


## MAIN POST-COVID-19 CARDIOVASCULAR SEQUELAE: AN INTEGRATIVE LITERATURE REVIEW

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### ABSTRACT

The disease caused by the new coronavirus, also known as COVID-19, can be understood as a severe acute respiratory syndrome caused by the SARS-CoV-2 virus. The objective of the study was to determine the possible sequelae in the cardiovascular system caused by covid-19 evidenced in the literature. It is an integrative literature review, based on six steps for its elaboration. The data search was carried out through the Lilacs, SciELO and PubMed databases, where the combination of COVID-19 and cardiovascular health descriptors was used, separated by the Boolean operator AND (COVID 19 AND cardiovascular). The study points out that the post-covid consequences related to the cardiovascular system have taken an important place in discussions about the sequelae caused by the disease, and the

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final sample evidenced nine scientific articles that were produced during and after the pandemic period. After their selection and analysis, two discussion categories were listed, grouping the articles: functional cardiac sequelae and secondary cardiac sequelae, both caused by the infection caused by COVID-19. In short, the cardiovascular sequelae caused by COVID-19 infection represent a serious global public health problem, being a significant aggravation and with the potential to reach other body systems, directly impacting the quality of life of affected individuals.

**Keywords:** SARS-CoV-2. Public Health. Cardiovascular System.

## INTRODUCTION

The disease caused by the new coronavirus, also known as COVID-19, can be understood as a severe acute respiratory syndrome caused by the SARS-CoV-2 virus, which belongs to the coronavirus family. The disease was first reported in December 2019, in the city of Wuhan, China. Its global spread was declared a pandemic by the World Health Organization (WHO) in March 2020 (PAHO, 2024).

The WHO declared COVID-19 a Public Health Emergency of International Concern (PHEIC) between January 30, 2020 and May 5, 2023, which is the Organization's highest level of alert. The end of the Emergency did not mean that the virus ceased to be a threat to public health, given that there are still victims, however it guides countries to manage the disease (PAHO, 2023).

The infection caused by the SARS-CoV-2 virus initially showed mild signs in patients, but ended up taking on greater proportions, leading to more severe symptoms, such as dyspnea and the involvement of immunocompromised systems in patients belonging to risk groups (Gomes et al., 2021; Borges et al., 2020).

To enter the host cell, the virus uses the angiotensin-converting enzyme 2 (ACE-2) receptor, which is expressed in various tissues, such as the respiratory tract, myocardium, kidneys, and gastrointestinal mucosa. In the lung, it is present in pneumocytes and macrophages, which are target cells of the virus, however, due to the presence of the enzyme in extrapulmonary sites, systemic dissemination and involvement of several organs becomes potential (Hoffmann et al., 2020).

Patients with pre-existing comorbidities, such as diabetes mellitus, hypertension, heart disease, and lung diseases, demonstrate greater susceptibility to clinical manifestations and complications in case of infection (Borges et al., 2020).

The cardiovascular system, also known as the circulatory system, has a crucial function, being responsible for transporting blood, gases, nutrients, and waste products around the body. It is made up of the heart and an extensive network of veins, arteries, and capillaries. The heart is a muscular organ responsible for pumping blood, while veins, arteries, and capillaries transport oxygenated and deoxygenated blood to maintain the effective functioning of the systems (Ferreira et al., 2021).

The mechanism of cardiovascular complication can be characterized in direct injuries or secondary complications, where initially the patient manifests flu-like symptoms and later can predispose to acute heart failure, thrombosis, arrhythmias, and myocarditis, worsening

the body's defense against the virus, consequently leading to a negative outcome of the condition (Santos et al., 2021). In view of the severity of the complications caused by the infection caused by the coronavirus, the present review study aims to determine the possible sequelae in the cardiovascular system caused by COVID-19 evidenced in the literature.

## **METHODOLOGY**

This study is an integrative literature review, based on six steps for its elaboration. These are: elaboration of the guiding question, search or sampling in the literature, data collection, critical analysis of the included studies, discussion of the results and presentation of the integrative review (Souza et al., 2010).

This type of study is a method whose purpose is to unite and systematize, in a comprehensive and organized way, the results of a specific theme or research question. Prioritizing the increase and deepening of knowledge and understanding of the topic under analysis.

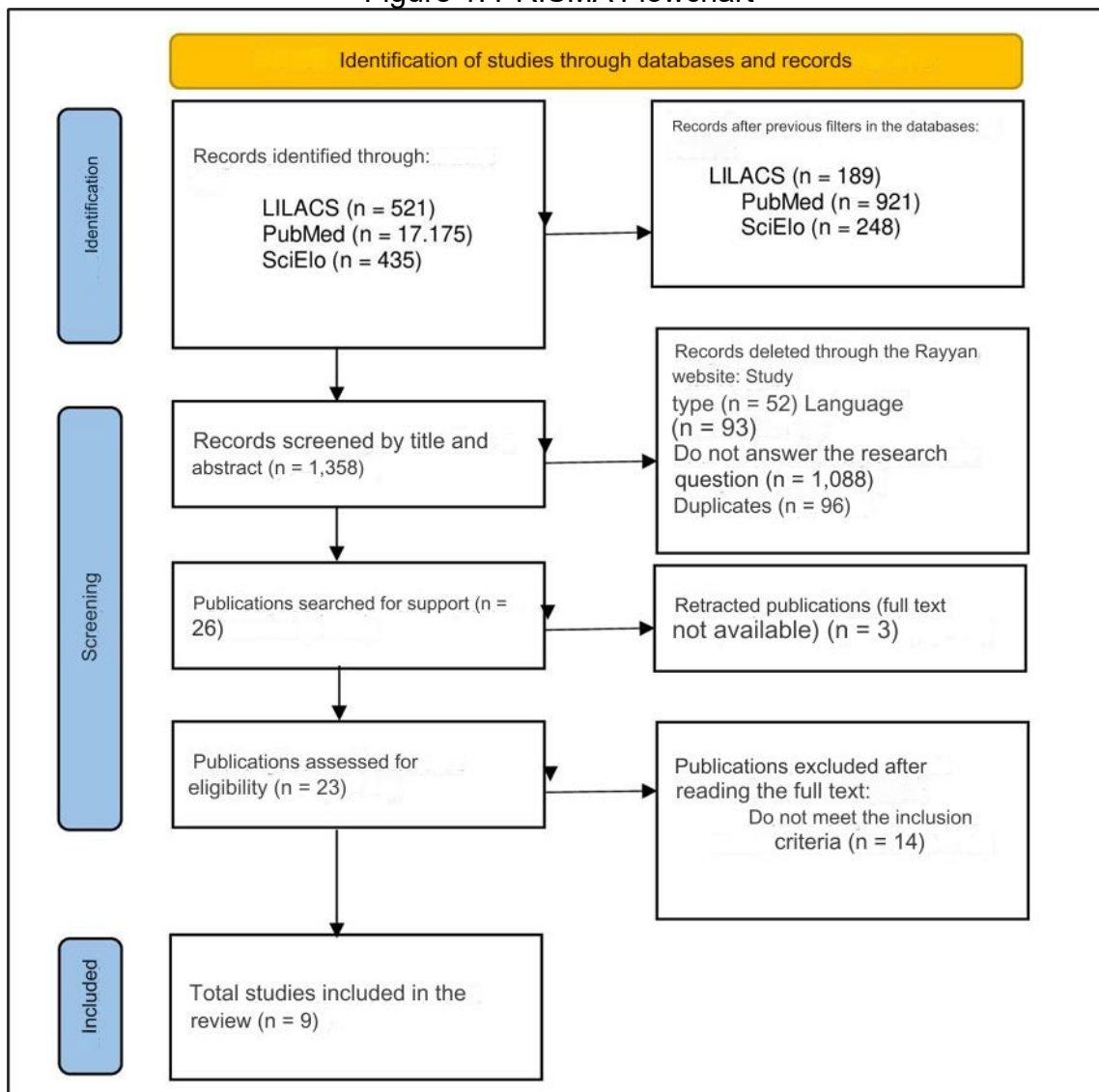
The study aims to answer the following guiding question: what are the possible sequelae in the cardiovascular system caused by COVID-19?

The data search was carried out through the Lilacs, SciELO and PubMed databases, where the combination of COVID-19 and cardiovascular health descriptors was used, separated by the Boolean operator AND (COVID-19 AND cardiovascular). The searches in the selected databases took place from April to June 2024.

The inclusion criteria were: free full articles published in journals indexed in the selected databases, published in the last five years (2019-2024), primary studies and in Portuguese and English. The exclusion criteria were: articles that did not answer the research question, review studies, theses, dissertations, newspaper articles, blogs, and experience reports.

During the search with the combination of descriptors and application of the inclusion and exclusion criteria, 189 publications were found in Lilacs, 248 in SciELO and 921 publications in the PubMed portal. Using the Rayyan website, 96 studies were removed because they were duplicates. After reading titles and abstracts, 1,091 articles were excluded because they did not answer the research question, 93 by language, and 52 by type of study, which were not filtered in the initial search. After reading the full text, 9 articles remained included for the composition of the study, as shown in Figure 1.

Figure 1. PRISMA Flowchart



Source: authors, 2024

Data extraction was carried out through a reading form created by the authors, selecting the main information provided by the selected studies (title, authors, year and contributions that answer the research question).

Based on the categorization defined by the authors, the information provided by the studies, through thematic content analysis, the results were organized, producing two categories of analysis: functional cardiac sequelae and secondary cardiac sequelae, the discussion of the findings was carried out in line with the production of other authors.

## RESULTS

The study points out that the post-COVID-19 consequences related to the cardiovascular system have taken an important place in discussions about the sequelae caused by the disease, and the final sample evidenced nine scientific articles that were produced during and after the pandemic period. Chart 1 presents the articles included, indicating number, title, author and year.

Table 1. Selected articles

NUMBER	TITLE	AUTHORS	ANUS
1	Disease Severity Affects Ventricular Repolarization Parameters in COVID-19 Patients	Mevlut Koc <i>et al.</i>	2020
2	COVID-19 - Endothelial Axis and Coronary Artery Bypass Graft Patency: a Target for Therapeutic Intervention?	Gokce Topal, Andrzej Loesch e Michael R. Dashwood	2020
3	Heart Failure with Preserved Ejection Fraction and COVID-19: a Pernicious Relationship	Evandro Tinoco Mesquita <i>et al.</i>	2020
4	Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19).	Valentina O. Puntmann <i>et al.</i>	2020
5	Myocardial injury and COVID-19: Serum hs-cTnI level in risk stratification and the prediction of 30-day fatality in COVID-19 patients with no prior cardiovascular disease.	Jiatian Cao <i>et al.</i>	2020
6	CardioVascular Mechanisms In Covid-19: methodology of a prospective observational multimodality imaging study (COSMIC-19 study).	Shirjel R. Alam <i>et al.</i>	2021
7	Cardiology referral during the COVID-19 pandemic.	Nathalia Conci Santorio <i>et al.</i>	2021
8	Incidence and predictors of development of new onset hypertension post COVID-19 disease.	Pooja Vyas <i>et al.</i>	2023
9	The long-term effects of the Covid-19 infection on cardiac symptoms.	Reza Golchin Vafa <i>et al.</i>	2023

Source: authors, 2024

After the selection and analysis of the scientific articles, two categories of discussion were listed, grouping them: a) functional cardiac sequelae; and b) secondary cardiac sequelae, both caused by the infection caused by the SARS-CoV-2 virus, as shown in chart 2:

Table 2. Categories chosen from the reading of the articles

Categories	Articles
Functional cardiac sequelae	1, 3, 4, 7
Secondary cardiac sequelae	2, 5, 6, 8, 9

Source: authors, 2024

## DISCUSSION

### FUNCTIONAL CARDIAC SEQUELAE

The COVID-19 pandemic has brought to light concerns beyond the immediate ones, causing a scenario of discomfort due to the lack of knowledge of possible sequelae that affect the body's systems. In particular, cardiovascular diseases have been studied and detailed in order to understand the specific causal factors of the infection.

In view of the importance of heart care, functional sequelae include possible cardiac dysfunctions, such as arrhythmia, inflammation of the heart muscle and chest pain, such dysfunctions can compromise the patient's health status, causing effects on all body systems. In this section, four scientific articles were selected, numbered as one, three, four and seven, which mention functional cardiac sequelae after COVID-19 infection.

Recently produced studies demonstrate the relationship between COVID-19 and myocarditis, an important inflammation in the heart muscle, where it can result in ventricular dysfunction, causing severe cardiac impairment. Thus, even after the individual's recovery, acute infection can leave sequelae in the heart muscle, resulting in a delayed and prolonged recovery, and may even be considered incomplete (Zhou et al., 2021).

Article three, prepared by Mesquita et al. (2020), selected due to the support of the theme, refers to heart failure and myocarditis, where they affirm a correlation, in addition to bringing with it a high morbidity and mortality rate and high cost to health services during and after COVID-19.

Cardiac arrhythmia can also be directly related to post-infection of COVID-19, the development is marked by atrial fibrillation and ventricular tachycardia. These events can be precipitated by systemic inflammation and also by oxidative stress, consequently contributing to a greater development of long-term cardiac complications (Huang et al., 2020).

As mentioned in article one (2020), cardiac complications do not occupy a single mechanism of action, but are multifactorial. Leading to the study of the electrocardiogram as an adjuvant in the discovery of cardiac arrhythmias. Thus, Mevlut Koc et al. (p.910, 2020) emphasize:

There are many electrocardiogram (ECG) parameters related to ventricular depolarization and repolarization. The parameters used in clinical practice are the QT and QTc intervals, the QT and QTc dispersion, and the Tpico-Tfim interval (Tpe).

The Tpe/QT and Tpe/QTc ratios obtained from these parameters are associated with ventricular transmural dispersion during repolarization.

The Tpe interval, when elevated, can be indicative of abnormal dissemination during ventricular repolarization, and is directly associated with an increased risk of developing ventricular arrhythmia.

During post-infection recovery from COVID-19, patients may have impaired functional capacity due to cardiorespiratory sequelae. Studies have described a decrease in physical activity tolerance and the ability to perform these activities in individuals who developed severe forms of the disease (Carfi et al., 2020).

Puntmann et al. (p.11, 2020), in article four, corroborate the findings, pointing out the development of respiratory disorders, such as severe dyspnea, which can cause an overload on the system. In addition to mentioning that the involvement of patients with pre-existing diseases does not change the fact of post-COVID-19 cardiac sequelae compared to healthy users.

It is necessary to consider the great impact of the functional cardiac sequelae of COVID-19 on the human body systems in the long term. In this case, multidisciplinary follow-up and cardiac rehabilitation are necessary to mitigate the risk of more serious complications and improve the quality of life of the affected population (Nishiga et al., 2020).

As cited in article seven, by Santorio et al. (2021), the referral of individuals to the cardiology service is challenging, there are still several obstacles, such as the accuracy of the diagnosis for subsequent effective resolutive treatment. He also mentions the complexity of training in recognizing such impairments during and after the pandemic.

Most of the productions carried out to date highlight the complexity of post-COVID-19 cardiovascular manifestations, highlighting the need for longitudinal studies to fully elucidate the underlying mechanisms and develop effective interventions (Puntmann et al., 2020).

Finally, the functional cardiac sequelae of COVID-19 elucidate a significant challenge for the world's health systems. Understanding these complications is essential for improving prevention, diagnosis, and management strategies for affected patients, aiming to ensure a humane and holistic approach to post-coronavirus health care (Madjid et al., 2021).



## SECONDARY CARDIAC SEQUELAE

Heart diseases resulting from initial pathologies may be causing serious dysfunction in the cardiac system, as they affect the functioning of vessels and blood coagulation. In this case, attention is paid to the formation of blood clots, which can cause acute myocardial infarction and even extreme tiredness, raising blood pressure to severe and chronic levels.

The prevalence of these complications demonstrates the need for effective and rigorous health monitoring, in addition to the implementation of strategies aimed at minimizing risks and promoting an improvement in the quality of life of users. Thus, five scientific articles were found and categorized that mention secondary cardiac sequelae, numbered as articles two, five, six, eight and nine.

Recently published studies carried out in Brazil have highlighted the involvement of patients with thromboembolism, causing significant repercussions on the cardiovascular system, which can increase the risk of thromboembolic events and even heart failure (Lopes et al., 2021).

As mentioned in articles two and nine, complications can affect far beyond the cardiovascular system, developing symptoms over time, such as palpitations, chest pain, and even fainting (Loesch; Dashwood, 2020; Vafa et al., 2023).

Secondary sequelae are often noticed in individuals recovered from COVID-19, who start to present extreme fatigue, even after the viral load is lowered and the infection is resolved (Borges et al., 2020).

A longitudinal study developed in Brazil has shown that patients who have undergone severe COVID-19 infection may present persistent structural and functional changes in the heart organ, causing an effect on vessels and capillaries, increasing the risk of adverse cardiovascular events, such as hypertension (Gomes et al., 2021).

Vyas et al. (2023), cite in article eight that, based on detailed studies, an increase in blood pressure was observed in patients already with the pathology and also in patients with no previous history.

High levels of cardiac markers are also considered a serious problem after COVID-19 infection, and cases of acute myocardial infarction have taken on a higher proportion, which may also contribute to the rates of the development of atherosclerosis (Costa et al., 2020).

In article six authored by Alam et al. (2021), there is a discussion that corroborates cardiac involvement through high troponin levels, stating that these patients have a lower survival rate than the others, and the chances of death were 80 times higher.

Other authors, Jiatian Cao et al. (2020, p.9670), reinforce and state that the viral infection caused by COVID-19 can leave sequelae in the cardiovascular system:

The mechanism of myocardial injury due to SARS-CoV-2 infection has not been fully elucidated, evidence suggests that it may involve direct viral infection of myocardial tissue and indirect pathways such as myocardial infarction, immune dysregulation, inflammation, and hypoxia.

In any case, regardless of cardiac involvement, rehabilitation has proven crucial in the management of post-COVID-19 cardiac sequelae. The exercise capacity and quality of life of affected patients have led to greater concern on the part of expert discussions (Santos et al., 2021).

Thus, it is worth emphasizing the importance of investing in health, so that effective measures can be created and related to each damage caused by COVID-19 to the cardiovascular system, which can avoid more serious damage in the long term and reduce the negative impact of the disease (Martins et al., 2020).

## **CONCLUSION**

Therefore, it was possible to respond to the objective of the research, demonstrating that the cardiovascular sequelae caused by COVID-19 infection represent a serious global public health problem, being a significant aggravation and with the potential to reach other body systems, directly impacting the quality of life of the affected population.

There are several studies that have identified these complications, such as arrhythmia, myocarditis, acute myocardial infarction, among other involvements, which may persist beyond the initial recovery from the disease. In order for proper treatment to occur and due importance to be given, a greater understanding of care is necessary, in order to mitigate potential future and avoidable complications in patients already affected by COVID 19 infection, in addition to conducting long-term clinical studies.

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