Short- and Long-term Effects of the COVID-19 Pandemic on Patients with Cardiovascular Diseases: A Mini-Review

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Abstract

The COVID-19 pandemic had profound implications for patients with cardiovascular diseases (CVDs), both in the short- and long-term. In this article, we provide an overview of the effects of the pandemic on individuals with preexisting cardiovascular conditions. In the short term, the severe acute respiratory syndrome coronavirus 2 infection increased the risk of many cardiovascular events. Furthermore, the pandemic has disrupted health-care systems worldwide, leading to constraints in routine care, and limited access to specialized cardiovascular services and procedure. This has resulted in increased morbidity and mortality rates among patients with CVD (coronary artery disease, hypertrophic cardiomyopathy, heart failure (HF), heart transplant recipients, atrial fibrillation, atrial flutter, previous stroke, or previous peripheral artery disease). In the long term, the COVID-19 impact on patients with CVD extends beyond the acute phase of the disease. Studies have highlighted the development of long-term cardiovascular complications in COVID-19 survivors, such as acute coronary syndrome myocarditis, HF, stroke, venous thromboembolism, and arrhythmias, which may lead to a surge of new cases associated with CVD in the postpandemic era. Health-care systems must prioritize cardiovascular care, developing strategies to identify the patients at higher risk and provide the care to minimize the impact of the pandemic on patients with CVD.

Keywords: Cerebrovascular disease, COVID-19, mortality, myocardial infarction, peripheral artery disease, severe acute respiratory syndrome coronavirus 2

Introduction

The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has disrupted lives worldwide, straining economies and societies, and posing unprecedented challenges to health-care systems. The SARS-CoV-2 was first identified in China in 2019 and then spread throughout all continents. This virus targets primarily the respiratory system, but it may exert profound effects on other organ systems, including the cardiovascular system. Furthermore, among the many complexities of this novel virus, its impact on individuals with preexisting medical conditions, especially cardiovascular disease (CVD), has emerged as a significant concern for health-care professionals and researchers alike. As the pandemic unfolded, clinicians and researchers quickly recognized the complex relationship between COVID-19 and cardiovascular health.

There is growing evidence that COVID-19 may have both short- and long-term consequences on patients with CVD, impacting their quality of life and potentially reshaping cardiovascular care for the future.

This article aims to reflect about the multifaceted repercussions of the COVID-19 pandemic on individuals living with cardiovascular conditions, elucidating both short- and long-term effects that have emerged since 2019.

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The Acute Cardiovascular Effect of the Severe Acute Respiratory Syndrome Coronavirus 2/COVID-19

The structure of SARS-CoV-2 consists of four proteins: the spike (S) protein with 2 subunits, the nucleocapsid protein, the envelope protein, and the membrane protein. The subunit S1 mediates the entrance of SARS-CoV-2 in human cells through the angiotensin-converting enzyme 2 (ACE2)[1,2] which is expressed in many tissues, including the cardiac tissues. Therefore, as expected, the effects of SARS-CoV-2 in the cardiovascular system were also acknowledged early in the pandemic period.

The effects are deemed to be mediated by viral injury and/or indirect injury through the hyperactivated inflammatory response with cytokine storm leading to endothelial injury and dysfunction, with concomitant inflammatory-related prothrombotic state.[3,4]

Severe SARS-CoV-2 infection can lead to myocardial injury[5] which has an incidence of approximately 50% in hospitalized patients, and evidence shows that myocardial injury has an impact on the prognosis.[5,6]

The prothrombotic effect of COVID-19 was also reflected in the increased risk of venous thromboembolism,[5,7] myocardial infarction, and stroke.[5] In the case of stroke, due to the increased risk of large vessel occlusion and possible consequent hemorrhagic transformation, the risk of mortality significantly increases in this context.[5,8,9]

The COVID-19 can also lead to arrhythmias,[5] and to myocarditis[10,11] (in with a frequency much higher compared with SARS-CoV-2 vaccination[12]).

The Acute Impact of COVID-19 on Patients with Preexisting Cardiovascular Disease

Due to the cardiovascular effects of SARS-CoV-2 with COVID-19 disease, the patients with previous known CVD are, expectedly, a population at higher risk of poor outcomes. Ahead we show some compelling data among patients with coronary artery disease (CAD), heart failure (HF), heart transplant recipients, and patients with previous stroke.

Coronary artery disease

In systematic reviews, the prevalence of known CAD among hospitalized patients with COVID-19 was about 12%–13%.[13,14] Preexisting CAD increased at least two-fold the risk of intensive care unit (ICU) admission (odds ratio [OR] = 2.25, 95% confidence interval [CI] [1.34–3.79]) and death [Figure 1]. However, the vital prognosis seems to be also influenced by age, the presence of hypertension, diabetes mellitus, or chronic kidney disease.[13,21]

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is one of the most relevant causes of inherited cardiac disease, and the impact of COVID-19 can lead to HF, arrhythmias, and/or thromboembolic events. The data about the impact of HCM in the prognosis of COVID-19 are scarce, but the Dilema International Cardiomyopathy and Heart Failure Registry and International SHaRe Registries provided unique data about these conditions.[15] The risk of death associated with HCM was nonsignificantly increased compared with controls (OR = 1.70, 95% CI [0.98–2.91]),[15] but in the cohort of patients 80 years old or less, HCM was associated with a 2-fold increase in the mortality risk (OR = 2.24, 95% CI [1.21–4.12]) [Figure 1]. In HCM patients, factors such as age, left ventricular outflow tract obstruction, and left ventricular systolic dysfunction were associated with increased risk of ICU admission or mortality.[15]

Heart failure

Patients with HF accounted for 9% of all COVID-19 patients evaluated in the different studies.[16] Preexisting HF was associated with an increased risk of death [Figure 1] and also hospitalization. Infections are a well-known cause of HF worsening, and cor pulmonale due to the COVID-19 infection explains at least part of the results. Another potential explanation was the upregulation of ACE2 in patients with

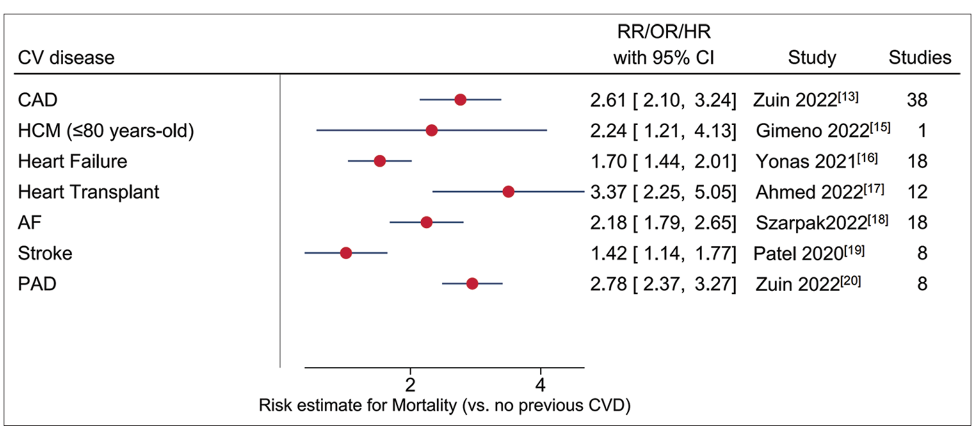

Figure 1: Summary of mortality risks associated with the presence of previous cardiovascular disease. AF=Atrial fibrillation, CAD=Coronary artery disease, CVD=Cardiovascular disease, HCM=Hypertrophic cardiomyopathy, HR=Hazard ratio, OR=Odds ratio, PAD=Peripheral artery disease, RR=Relative risk

HF.[22] However, as observed with ACE inhibitors and angiotensin receptor blockers – medications that increase ACE2 levels and are potential treatments for heart failure – this mechanism does not seem to influence the risk of disease and prognosis.[23,24] On the other hand, the withdrawal of drugs that influence the outcomes of HF is known to increase the mortality in COVID-19 and can explain part of the negative results of SARS-CoV-2 infection in patients with HF.

Heart transplant recipients

Heart transplant recipient patients are also a special population. These patients receive immunosuppressant drugs, and their overall physiological reserve is decreased due to the primary cardiac dysfunction that led to transplantation on top of comorbid risk factors. Despite the recommendation for the use of immunosuppressant drugs for COVID-19 treatment, being a heart transplant recipient remains at increased risk of mortality compared to the individuals without this condition [Figure 1].[17] Furthermore, similar trends were also seen in kidney transplant recipients infected with SARS-CoV-2 which further supports this hypothesis.[25]

Atrial fibrillation or atrial flutter (atrial arrhythmias)

New-onset atrial arrhythmias such as atrial fibrillation or atrial flutter, in the context of a SARS-CoV-2 infection, can range from 2% to 9% according to the severity of the disease.[26,27] The mechanisms thought to be related to the development of these arrhythmias in COVID-19 are systemic inflammation and autonomic imbalance. Atrial fibrillation also increases the risk of death in COVID-19, both for new-onset (relative risk [RR] = 1.86, 95% CI [1.54–2.24]) and previously diagnosed (2-fold increase, RR = 2.18, 95% CI [1.79–2.65], [Figure 1]).[18] This result was somehow expected because the risk factors for atrial fibrillation (such as hypertension, obesity, diabetes, smoking, and obstructive sleep apnea) that frequently coexist with arrhythmia are also risk factors for severe COVID-19 disease.[18]

Stroke and peripheral artery disease

The preexisting cerebrovascular disease, namely stroke, was seen in 4% of the patients with COVID-19. This comorbidity has been associated with an increased risk of ICU admission, mechanical ventilation, and mortality [Figure 1].[8,19,28] This pattern was similar to those seen in severe acute respiratory syndrome and Middle-East respiratory syndrome caused by other coronaviruses.[29,30] The role of previous stroke in the prognosis is not well established but is deemed to be related to age and the presence of other cardiovascular risk factors.

As for peripheral artery disease (PAD), the prevalence of this condition was around 5% of COVID-19 patients.[20] Preexisting PAD increased 2-fold the risk of mortality based on a systematic review of 8 studies [Figure 1].[20] In patients with acute limb ischemia, the presence of COVID-19 also increased the risk of mortality compared with those without COVID-19.[31]

Cardiovascular disease as a risk factor for mortality in international cohort studies

In a systematic review of European cohort studies, arrhythmia and ischemic heart disease were linked to increased inhospital COVID-19 mortality, and a history of HF and stroke were associated with increased COVID-19 mortality in community-based studies.[32]

Impact of COVID-19 on the Health-Care Delivery Related to Cardiovascular Diseases

The COVID-19 pandemic had a detrimental impact on the care provided to patients with acute CVD. Several factors have contributed to a decline in the quality of care during this global health crisis:

1. Fear of seeking medical care/help: Patients might have been hesitant to seek medical attention due to the fear of contracting being infected with SARS-CoV-2 in health-care settings. This delay in seeking care can lead to a missed window of opportunity for timely diagnosis and treatment, potentially resulting in poorer outcomes
2. Strained health-care system: The peak incidence of COVID-19 cases has strained health-care systems, causing hospitals and emergency departments to become overcrowded
3. Disruption of cardiac services: The COVID-19 outbreak has disrupted the normal functioning of cardiac services, including outpatient clinics, diagnostic procedures, and elective surgeries. Canceled or postponed appointments, procedures, and rehabilitation programs have further delayed the management of ACS patients, impacting their overall care
4. Staff shortages and burnout: Health-care professionals are facing increased workloads and immense pressure during the pandemic. Staff shortages resulting from illness, quarantine, or burnout can negatively affect the quality and continuity of care provided to ACS patients. The heightened stress levels and burnout among health-care workers can also impact decision-making and patient outcomes.

The following data detail more specifically some health-care bundles that were affected by the COVID-19 pandemic.

In the setting of the COVID-19 pandemic, there was a decline in the occurrence and admission rates of ACS. The time between the onset of symptoms and the first medical contact was prolonged, while there was an increase in cases where ACS patients were managed outside of hospital settings.[33] In addition, a shift toward less invasive treatment approaches was observed.[33] Unfortunately, ACS patients who presented during the pandemic experienced poorer outcomes with a high risk of mortality and/or HF [Table 1].[33] Despite the heterogeneity among the data, there are studies suggesting that race/ethnicity could have influenced the myocardial infarction care and outcomes in COVID-19 pandemic period.[37-39] Black and Asian patients were less likely to receive invasive treatment and had a higher risk of death.[38,39]

To enhance the prognosis of ACS patients in future pandemics, it is crucial to implement such initiatives and strategies that encourage individuals with ACS symptoms to promptly seek for medical care and avoid inequity in the health-care access.[40] Furthermore, initiatives like early discharge of low-risk myocardial infarction patients should be considered to alleviate the strain on the health-care system.[41]

Regarding stroke care, hospital admissions were reduced in the beginning of the pandemic with the social distancing/isolation. Some reports have shown that stroke admission decreased by 35% while the recanalization therapy was not affected [Table 1].[34] However, the performance measures for recanalization, namely the response time, showed some patient and system-related delays in recanalization-eligible patients.[35]

The volume of cardiac testing modalities has suffered a 77% reduction during the pandemic, but 1 year later, there was a recovery in the volume of examinations similar to prepandemic values [Table 1].[36] The problem is that this recovery might not compensate the absence of cardiac testing with possible prognostic implications.

Despite all these constraints, it is worth noting that a fast adoption of digital technology in the cardiac rehabilitation setting and the building of structured home-based digital-aided interventions were successful in maintaining the cardiovascular health of secondary prevention patients during the pandemic.[42,43]

Long-Term Cardiovascular Effects of COVID-19

This persistence of ongoing COVID-19 signs and symptoms, including symptoms associated with CVD beyond 3 months after recovery from COVID-19, has been internationally recognized as "long-COVID" and "post-COVID."[40,44,45]

The pathophysiology of long-COVID is not well established but it was hypothesized that the persistence of viral particles[46] could lead to inflammation, autoimmune reactions, and/or endothelial/microvascular circulation impairment/microthrombosis,[47] among other potential mechanisms that neurologic involvement and/or psychological factors.[48]

The risk of long-COVID is proportional to the severity of the acute SARS-CoV-2 infection,[49-51] including long-term cardiovascular involvement.[51] However, even mild acute cases are not excluded from long-COVID consequences.[50]

Some of the long-term effects of COVID-19 in cardiovascular manifestations include exercise-induced dyspnea/fatigue (despite most of the cases being related to inefficient oxygen extraction by the muscles[52]), palpitations, dysautonomia related to postural tachycardia syndrome, orthostatic intolerance, and inappropriate sinus tachycardia [Table 2].[53,54]

The new-onset cases of arterial hypertension and diabetes mellitus (up to 1.3% and 2.4% of the cases) increased significantly in patients with COVID-19.[55,56]

Table 1: The impact of COVID-19 on the health-care delivery in acute cardiovascular events/disease

Study	Effects
	ACS/STEMI care
Nadarajah *et al*., 2022[33]	Decline 21% in STEMI hospitalization
	Average increase of symptoms to first medical contact in 69 min
	Similar door-to-balloon times
	Decrease in 27% of revascularization procedures
	Increased use of thrombolysis in STEMI, particularly in lower-income populations
	Post-STEMI heart failure increased in 8% in lower-income countries
	Stroke care
Romoli *et al*., 2021[34]	Stroke admission decreased by 35%
	Overall recanalization therapy did not change significantly
	Average increase in 32 min in the onset-to-door time
Nawabi *et al*., 2022[35]	Increased time of door-to-reperfusion
	Cardiac testing
Einstein *et al*., 2022[36]	Change in stress/ischemia examinations versus prepandemic period
	2020: −77%
	2021: −12%
	Change in CCTA versus prepandemic period
	2020: −54%
	2021: +14%
	Change in ICA versus prepandemic period
	2020: −61%
	2021: 0%

CCTA=Coronary computerized tomography angiogram, ICA=Invasive coronary angiography, STEMI=ST-segment elevation myocardial infarction, ACS=Acute coronary syndrome

Table 2: Selected possible manifestations related to long-term effects of COVID-19 infections

Possible signs and symptoms	Possible conditions/events
Dyspnea/fatigue	Hypertension
Palpitations/tachycardia	Diabetes
Postural tachycardia syndrome	Deep venous thrombosis
Orthostatic hypotension	Pulmonary embolism
Inappropriate sinus tachycardia	AF
	Stroke
	ACS

ACS=Acute coronary syndrome, AF=Atrial fibrillation

Patients who recovered from COVID-19 are also prone to deep venous thrombosis and pulmonary embolism. The incidences of deep venous thrombosis and pulmonary embolism were 2.3% and 1.2%.[57] The risk of these venous thromboembolic events was 2-3-fold higher among COVID-19 patients than in individuals without COVID-19. This risk was higher in the elderly and female patients, being lower as time goes away from the COVID-19 event.[57]

The risk of increased acute arterial cardiovascular events such as acute coronary syndromes or stroke was stressed by Wan *et al*. These researchers showed that individuals who recovered from COVID-19 are still at risk of cardiovascular events (hazard ratio [HR] = 1.3, 95% CI [1.1–1.6]) and all-cause mortality (HR = 4.5, 95% CI [3.9–5.2]) at 18 months of follow-up, according to the data of the UK Biobank.[58]

Al-Aly *et al*. showed that for each 1,000 COVID-19 patients, there were additional 45 cases of cardiovascular events, 23 cases of major adverse cardiovascular events, 10 cases of atrial fibrillation, and 10 cases of venous thromboembolism at 1 year after the infection. The odds for having any of these complications were proportional to the severity of the index event.[59,60]

All these cardiovascular manifestations are particularly relevant in patients with previous CVD, as COVID-19 may worsen the cardiovascular risk profile and elderly patients as well as those with CVD are at higher risk for long-COVID.[61]

Thus, the intersection between long-COVID and preexisting CVD poses a significant health concern. Patients with a history of cardiovascular conditions, such as myocardial infarction, HF, or stroke, may be at an increased risk of experiencing more severe long-COVID symptoms and prolonged recovery periods, but the data are scarce for this phenomenon.

The long-term impact on these individuals can be debilitating, affecting both their physical and mental well-being which also increases the risk of cardiovascular events. To investigate and manage cardiovascular long-COVID symptoms, physicians should consider beyond the standard clinical examination, doing an electrocardiography, transthoracic echocardiogram, and blood analyses. According to the symptoms of the patients, an investigation should be carried out using Holter monitoring for arrhythmias, tilt test for dysautonomia/postural orthostatic tachycardia, coronary computerized tomography scan with contrast or functional ischemia examinations for coronary disease, cardiac magnetic resonance for myocarditis evaluation, and pulmonary computerized tomography scan with contrast or pulmonary scintigraphy for pulmonary embolism.[53]

Conclusion

The COVID-19 pandemic has further disrupted the health of patients with CVD in unprecedented ways. From the immediate exacerbation of these baseline conditions to the long-term implications on cardiovascular health, the effects of the pandemic have been complex and are still not completely understood. The data are particularly compelling for patients with CAD, HF, heart transplant, and stroke. Understanding and addressing these short- and long-term consequences is crucial to guide clinical decision-making, reshape health-care delivery, and ensure the optimal care of patients with CVD in the post-pandemic era. The lessons taken from this global health crisis are important for the enhancement of healthcare systems to improve patient outcomes and pave the way for a more equitable and robust cardiovascular care. Future data are still needed to better understand and tackle the long-COVID consequences.

Author contributions

Daniel Caldeira designed the study and wrote the first draft of the manuscript with Joana Brito, Catarina Gregório, Rui Plácido, and Fausto J Pinto. Each co-author contributed to either the delivery of the study or helped with the writing. All authors have given final approval for the current version to be published.

Ethical statement

The ethical statement is not applicable to this article.

Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Conflicts of interest

Prof. Fausto J. Pinto is an Editorial Board Member of the *Heart and Mind* journal. The article was subject to the journal's standard procedures, with peer review handled independently of Prof. Fausto J. Pinto and the research groups. There are no conflicts of interest.

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