
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 commentary: Cardiac arrhythmias in the era of COVID-19 pandemic ☆

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Coronavirus disease-19 (COVID-19) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection has quickly spread across the world since it was officially reported in Wuhan, China in Dec 2019 and emerged as a global pandemic leading to significant morbidity, mortality, economic affliction, and social disruption. Cardiac injury is one of the known complications of COVID-19 through various mechanisms [1]. Cardiac injury increases the risk of critical illness, morbidity, and mortality. It also increases the risk of cardiac arrhythmias. Current understanding of the impact of COVID-19 on arrhythmias is still in its infancy. However, it continues to evolve as new data from reliable studies emerge [2]. Cardiac arrhythmias are more common in critically ill COVID-19 patients. The exact mechanisms that could result in arrhythmogenesis is not completely known yet, but hypoxia caused by pulmonary disease, myocarditis, exaggerated host immune response, myocardial ischemia, electrolyte imbalance, and medication side effects have been proposed as a potential cause [3].

Manolis and colleagues [4] in this issue of Trends in Cardiovascular Medicine summarize current knowledge regarding arrhythmic complications of COVID-19 and discuss potential mechanisms. They further touch upon treatment, management, and monitoring strategies for COVID-19 patients. Different cardiac rhythm disturbances of COVID-19 have been reported so far. Amongst them sinus tachycardia is the most common due to multiple causes including systemic infection, fever, respiratory failure, and pain. Sinus bradycardia, on the other hand, has been observed in a few studies emphasizing the need for close monitoring of these patients. Bradycardia has been suggested as a warning sign of the onset of a serious cytokine storm suggesting that inflammatory injury of the sinus node is likely the contributing factor. The presence of right bundle branch block, intraventricular block, premature atrial contractions, or abnormal PR interval behavior (paradoxical prolongation or lack of shortening) increased mortality [5].

According to one survey, atrial fibrillation (AF) was the most commonly encountered cardiac arrhythmia in COVID-19 patients [6]. The authors discuss the impact of national lockdown on the rate of AF diagnosis, reporting a significant drop in registered new-onset AF cases during the pandemic [7]. Their guidance on management of atrial fibrillation is similar as treatment for non-COVID-19 patients albeit with several specific recommendations. First, aside from those with hemodynamic compromise, rate control should be considered the backbone of treatment in those ill with COVID-19. Second, caution should be exercised with initiation of QT prolonging antiarrhythmic medications, given heightened concerns about pro-arrhythmia and potentially drug-drug interactions with other therapies directed at COVID-19 infection. As with all AF patients, initiation of anticoagulation is necessary. Current recommendations support initiation of intravenous heparin with potential for reduction of other embolic events. It is unclear if other agents such as direct oral anticoagulants are immediately beneficial.

Additionally, the article discusses the common incidence of acute myocardial injury in COVID-19 patients, which can be a potential substrate for ventricular arrhythmia. The authors note that in comparison to the year prior there was an increased incidence of out-of-hospital cardiac arrest observed during the pandemic [8]. While the correlation between the increase in cardiac arrest and COVID-19 infections is high, this increase may be attributable to delayed routine cardiac care and apprehension of seeking medical attention during the lockdown. A recent study showed increased incidence of stress-induced cardiomyopathy during the pandemic, a condition that is well-known for its predisposition for life-threatening arrhythmias [9].

Unfortunately, treatments for acute COVID-19 infection that have been attempted can also have detrimental cardiac effects. The authors describe the QT prolonging effects of several therapies, particularly macrolides and hydroxychloroquine, and the need for close monitoring of QT interval in those patients receiving these medications. These potentially pro-arrhythmic changes can occur through direct effects of treatment, drug-drug interactions, or uncovering of silent genetic variants of congenital QT syndrome. Although serial electrocardiograms (ECG) have been used traditionally to monitor QTc, outpatient cardiac telemetry has emerged as an alternative method. New QT detection algorithms on mobile cardiac outpatient telemetry systems, and consumer heart rate and even oximetry monitors will likely change the approach for the future. However, while it is potentially a safer option for monitoring as it minimizes the need for hospitalization and mitigates risk of coronavirus transmission from other patients or healthcare

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workers, large scale validation studies on this approach have not been performed. The authors also caution the medical community of using QT-prolonging drugs in patients with a QTc ≥500 ms or a change of QTc of >60 ms during treatment with QT prolonging medications. Despite all advancements in QTc monitoring, torsade de pointes (TdP) is still seen in clinical practice, which necessitates immediate attention and management with defibrillation and intravenous magnesium sulfate. In cases of TdP that occurs in the setting of profound bradycardia or in patients with incessant VT, isoproterenol infusion and ventricular pacing to heart rate of 90–110 beats per minute can reduce further ventricular arrhythmias.

The authors also elucidate potential pharmacological interactions that can be seen in patients taking antiarrhythmic drugs (AAD) and COVID-19 therapies via different mechanisms such as direct QT prolongation, as mentioned earlier, or their effects on cytochrome enzymes, which metabolize several and commonly used AAD. Hence, extra caution should be implemented before initiating or continuing AAD in COVID-19 patients, whom new antimicrobial or anti-inflammatory therapies are commenced. Additionally, the authors shed light on other potential mechanisms of arrhythmias in COVID-19 patients, which include direct viral damage to the vagus nerve nucleus in the brain stem that result in dysregulation of parasympathetic nervous system, and consequently bradycardia. Conversely, pulmonary and cardiometabolic disease seen in COVID-19 can enhance the sympathetic activity, which may play a major role in various arrhythmia pathogenesis, commonly seen in the infected patients. The authors further discuss the use of various antiarrhythmic medications in COVID-19 patients when taken in conjunction with antiviral, anti-inflammatory, or antimicrobial medications that have been used in this patient's population, which falls again with the widely accepted guidelines that cautions healthcare providers of potential pharmacological interactions between antiarrhythmic and different class of medications. A major limitation to understanding of safety of antiarrhythmic medications in COVID-19 patients is still lack of studies or even case series that examine patients who are treated with those medications. Furthermore, the literature at the present time does not have substantial data explaining the mechanisms of arrhythmia in COVID-19.

Ultimately, hindsight and retrospective analysis of the cardiac impact of COVID-19 will tell us if the standard treatments used for treating arrhythmias in other individuals were beneficial or detrimental to coronavirus patients. Particular focus on evaluating the safety of anti-arrhythmic drugs, different anticoagulants, or clinical factors that influence management is paramount. Until we have more data, clinicians will have to apply clinical judgment when treating these patients.

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