South Health and Policy. 2025; 4:241
doi: 10.56294/shp2025241

REVIEW

Update on Cardiac Arrhythmias in Patients with COVID-19

Actualización sobre las arritmias cardiacas en pacientes con la COVID-19

Dania María García Rodríguez[1], Dionis Ruiz Reyes[1], Madyaret Águila Carbelo[1], Adriel Herrero Díaz[1], Ileana Beatriz Quiroga López[1]

[1]Universidad de Ciencias Médicas de Villa Clara. Facultad de Medicina. Hospital Provincial Clínico Quirúrgico "Arnaldo Milián Castro". Villa Clara. Cuba.

Cite as: García Rodríguez DM, Ruiz Reyes D, Águila Carbelo M, Herrero Díaz A, Quiroga López IB. Update on Cardiac Arrhythmias in Patients with COVID-19. South Health and Policy. 2025; 4:241. https://doi.org/10.56294/shp2025241

Submitted: 24-05-2024 **Revised:** 26-10-2024 **Accepted:** 10-03-2025 **Published:** 11-03-2025

Editor: Dr. Telmo Raúl Aveiro-Róbalo

Corresponding author: Dionis Ruiz Reyes

ABSTRACT

Currently the world population is besieged by COVID-19, a disease caused by the SARS-CoV-2 coronavirus; and it has been declared by the WHO as a pandemic. COVID-19 disease usually presents with mild respiratory symptoms, some patients have pneumonia, and in severe cases, acute respiratory distress syndrome (ARDS) and shock are seen. Cardiovascular complications in the course of COVID-19 are responsible for high mortality. A bibliographic review was carried out in order to characterize the pathophysiology of heart rhythm disorders caused by COVID-19 and its complications. A total of 22 bibliographic references were reviewed between books, medical journals and web pages of the Scielo and Infomed platforms. It is evident that those who suffer from previous heart disease are at risk of decompensation and have higher mortality. The drugs used during the treatment of this condition confer a proarrhythmogenic effect.

Keywords: Arrhythmias; COVID-19; Cardiac Pathophysiology.

RESUMEN

Actualmente la población mundial se encuentra asediada por la COVID-19, una enfermedad causada por el coronavirus SARS-CoV-2; y ha sido declarada por la OMS como una pandemia. La enfermedad COVID-19 suele presentarse con síntomas respiratorios leves, algunos pacientes tienen neumonía y, en casos severos, se observa un síndrome de distress respiratorio agudo (SDRA) y shock. Las complicaciones cardiovasculares en el curso de la COVID-19 son responsables de alta mortalidad. Se realizó una revisión bibliográfica con el objetivo de caracterizar la fisiopatología de los trastornos del ritmo cardiaco por la COVID-19 y sus complicaciones. Se revisaron un total de 22 referencias bibliográficas entre libros, revistas médicas y páginas web de las plataformas Scielo e Infomed. Se evidencia que quienes padecen de cardiopatías previas están en riesgo de descompensación y tienen mayor mortalidad. Los fármacos empleados durante el tratamiento de esta afección confieren un efecto proarritmogénico.

Palabras clave: Arritmias; COVID-19; Fisiopatología Cardiaca.

INTRODUCTION

In December 2019, in the city of Wuhan, Hubei province, China, health authorities reported several cases of pneumonia of unknown cause, specifying later that the causative pathogen was a new type of coronavirus.[1]

The type 2 coronavirus that causes severe acute respiratory syndrome, abbreviated SARS-CoV-2 (from

severe acute respiratory syndrome coronavirus 2), is the cause of the 2019 coronavirus disease, COVID-19.[1]

This disease spread rapidly worldwide due to its efficient transmission capacity, resulting in a pandemic. 1On March 11, 2020, the WHO declared a pandemic due to the high number of infected people worldwide.[2]

As of March 25, 2021, the new coronavirus continues to spread across the globe, with more than 2,7 million deaths and more than 125,7 million people infected. The country most affected in absolute terms is the United States, with more than 30 million infections and over 546 000 deaths, followed by Brazil, with more than 12,3 million cases and 303 000 deaths, and India, with more than 11,8 million cases and 160 000 deaths. The primary focus of the pandemic is once again in Europe, which faces the threat of a fourth wave on the horizon.[3]

The countries most affected by the new type of coronavirus in Latin America are Brazil, Colombia, Mexico, Argentina, Peru, Chile, and Ecuador.[4]

According to the official website of the Ministry of Public Health in Cuba, as of March 25, 2021, there were 70,634 confirmed cases of the disease and 413 deaths.[5]

At the end of March 2021, Villa Clara reported an incidence rate of 16,2 per 100 000 inhabitants.[6]

COVID-19 usually presents with mild respiratory symptoms, some patients have pneumonia, and in severe cases, acute respiratory distress syndrome (ARDS) and shock are observed. Although the manifestations of COVID-19 are mainly respiratory, other effects, such as cardiac effects, have recently been studied more frequently.[7]

Cardiovascular disorders have been observed in patients with COVID-19. In the heart, SARS-CoV-2 is capable of causing direct cardiac damage and fulminant myocarditis, mediated by the systemic inflammatory process and cytokine storm. Cardiac damage manifests as myocarditis, heart failure, cardiogenic shock, acute coronary syndrome, and cardiac arrhythmias and is detected by elevated cardiac biomarkers (troponins, CK-MB, and LDH). The presence of underlying comorbidities, pathophysiological changes imposed by the disease, and concomitant polypharmacy increases the likelihood of life-threatening arrhythmias in these patients.[8,9]

A January 1 to 20, 2020, report on 130 patients hospitalized at Zhongnan University Hospital in Wuhan shows that 26 % required intensive cardiac care. Of these, 16,7 % developed arrhythmias and 7,2 % experienced acute coronary syndrome. Many of them also had elevated levels of high-sensitivity cardiac troponin I, suggesting myocardial injury. In other cases that tested positive for COVID-19, cardiac symptoms (palpitations and chest pain) were the first manifestations.[2]

Information on the incidence of ventricular arrhythmias in patients with COVID-19 infection is limited. A single-center retrospective study in Wuhan identified ventricular arrhythmias in 187 patients and malignant events [ventricular tachycardia (VT)/ventricular fibrillation (VF)] in 5,9 %. Thirty-five point three percent had underlying cardiovascular disease, hypertension (32,6 %), coronary artery disease (11,2 %), cardiomyopathies (4,3 %), and 27,8 % had elevated troponin T levels. The overall mortality rate was 23 %.[8]

COVID-19 is a global pandemic that has affected millions of people worldwide due to its high virulence. SARS-CoV-2 infection causes various conditions in various body systems, including the respiratory, renal, cardiovascular, and nervous systems. These conditions are due to the pathophysiology of the virus. Given the importance of understanding the cardiac pathophysiology of SARS-CoV-2, which leads to an increased likelihood of arrhythmias in patients, we have decided to conduct this literature review to further our knowledge on the subject.

Objective: To characterize the pathophysiology of cardiac rhythm disorders caused by COVID-19 and its complications.

DEVELOPMENT

Pathophysiology of cardiac disease caused by SARS-CoV-2

SARS-CoV-2 is a single-stranded ribonucleic acid (RNA) virus enveloped with surface projections corresponding to spike glycoproteins (protein S) with two subunits, S1 and S2, which give it a crown-like appearance. S1 contains the binding domain receptor that will bind to the angiotensin-converting enzyme 2 (ACE2) peptidase, and S2 is responsible for membrane fusion. The first step in viral entry is binding the coronavirus S protein to the host's trimeric ACE2 protein.[10]

Angiotensin-converting enzyme II (ACE-2) is a membrane exopeptidase in type 2 pneumocytes, cardiomyocytes, pericytes, endothelium, and possibly other cell types.[2,10]

ACE2 is a multifunctional protein. Its primary function is the enzymatic conversion of angiotensin 2 (Ang II) to angiotensin (Ang)-(1-7) and Ang I to Ang-(1-9), which are cardiovascular protectors.

ACE2 plays a role in lung protection. Therefore, viral binding to this receptor dysregulates a lung protection pathway, contributing to viral pathogenicity.[11]

After endocytosis, the ACE2 surface is downregulated, accumulating angiotensin II, whose effects include increased inflammation, vasoconstriction, fibrosis, vascular permeability, and a propensity for thrombosis. Within the host cell's cytoplasm, RNA from the viral genome is released and replicated, leading to newly formed genomic RNA, which is processed into vesicles containing virions that fuse with the cell membrane to release

the virus.[10]

SARS-CoV-2 infection is characterized by three phases:[12]

- Phase 1 or early infection: characterized by anosmia, fever, dry cough, and constitutional symptoms as clinical manifestations, with biomarkers including lymphocytopenia, increased D-dimer levels, increased LDH levels, and increased cytokine levels.
- Phase 2 or pulmonary: dyspnea and tachypnea are the clinical manifestations, and biomarkers include decreased O2 saturation, increased D-dimer levels, and pulmonary infiltrates (CT).
- Phase 3 or severe hyperinflammation: clinical manifestations include acute respiratory distress syndrome (ARDS), septic shock, acute renal failure, acute heart failure, disseminated intravascular coagulation (DIC), and biomarkers include a significant decrease in O2 saturation, a greater increase in D-dimer, increased coagulation times, increased ferritin, increased interleukin 6 (IL-6), tumor necrosis factor **α** (TNF**α**), PCR, and increased troponin levels.

Severe cases of COVID-19 have been found to have very high levels of angiotensin II. Angiotensin II levels have been correlated with viral load due to ACE-2 inhibition by the virus.[2]

The pathophysiology of cardiovascular system disorders is not yet well defined, as many factors can alter it, such as the patient having a pre-existing heart condition, comorbidities (hypertension, diabetes, some degree of obesity, cancer) or use of medications such as angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), or antivirals. However, it has been reported that, at the beginning of the interaction between the virus and the cells to be infected, transmembrane serine protease 2 (TMPRSS2) cleaves the S protein of the virus, causing its internalization by ACE2, induced by the S2 subunit. This first point could explain some manifestations because when ACE2 is damaged, it loses its regulatory function with angiotensin II, promoting increased blood pressure and a proinflammatory state, mainly affecting the lungs. In addition to endothelial dysfunction, there is activation of the innate immune system that causes cytokine storms, triggering an unbalanced response by type 1 and 28 T helper cells, causing damage to the microvascular system, hypoxemia, and activation of the coagulation system with inhibition of fibrinolysis. All these alterations lead to disseminated intravascular coagulation, which causes a general microcirculatory disorder contributing to myocardial cell damage and, subsequently, to a synergistic effect with other organic alterations in systemic failure.[1]

The research team suggests that the virus's pathogenicity, which causes complications in different organ systems, is due to the entry point, ACE II, found in the membranes of type 2 pneumocytes, cardiomyocytes, pericytes, endothelium, and possibly other cell types. The complications are due to the dysfunction of this protein, which causes increased blood pressure and a proinflammatory state.

Cardiac complications during COVID-19

Although patients with SARS-CoV-2 frequently present with respiratory symptoms, it is not unusual for clinical presentation to include symptoms that point to the cardiovascular sphere.

The most common forms of presentation are listed below.

1-Myocarditis

There is evidence of direct damage to the myocardium by coronavirus. One of the clinical presentations of COVID-19 can be chest pain, accompanied by alterations in the PR and ST segments on the electrocardiogram, with elevated blood biomarkers that suggest a diagnosis of myocarditis. Current evidence is insufficient to determine whether these patients preferentially present with preserved or reduced ejection fraction. The severity of the clinical picture will depend on the extent of myocardial damage and the levels of inflammatory mediators, such as interleukin 6 (IL-6). The outcome can be dramatic in those who develop fulminant myocarditis with cardiogenic shock.

Inciardi RM et al.[13] describe the case of a patient with no history of cardiovascular disease who was admitted for COVID-19 with dysfunction.

significant left ventricular enlargement, which had severe acute myopericarditis. SARS-CoV-2 infection causes focal or global myocardial inflammation, with necrosis areas that produce electrocardiographic and echocardiographic abnormalities and elevated myocardial damage markers that can be confused with acute coronary syndrome.[14]

2-Decompensated heart failure

Presentation as heart failure (HF) is common, affecting nearly 23 % of those infected with SARS-CoV-2. However, doubts remain as to whether it is more often due to an exacerbation of pre-existing disease or a de novo phenomenon secondary to myocarditis or stress cardiomyopathy.[7] Acute viral myocarditis, in this case caused by SARS-CoV-2, is not the only cause of acute heart failure, which can be severe. The enormous

machinery of molecular and cellular mechanisms involved in the pathophysiology of COVID-19 in its most advanced stages explains why ventricular dysfunction occurs, regardless of the virus's direct involvement in the myocardium. The hypoxia caused by respiratory distress reduces the oxygen supply to the myocardium, which has increased demands for this gas due to sympathetic stimulation secondary to the infection. Furthermore, systemic inflammatory response syndrome promotes an increase in cytokines, which have a known depressant effect on the myocardium.[14]

3-Acute coronary syndrome

Patients with a history of ischemic heart disease or those at risk of atherosclerotic disease are at increased risk of developing ACS. Infection causes increased myocardial oxygen demand, usually linked to respiratory failure, which can trigger type II acute myocardial infarction secondary to an imbalance in oxygen supply/demand. On the other hand, the systemic inflammatory response can destabilize coronary atherosclerotic plaques, causing type I acute myocardial infarction.7Noria S et al 7 found that in a series of 19 patients with ST-elevation ACS and SARS-CoV-2 infection, there was wide variability in presentation, with a high prevalence of non-obstructive coronary artery disease and poor prognosis (72 % in-hospital mortality).

4-Thromboembolic events

The response to viral infection produces a state of hypercoagulability which, together with inflammation of the endothelial cells, can lead to platelet dysfunction and a predisposition to thrombus formation. Although these are more frequently venous, they can also occur in the arterial system and cause heart attacks at any level, as well as pulmonary thromboembolism and hypertension.[14]

Spiezia L et al15 found that the hypercoagulable state presented by COVID-19 patients is associated with an increase in fibrinogen levels with excessive fibrin polymerization secondary to infection; this virus promotes massive fibrin formation, which would explain the high levels of D-dimers, and this would not be associated with consumption coagulopathy. Patients infected with SARS-CoV-2 are at increased risk of venous thromboembolism, reaching 25 % in those admitted to the ICU. Antithrombin levels are lower in COVID-19 cases, and D-dimer and fibrinogen levels are higher than in the general population. In addition, the progression of disease severity is linked to a gradual increase in D-dimer. The maximum expression of this disorder is the presence of a coagulopathy similar to antiphospholipid syndrome or the establishment of disseminated intravascular coagulation.[2,7,14]

IL-6 plays an important role in the network of inflammatory mediators and can cause coagulation disorders through various pathways, such as hepatic stimulation for thrombopoietin and fibrinogen synthesis, increased expression of vascular endothelial growth factor, expression of monocyte tissue factors, and activation of the extrinsic coagulation system. The thrombin generated in turn can induce the vascular endothelium to produce more IL-6 and other cytokines. Cytokine storms and coagulation disorders thus feed back into each other.[2]

Based on the above, it is recommended that infected patients receive thromboprophylaxis, not only during hospitalization, but also for 45 days in individuals at high risk (reduced mobility, active cancer, elevated D-dimers).[7]

The research team suggests that the main cardiovascular complications caused by COVID-19 are due to damage to cardiomyocytes or dysfunction of another organ system, since myocarditis is due to damage to cardiomyocytes, causing elevated biomarkers. On the other hand, ACS is due to an imbalance in oxygen supply/demand due to respiratory system involvement or endothelial discontinuity. This leads to coagulation activation, causing prothrombotic events throughout the body.

Arrhythmias

Cardiac arrhythmias are another common manifestation in infected patients, with an approximate incidence of 16 %, which increases significantly with the severity of the disease (44 % in ICU patients). The presence of malignant arrhythmias such as ventricular tachycardia/fibrillation was reported in 5,9 % of cases. Myocardial injury, manifested by elevated troponin levels, has also been observed in these patients. Although the underlying mechanisms are still under investigation, they are attributed to hypoxia, metabolic alterations, and inflammatory and neurohumoral stress. Brugada-like electrocardiographic patterns have also been described, further complicating the correct differential diagnosis.[1,7]

Wang D et al.[16] found in their study that arrhythmias were present in 16,7 % of the patients studied and are one of the main complications during hospitalization. Although the type of arrhythmia or definition was not specified, its relationship (as well as acute myocardial damage) with admission to the ICU and older patient age was mentioned.

Three scenarios in which cardiac arrhythmias occur in COVID-19 are highlighted:[8]

1. Cardiac arrhythmias caused by COVID-19.
2. History of cardiac arrhythmias in patients with COVID-19.

3. Proarrhythmia secondary to COVID-19 treatment.

Cardiac arrhythmias caused by COVID-19

In patients with COVID-19, infection is a sufficient condition to cause cardiac arrhythmias in the absence of previous structural heart disease. Direct cardiac damage, myocarditis, myocardial ischemia, and heart failure are favorable scenarios for the development of atrial fibrillation (AF) and ventricular arrhythmias.[8]

The severe inflammatory reaction observed in some patients may, in theory, promote arrhythmias through sympathetic hyperactivity and the effect of interleukins (especially IL-6) on potassium channels and CYP3A4, which can lead to repolarization prolongation.[17]

The substrates, triggers, and modulators for the genesis and perpetuation of AF in this context are multiple, complex, overlapping, and difficult to control. Noteworthy are myocardial injury, hypoxia, ischemia, inflammation, hypokalemia and hypomagnesemia, metabolic acidosis, use of inotropic agents (dobutamine, dopamine, and norepinephrine), ventilator dyssynchrony, volume overload, increased sympathetic tone, and concomitant bacterial infection.[8]

No specific electrocardiographic changes have been described for COVID-19. Case reports have found a transient S1Q3T3 pattern and AV block, which have been explained by acute right ventricular overload and myocardial inflammation, respectively. ST elevation has also been reported, which has been linked to myocarditis. The limited information available is possibly associated with the difficulty of performing electrocardiograms in these patients due to the risk of spreading the infection through electrocardiographs and the risk to healthcare workers.[17]

The incidence of AF in patients with severe pneumonia, ARDS, and systemic inflammatory response syndrome is high. Ambrus et al.18 reported a 10 % incidence of recent-onset AF in critically ill patients with sepsis or ARDS.

History of cardiac arrhythmias in patients with COVID-19

Patients with hypertension, ischemic heart disease, cardiomyopathies, DM, obesity, and channelopathies constitute, per se, a high-risk subgroup for cardiac complications, which is increased in the context of COVID-19,[8] according to recent epidemiological studies. However, according to the literature reviewed, the magnitude of the association between cardiovascular comorbidity and the presence of symptoms at the time of diagnosis has not been determined in this type of patient.[19]

The comorbidities above are associated with a higher incidence of AF, atrial flutter (AFL), and VT.[8]

There are no data on what happens to baseline arrhythmias in patients with COVID-19. Given the relationship between atrial fibrillation (AF) and sepsis, events may be exacerbated. A study including 8 910 patients evaluated mortality and found, in a multivariate analysis, that a history of arrhythmias conferred a higher risk (OR 1,95, 95 % CI 1,33-2,86). However, there is also no information on the type of arrhythmia or the effect of each type on this risk.[17]

Similarly, in the face of severe infection and increased metabolic requirements, cases of ventricular arrhythmias may increase in patients with underlying heart disease.[17]

Pre-existing structural heart disease with scarring, fibrosis, and sutures creates areas with heterogeneous electrophysiological properties that determine the arrhythmogenic substrate. In critically ill patients, infection, hydroelectrolytic and acid-base disturbances, hypoxemia, ischemia, cytokine storm, and increased sympathetic nervous system tone are triggers and modulators of the preexisting arrhythmic substrate. Thus, a vicious circle is established; cardiac arrhythmias and their underlying conditions increase the risk of severe disease, while in the most severe forms, triggers and modulators of cardiac arrhythmias are more frequent.[8]

The existence of arrhythmias before COVID-19, regardless of whether they are atrial or ventricular in origin, poses a challenge in the management of patients. Comorbidity makes them vulnerable to developing severe forms of the disease with a poorer response to therapy. The most severe forms provide triggers and modulators of cardiac arrhythmias, and the prior use of antiarrhythmic drugs often limits protocol-based therapy and their interaction is potentially proarrhythmic.[8]

Proarrhythmia secondary to COVID-19 treatment

Proarrhythmia is defined as the generation of a new arrhythmia or the worsening of a pre-existing arrhythmia due to drugs used in doses considered non-toxic. It generally occurs in patients with structural heart disease; there is individual susceptibility, it is genetically determined, it is the result of abuse, misuse, or inherent to the drug, and it is often unpredictable.[8]

Many clinical trials are underway in patients with coronavirus disease 2019 (COVID-19) to test drugs that may be useful for its management. Some of these are associated with prolonged cardiac ventricular repolarization (evidenced on a conventional electrocardiogram as QT prolongation), which occurs due to alteration of various ion channels in the cell membrane of cardiac myocytes.[20]

The QT interval is the electrocardiographic representation of cardiac myocytes' depolarization and repolarization.[20]

The QT interval can be prolonged by multiple medications that directly or indirectly inhibit potassium ion channels (Ik). Inhibition of these channels will lead to an abnormal prolongation of phase 3 of the action potential, which is reflected electrocardiographically as T wave abnormalities or the appearance of the U wave. Prolongation of phase 3 may lead to early post-depolarizations due to the activation of calcium channels that allow calcium to enter the cell; the latter is what causes ventricular arrhythmias, mainly torsade de pointes.[20]

Prolongation of the QT interval predisposes to the onset of ventricular arrhythmias that can cause death. The arrhythmia most closely related to QT interval prolongation is torsade de pointes, which can rapidly degenerate into ventricular fibrillation. It is also important to mention that for every 10 ms of QT interval prolongation, the risk of torsades de pointes increases by 7 %.[20]

Some patients have ion channel abnormalities due to genetic mutations that cause pathological QT interval prolongation, a condition known as long QT syndrome. Currently, there are multiple types of this syndrome, and it is one of the hereditary conditions most frequently associated with sudden death. Great caution should be exercised with drugs prescribed to these patients, as they could further prolong the QT interval and precipitate malignant arrhythmias. At present, there are no reports of cases of long QT syndrome and COVID-19. Still, if any arise, great caution should be exercised with the drugs used.[20]

The appearance of early post-potentials has been demonstrated for drugs that prolong the QTc, hypokalemia, hypoxia, increased partial pressure of carbon dioxide, elevated catecholamine concentrations, and bradycardia and pauses. All of these conditions can occur in patients with COVID-19. Their confluence is associated with an increase in Na2+ or Ca2+-dependent inward currents, or with a decrease in K2+-dependent outward currents, which causes prolongation of the action potential and, in susceptible cases, generates post-potentials that trigger TdP.[8]

Pharmacological treatment protocols for SARS-CoV-2 include a combination of drugs that seek a synergistic effect. Despite limited evidence on the efficacy of many of these drugs, those believed to have an effect against the virus are being used. The drugs used are: chloroquine/hydroxychloroquine, protease inhibitors (lopinavir-ritonavir), remdesivir, azithromycin, interferon, glucocorticoids, and monoclonal antibodies (tocilizumab).[8]

The Cuban protocol defines six therapeutic scenarios. The first three are community population, traveler surveillance centers, and contact isolation centers; they apply prophylactic measures to administer prevengo vir and biomodulin T to vulnerable patients at higher risk. Patients in care centers for suspected cases are treated with oseltamivir, azithromycin, and interferon alfa 2b. Patients hospitalized in open wards are given Kaletra (lopinavir-ritonavir), chloroquine, and interferon alfa-2 b. In units for seriously and critically ill patients, they are treated with Kaletra, chloroquine, tocilizumab, erythropoietin, sulfacetamide, and plasma. These treatments are part of clinical trials, as there is currently no specific treatment for COVID-19.[8]

Chloroquine and its structural analogue, hydroxychloroquine, are antimalarial agents with therapeutic properties for connective tissue diseases such as systemic lupus erythematosus and rheumatoid arthritis. They also have powerful immunomodulatory effects, including the reduction of cytokines such as interleukin 1 and 6 (IL-1, IL-6), tumor necrosis factor (TNF), and interferon (IFN). In vitro activity has been demonstrated against RNA viruses (rabies, poliovirus, dengue, Ebola) and coronaviruses (SARS-CoV-1 and MERS-CoV) and is currently used for COVID-19 disease. Its antiviral effect occurs by limiting the binding of viral particles to the cell surface, preventing endocytosis, suppressing virus fusion with endosomes, and limiting the virus maturation process. Adverse events associated with its use include ventricular repolarization disorders (prolonged QT interval) with increased susceptibility to developing serious ventricular arrhythmias, such as torsade de pointes, ventricular fibrillation, and sudden death. This effect is dose-dependent and is due to the blockade of the KCNH2 potassium channel.[21]

A concern with the use of these drugs is that they can cause QTc prolongation, thereby increasing the possibility of TdP and sudden death. Another effect on the cardiovascular system that is of concern is the decrease in intracardiac conduction velocity, which becomes evident with conduction disorders of varying degrees. Adverse effects on the heart are rare and associated with long-term treatment; however, they should be monitored due to their implications regarding mortality.[8]

Therefore, it is advisable not to administer hydroxychloroquine if you have a baseline QTc > 550 ms. If QTc < 500 mg, with narrow QRS, reevaluate at the second and fourth doses of the medication. If 550 mg is exceeded, discontinue and consult a cardiologist (either at the second or fourth dose). If the QTc is not prolonged (value < 550 ms), treatment may be continued with daily monitoring of the QTc.[22]

Azithromycin is an antimicrobial belonging to the macrolide family. Its use in patients with COVID-19 is based on minimal evidence from a small study. Six patients in the hydroxychloroquine arm were also treated with azithromycin. A significant reduction in SARS-CoV-2 positivity in nasopharyngeal secretions was found compared with hydroxychloroquine alone. Macrolides are capable of prolonging the QT interval and inducing ventricular arrhythmias. It has been proposed that chronic exposure to azithromycin increases the current of Sodium

(Na+), which promotes QT prolongation and cardiac arrhythmias. Azithromycin has been associated with QTc prolongation and TdP in isolated cases, mainly in individuals with additional risk factors.[21]

Kaletra (lopinavir-ritonavir) is a combination of protease inhibitors useful in the treatment of HIV infection. In vitro and animal activity against other coronaviruses, such as SARS and MERS, has been reported. In patients with severe COVID-19, it showed no additional benefit over standard treatment. No major proarrhythmic adverse events were reported in either arm of the study, and there was only one case of QTc prolongation in the lopinavir-ritonavir arm (no details on the degree or existence of other risk factors for concomitant QTc prolongation). Its use carries a moderate risk of affecting atrioventricular (AV) conduction, with reports of AV block and QTc prolongation, but a low risk of TdP when used alone.[21]

The risk of proarrhythmia from the use of these drugs is low when used individually; however, in the context of COVID-19, several of them are almost always included at the same time. In addition, special attention should be paid to patients undergoing treatment with antiarrhythmic drugs due to the risk of ventricular arrhythmias secondary to proarrhythmia, due to interaction with the drugs included in the COVID-19 treatment protocol.[8]

In the case of interferon alfa 2b, oseltamivir, tocilizumab, erythropoietin, and sulfacen, there is no evidence of reports of proarrhythmia, nor are there any theoretical elements regarding their mechanism of action that would justify their occurrence.[8]

The research team suggests that the causes of arrhythmias in COVID-19 are due to QT interval prolongation, which is caused by myocardial damage from the disease or exacerbated by it due to a previous history, or by the proarrhythmic effects of some drugs used in the treatment of this disease, hence the importance of monitoring and ECG control when starting and continuing treatment with these drugs.

CONCLUSIONS

The COVID-19 pandemic has affected millions of people around the world. The SARS-CoV-2 virus (the causative agent of COVID-19) enters the body by binding to angiotensin-converting enzyme receptors in the host. Numerous manifestations of the disease related to the cardiovascular system have been described, such as myocarditis, arrhythmias, acute coronary syndrome, sudden death, or heart failure, which could be associated with the activation of coagulation pathways, proinflammatory effects, or endothelial dysfunction. These effects are caused by structural damage from the virus or are associated with hypoxia, neurohumoral stress, cytokine release, electrolyte disturbances, or blood viscosity due to reported massive thrombosis. Coronavirus causes a prolongation of the QT interval, leading to arrhythmias, some of which are malignant and cause sudden death due to myocardial damage. The drugs used to treat this condition have a proarrhythmogenic effect, mainly due to QTc prolongation, and may interact with cardiovascular medications. Diagnostic, preventive, and treatment measures must therefore be established in these patients due to the risk of torsade de pointes and death.

BIBLIOGRAPHICAL REFERENCES

1. Clemente-Herrera A, Sánchez-De la Torre EJ, Enríquez-Contreras JM. Manifestaciones cardiológicas en pacientes con COVID-19. Med Int Méx [Internet]. 2020 [citado 23 Mar 2021]; 36(3): 357-364. Disponible en: https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.medigraphic.com/pdfs/medintmex/mim-2020/mim203k.pdf&ved=2ahUKEwi13IL9huXvAhUinuAKHWc5BQsQFjABegQIARAG&usg=AOvVaw2ix9pcnguHyM5nKCu8KWC-

2. Fonseca MYI, Díaz RYL, Vargas FMÁ. Relación entre la COVID-19 y las enfermedades cardiovasculares. 16 de abril. 2020;59(277):1-6.

3. World Health Organization. Coronavirus (COVID19) – WHO Health Emergency Dashboard [Internet]. 2020 [citado 23 Mar 2021]. Disponible en: https://covid19.who.int/

4. Estadísticas en América Latina[Internet].[citado 18 May 2021]. Disponible en: https://es.statista.com/estadisticas/1105121/numero-casos-covid-19-america-latina-caribe-pais/

5. Sitio Oficial del Ministerio de Salud Pública de Cuba[Internet].[citado 18 May 2021]. Disponible en: https://salud.msp.gob.cu/category/covid-19/

6. Perez Fernandez GA, Isidor Santana G, Martín Rodriguez, Suarez Hernandez R, Rodriguez Gonzalez E, Sarda Rojas J. Aspectos epidemiológicos y de laboratorio en pacientes con cardiopatía y diagnostico de COVID-19 en Santa Clara (Cuba). Rev.CorSalud[Internet]. 2020 [citado 23 Mar 2021]; 12(2):129-137. Disponible en: http://www.revcorsalud.sld.cu/index.php/cors/article/view/622/1171

7. Noria S, Bachini JP, Ramos MV. Coronavirus y sistema cardiovascular. Rev.Urug.Cardiol[Internet]. 2020 [citado 23 Mar 2021]; 35(2):193-208Disponible en: http://www.scielo.edu.uy/scielo.php?script=sci_

arttext&pid=S1688-04202020000200193. Epub 01-Ago-2020. http://dx.doi.org/10.29277/cardio.35.2.13

8. Gutierrez Lopez A, Cruz Cardentey M, Mengana Betancourt A, Castañeda Chirino O, Martinez Lopez F, Falcon Rodriguez R. Arritmias cardiacas en pacientes con la Covid-19. Escenarios y tratamiento. Rev.cuba. cardiol. Sir.cardiovasc. [Internet]. 2020. [citado 23 Mar 2021]; 26(3): 2-6. Disponible en: http://revcardiologia.sld.cu/index.php/revcardiologia/article/view/1006

9. Kunal Karamchandani MD, Quintili A, Landis T. Arritmias cardiacas en pacientes críticos con Covid-19. Journ. Cardioth. Vasc. Anesth. [Internet]. 2020. [citado 23 Mar 2021]. Disponible en: https://www.jcvaonline.com/article/S1053-0770(20)30807-7/fulltext#articleInformation

10. Arregui Costales RA, Alomia Arevalo CA, Arequipa Herrera JA, Barrera Valdivieso MA et al. Consenso Interino De Cardiologia Informado en la evidencia sobre complicaciones cardiovasculares de SARS-CoV-2/COVID-19. [Internet]. 2020. [citado 23 Mar 2021]. Disponible en: https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.salud.gob.ec/wp-content/uploads/2020/05/CONSENSO-DE-CARDIOLOG%25C3%258DA-SOBRE-MANEJO-DE-COMPLICACIONES-CARDIOVASCUARES-ASOCIADAS-A-SARS-COv2COVID19-versi%25C3%25B3n.pdf&ved=2ahUKEwjp29jJi-XvAhVuh-AKHRcZDaMQFjAAegQIBRAC&usg=AOvVaw0CcTblFTzz72z-6dp52p4b

11. Alfonso Rodriguez E, Llerena Rojas LD, Rodriguez Nande LM. Consideraciones para pacientes con enfermedades cardiovasculares durante la pandemia de la COVID-19. Rev Cubana Invest Bioméd. [Internet]. 2020. [citado 23 Mar 2021]; 39(3): e795. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0864-03002020000300023

12. Rozadoa J, Ayestaa A, Morísa C, Avanzas P. Fisiopatología de la enfermedad cardiovascular en pacientes con COVID-19. Isquemia, trombosis y disfunción cardiaca. Rev Esp Cardiol Supl. [Internet]. 2020. [citado 23 Mar 2021];20(E):2-8. Disponible en: https://www.revespcardiol.org/es-fisiopatologia-enfermedad-cardiovascular-pacientes-con-articulo-S1131358720300285

13. Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, et al. Cardiac involvement in a patient with Coronavirus Disease 2019 (COVID-19). JAMA Cardiol [Internet]. 2020 [citado 18 May 2021]. Disponible en: http://doi.org/10.1001/jamacardio.2020.1096

14. Moreno-Martinez FL, Moreno-Lopez FL, Oroz Moreno R. Repercusión cardiovascular de la infección por el nuevo coronavirus SARS-CoV-2 (COVID-19). Corsalud. [Internet]. 2020. [citado 23 Mar 2021]; 12(1): 3-17. Disponible en: http://www.revcorsalud.sld.cu/index.php/cors/article/view/588

15. Spiezia L, Boscolo A, Poletto F, et al. COVID-19-related severe hypercoagulability in patients admitted to Intensive Care Unit for acute respiratory failure. Thromb Haemost[Internet] 2020[citado 17 May 2021]; 120(6): 998-1000. https://doi.org/10.1055/s0040-1710018

16. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA J Am Med Assoc[Internet]. 2020[citado 17 May 2021];323(11):1061-9. Disponible en: 10.1001/ jama.2020.1585

17. Mora G. Covid-19 y arritmias. Relación y riesgo. Rev. Colomb. Cardiol. [Internet]. 2020. [citado 23 Mar 2021]; 27(3): 153-159. Disponible en: https://www.elsevier.es/es-revista-revista-colombiana-cardiologia-203-articulo-covid-19-arritmias-relacion-riesgo-S0120563320300930#:~:text=En%20la%20pandemia%20por%20COVID,parcialmente%20por%20da%C3%B1o%20mioc%C3%A1rdico%20agudo.

18. Ambrus DB, Benjamin EJ, Bajwa EK, Hibbert KA, Walkey AJ. Risk factors and outcomes associated with newonset atrial fibrillation during acute respiratory distress syndrome. J Crit Care[Internet] 2015[citado 17 May 2021];30(5):994-7. Disponible en: https://doi.org/10.1016/j.jcrc.2015.06.003

19. Dr.C. Pérez Fernández GA, Dra. Santana GI, Dra. Martín Rodríguez L, Dr. Suárez Hernández R, Dr. Rodríguez González E, Dr. Sarda Rojas J. Aspectos epidemiológicos y de laboratorio en pacientes con cardiopatía y diagnóstico de COVID-19 en Santa Clara (Cuba). CorSalud. [Internet]. 2020. [citado 23 Mar 2021]; 12(2):129-137. Disponible en: http://www.revcorsalud.sld.cu/index.php/cors/article/view/622/1171

20. Cueva-Parra Á, Neach-De la Vega D, Ortiz-Solís W, et al. Protocolo para la prevención de arritmias ventriculares debido al tratamiento en pacientes con COVID-19. Cardiovasc Metab Sci[Internet] . 2020[citado 17 May 2021];31(Suppl: 3):222-228. Disponible en: 10.35366/93952.

21. Medeiros-Domingo A, Carrasco OF, Berni-Betancourt A. Potenciales efectos proarrítmicos de la farmacoterapia contra SARS-CoV-2. Cardiovasc Metab Sci . 2020;31(Suppl: 3):199-204.

22. Barja LD, Dr. Fitz Maurice M y Dr.C. Chávez González E. Hidroxicloroquina y azitromicina: riesgo cardiovascular, prolongación de QTc y muerte súbita en el nuevo escenario de la pandemia por COVID-19. CorSalud. [Internet]. 2020 [citado 23 Mar 2021];12(1):54-59. Disponible en: http://www.revcorsalud.sld.cu/index.php/cors/article/view/601/1097

FINANCING

None.

CONFLICT OF INTEREST

None.

AUTHORSHIP CONTRIBUTION

Conceptualization: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Data curation: Dania María María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Formal analysis: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Research: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Methodology: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Project Management: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Resources: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Software: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Supervision: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Validation: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Visualization: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Writing - original draft: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

Writing - revision and editing: Dania María García Rodríguez, Dionis Ruiz Reyes, Madyaret Águila Carbelo, Adriel Herrero Díaz, Ileana Beatriz Quiroga López.

https://doi.org/10.56294/shp2025241 ISSN: 3072-7677