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Cardiac Arrhythmia Mechanisms in COVID-19: Review Article

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ABSTRACT

Background: The World Health Organization has declared SARS-CoV-2 a public health emergency and pandemic because of its fast spread [COVID-19 (coronavirus disease 2019)]. Cardiogenic shock and arrhythmias such as acute coronary syndrome and myocarditis have been documented in the scientific literature. Heart arrhythmias in COVID-19-infected patients have been the subject of several recent articles in the scientific literature. It was also shown to be linked to an increased mortality risk. Atrial fibrillation, atrial flutter, ventricular tachycardia, and ventricular fibrillation have all been recorded in the literature so far. Unexpectedly, a study found that 7 % of patients who didn't require intensive care unit treatment experienced arrhythmias, but 44 % of patients who required to be hospitalized in ICU. Repletion of electrolytes, withdrawal of drugs that cause arrhythmia, volume status management, or suppression of catecholamine surges in COVID-19 are some of the treatment options for arrhythmias.

Objective: This study aimed to evaluate the potential mechanisms of cardiac arrhythmias especially of supraventricular tachycardia in COVID-19.

Methods: The databases were searched for articles published in English in 4 data bases. PubMed, Google scholar, science direct and Boolean operators (AND OR NOT) had been used such as cardiac arrhythmia mechanisms, Covid-19 OR SARS-CoV-2 and in peer-reviewed articles between March 2005 and October 2021.

Conclusion: The pathophysiology of COVID-19 can be divided into a series of different ways. Metabolic imbalances, acidosis, and hypoxia are all possibilities as causes. Additional research suggests neurohormonal and catecholaminergic stress may have a significant influence.

Keywords: Cardiac arrythmia, COVID-19.

INTRODUCTION

SARS-CoV-2, a newly discovered coronavirus in 2019, is to blame for the current outbreak of Coronavirus disease. In December of that year, Wuhan in Hubei Province, China, found the virus [(1)].

COVID-19-related inflammation has been linked to a significant incidence of supraventricular arrhythmias, particularly in patients with COVID-19-associated systemic inflammation [(2)]. Patients with COVID-19 have a higher or lower incidence of arrhythmias and illness of the conduction system, depending on the population. Atrial fibrillation can begin anywhere from a few days to a week after contracting the virus, according to several case reports. However, it can take much longer in other cases [(3)].

There were 19 COVID-19 patients who developed atrial tachyarrhythmias that were not present on entry, all of whom were admitted to the MICU (27.5% of MICU patients). In 12 of these patients, atrial fibrillation was found, whereas in six patients, it was found to be atrial flutter [(4)]. Individuals admitted to critical care units with COVID-19 who had atrial tachyarrhythmias were frequently followed by hemodynamic worsening, according to the results of one recent research [(5)].

248 of 301 patients admitted to the ICU with COVID-19 infection were studied in another study. Thirty-seven of them (14.9%) were newly diagnosed with AF (NOAF). It took an average of 10.0 (5.0-17.0) days from the time that COVID-19 infection symptoms began to develop until NOAF appeared. As a general rule, patients who were admitted to intensive care units were admitted for a median time of 3.0 (0.0-10.0) days before they developed NOAF [(6)].

A lack of knowledge about the pathophysiology of COVID-19-related AF has led some researchers to propose a variety of mechanisms, including a decrease in the availability of the angiotensin-converting enzyme 2 (ACE2) receptor, surge in pro-inflammatory signalling that results in inflammation, damage to viral endothelium cells, and aberrant electrolyte and acid-base balance during the acute phase, due to a CD147-sialic acid spike protein interaction . Atrial fibrillation and other supraventricular tachyarrhythmias are more frequently linked to sympathetic nervous system activity than ventricular tachyarrhythmias. Thus, COVID-19 individuals are more likely to have supraventricular tachyarrhythmias because of their increased sympathetic activity [(7)].

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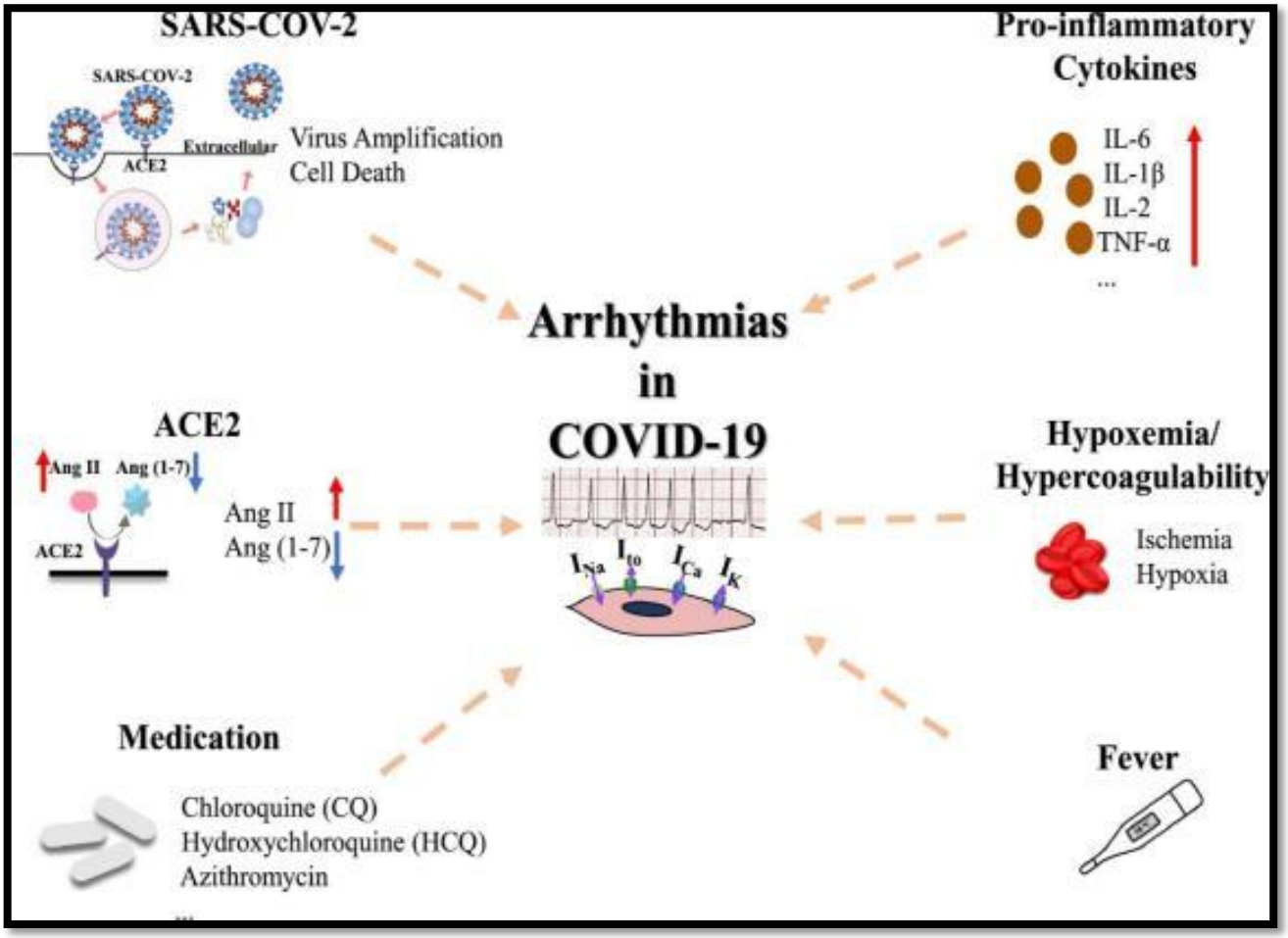

Figure (1): COVID-19's Cardiac Arrhythmias: Possible Mechanisms [4]

ACE2: Angiotensin converting enzyme-2, SARSCoV-2: severe acute respiratory syndrome coronavirus-2, , I K: potassium channel, I Na: sodium current, I Ca: Ca2+ current, IL: Interleukin , Ang II: Angiotensin II, Ang (1-7): Angiotensin (1-7).

(1) ACE2-related signalling pathways:

The coronavirus receptor ACE2 was discovered to be a membrane-bound protease. The entrance of SARS-CoV-2 has been found to be facilitated by additional human cell surface receptors/facilitators, like extracellular matrix metalloproteinase inducer (CD147) as well as sialic acid [8].

As far as we can tell, the primary entrance point is ACE2. When the transmembrane protease serine 2 cleaves the SARS-CoV-2 viral spike protein. Endothelial cells, macrophages, pneumocytes, cardiomyocytes as well as pericytes are among the host cells infected by SARS-CoV-2, which uses ACE2 to do [9].

It is possible that decreases in kidney tubular epithelial cell surface ACE2 contribute to renal damage and hypertension as well as the development of atrial fibrillation (AF) [10].

(2) Sialic acid spike protein-CD147 interaction:

CD147, an immunoglobin superfamily transmembrane glycoprotein with another term ECM metalloproteinase inducer, aids SARS-CoV-2 invasion. Increased cytokine production results in cardiomyocyte oxidative stress and negative inotropic effects, which can lead to heart disease [11].

CD147 is a crucial participant in adult mouse cardiomyocyte IL-18 gene expression and protein synthesis. Cardiovascular remodelling is caused by the activation of metalloproteinases and the breakdown of extracellular matrix components by IL-18. In addition, it has been found that circulating levels of IL-18 are linked to the development of atrial fibrillation [12].

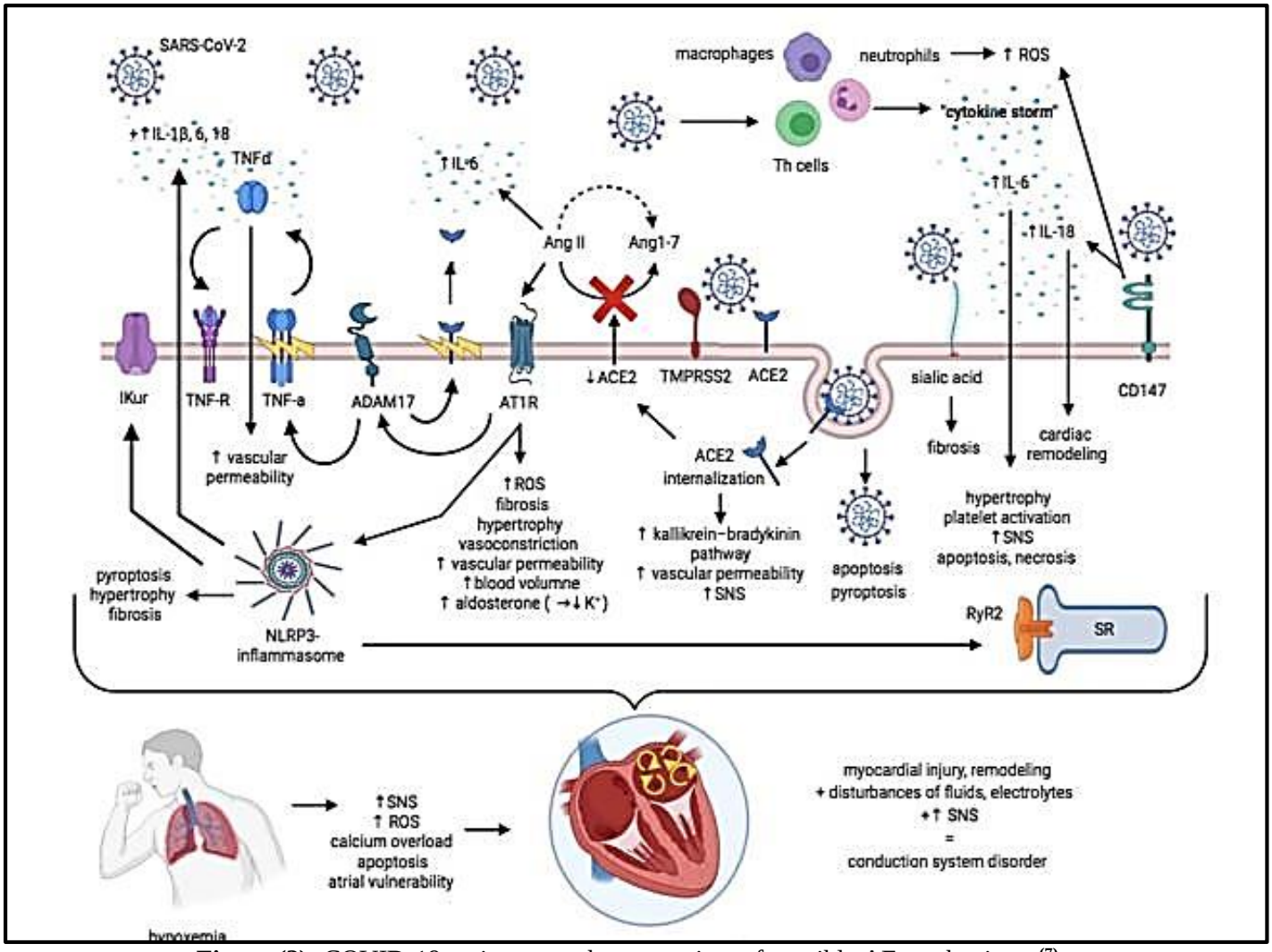

Figure (2): COVID-19 patients may have a variety of possible AF mechanisms [7]

(3) Cytokine storm:

In SARS-CoV-2 infection, an imbalance between Th1 and Th2 cells results in a cytokine storm, which results in an increase in cytokine release like interferon gamma (IFN), Interleukins (1-b, 2, 6 and 7), IFN-inducible protein-10 (IP-10), monocyte chemoattractant protein-1 (MCP-1), TNF-a as well as macrophage inflammatory protein-1A (MIP-1A) [13].

Myocardial necrosis and apoptosis may occur as a result of the release of proinflammatory cytokines, anomalies in atrial repolarization and conduction are possible consequences of this. This cytokine (IL-6) has been demonstrated to have direct effects such as increasing the formation of vascular smooth muscle, activating endothelial cells and triggering platelet activation in studies. A multicenter investigation on COVID-19 patients found that non-survivors had higher IL-6 levels than survivors, suggesting that virally-induced hyperinflammation and greater vulnerability to deadly arrhythmias may be to blame for the increased mortality [14].

(4) Leakage from the blood vessels and malfunction of the endothelium:

Patients with severe COVID-19 experience endothelial dysfunction for a variety of reasons:

-A decrease in the activity of the ACE2 receptor on cells stimulates the kallikrein–bradykinin pathway, increasing the permeability of blood vessels [15].

-Histotoxic mediators such as reactive oxygen species are produced by endothelial cells by activated neutrophils. Endothelial cell contraction and inter-endothelial junction loosening are induced by vasoactive molecules (thrombin, histine, bradykinin, thromboxane A2 and vascular endothelial growth factor), inflammatory cytokines (IL-6, IL-8 and TNFa), and immune cells. Degradation of the glycocalyx by IL-1b and TNFa activates glucuronidases that upregulate hyaluronic acid synthase type-2, resulting in an increase in the extracellular matrix deposition of hyaluronic acid and fluid retention [16].

(5) Fluid, electrolyte, and acid-base balance disturbances:

Most COVID-19 patients have hypokalemia, which can be life-threatening in up to 61% of patients who are admitted to the hospital. This is thought to be owing to an increase in potassium excretion from the urine and gastrointestinal tracts. SARS-CoV-2 binds to ACE2 and speeds up its degradation, decreasing the anti-renin-AngII system actions of ACE2. Increased salt and water absorption is the end result, followed by higher blood

pressure and increased potassium excretion. Diarrhoea and vomiting are common in persons with COVID-19, and this lowers the potassium supply to the body and further complicating matters [(4)].

(6) Hypoxia:

Pneumonia can cause significant gas exchange and airway obstruction deficits in people with severe SARS-CoV-2 infection. The cell membrane's phospholipid layer could be damaged by hypercapnia and oxygen free radicals, resulting in intracellular acidosis and damage to oxygen free radicals. This calcium influx also leads to cardiomyocyte necrosis and damage in the presence of hypoxia [(17)].

Airflow restriction and dynamic hyperinflation impact blood gas levels and pressure gradients in a COVID-19 infection. Pulmonary hypertension can cause tricuspid regurgitation by damaging the right atrium in particular [(18)].

(7) Myocardial ischemia:

Ischemia can be caused by a hyperinflammatory state and microvascular dysfunction, in an atherosclerotic plaque, which activates inflammatory cells and causes vasoconstriction due to a malfunction of the coronary endothelium system [(19)]. Disseminated intravascular coagulation related to hyperinflammation and immunological activation was discovered in a study of microvascular dysfunction [(20)].

Excessive extracellular potassium levels in hypoxic tissues increase electrical conduction speed by lowering the threshold for depolarization. Gap junction connexin 43 dephosphorylation can also impair electrical coupling and tissue anisotropy owing to hypoxemia [(21)].

CONCLUSION

The pathophysiology of COVID-19 can be divided into a series of different ways. Metabolic imbalances, acidosis, and hypoxia are all possibilities as causes. Additional research suggests neurohormonal and catecholaminergic stress may have a significant influence.

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