

## Letters to the Editor

# Increased Risk of Arrhythmia in COVID-19 Patients: Possible Roles of Both the Disease Pathophysiology and Adverse Drug Reactions

Dear Editor,

Coronavirus disease 2019 (COVID-19) is a newly emerging and highly contagious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that was first reported in December 2019 and was announced as a pandemic disease on March 11, according to the World Health Organization warning.<sup>[1]</sup> The clinical sign and symptoms of COVID-19 mostly include fever (98.6%), fatigue (69.6%), dry cough (59.4%), anorexia (39.9%), myalgia (34.8%), and dyspnea (31.2%), and it causes the most involvement in lung tissue.<sup>[2]</sup> However, in addition to lung involvement, other organs can also be involved in COVID-19, including the heart, and causes complications such as acute cardiac injury and arrhythmia (which reported in 44.4% of intensive care unit [ICU] patients and 6.9% of non-ICU patients).<sup>[2,3]</sup> Major mechanisms that predispose COVID-19 patients to arrhythmia include the direct effect of the SARS-CoV-2 on the heart and lung tissue (causing hypoxia and has an indirect effect), diarrhea and electrolyte disturbances (especially hypokalemia), cytokine storm, and interleukin (IL)-6 effects on sympathetic tone, cardiomyocyte ion channels (hERG-K<sup>+</sup>), and fever (causing Brugada syndrome).<sup>[4]</sup> However, these mechanisms are not the only risk factors for arrhythmia in COVID-19 patients, but medications prescribed can also be significant risk factors.

Among the most common medications used to treat COVID-19 are aminoquinolines (chloroquine and hydroxychloroquine), of which cardiac arrhythmia is one of the most important side effects. On the other hand, azithromycin and lopinavir/ritonavir (Kaletra) are two drugs that often prescribed in combination with chloroquine and hydroxychloroquine, and due to their arrhythmogenic effects and CYP3A4 inhibitory effect of Kaletra (which can interfere with chloroquine, hydroxychloroquine, and azithromycin metabolism), they can increase the risk of arrhythmia. Furthermore, it has been reported that IL-6 by cytochrome P450, particularly CYP3A4, inhibitory effects and SARS-CoV-2 by causing liver and kidney injuries, can interfere with chloroquine, hydroxychloroquine, azithromycin, and Kaletra metabolism and possibly increase their serum concentration and risk of arrhythmia.<sup>[4,5]</sup>

As a result, COVID-19 can be a reason for heart damage and arrhythmia, or it can provide conditions for arrhythmia, especially in patients who receive arrhythmogenic drugs, such as chloroquine, hydroxychloroquine, azithromycin, and Kaletra. Hence, constant monitoring of the electrocardiogram, electrolyte

levels (especially potassium), body temperature, and troponin (a marker of myocardial damage) is essential and can be life-saving in COVID-19 patients.

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### Conflicts of interest

There are no conflicts of interest.

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