 2018;11(7):e006273. <https://doi.org/10.1161/CIRCEP.118.006273>.

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