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REVIEW PAPER

A brief review of the cardiovascular complication of COVID-19 – what is the pathophysiology of arrhythmia during infection?

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ABSTRACT

Introduction and aim. COVID-19, caused by SARS-CoV-2, significantly affects the cardiovascular system beyond its respiratory manifestations. This review examines the intricate relationship between COVID-19 and cardiovascular complications, focusing on cardiac arrhythmias and their underlying pathophysiology.

Material and methods. A comprehensive literature search was conducted in PubMed and Google Scholar from its inception to December 2024, including peer-reviewed articles published in English.

Analysis of literature. In COVID-19, a spectrum of cardiovascular complications is observed, including acute myocardial infarction, arrhythmias, myocarditis, venous thromboembolism, and heart failure/cardiac shock. The pathophysiology of cardiovascular damage in COVID-19 involves multiple mechanisms, primarily including direct viral cardiotoxicity, systemic inflammation, and hypercoagulability. Arrhythmias are a common cardiac complication in COVID-19, encompassing a range of disturbances, from bradycardia to ventricular fibrillation. The mechanisms underlying arrhythmias in COVID-19 are multifaceted, including direct viral injury to cardiomyocytes, hypoxia, systemic inflammation, hyperthermia, autonomic imbalance, electrolyte imbalances, side effects of medications, and drug-drug interactions.

Conclusion. Understanding the complex interplay of these factors is crucial for the early diagnosis and appropriate management of cardiac complications in patients with COVID-19. To mitigate cardiovascular morbidity and mortality in individuals with COVID-19, cardiovascular monitoring and the development of targeted therapeutic strategies are highly recommended.

Keywords. arrhythmias, cardiovascular diseases, coronavirus, COVID-19, pathophysiology

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has presented an unprecedented global health crisis, requiring a comprehensive understanding of its multifaceted impact on human physiology.[1] While the virus primarily targets the respiratory system, a growing body of evidence reveals a complex and significant interplay between SARS-CoV-2 and the cardiovascular system, echoing observations from previous coronavirus outbreaks such as SARS and MERS.[2,3] This cardiovascular involvement extends beyond the

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acute phase of the disease, raising concerns about long-term cardiac sequelae and contributes significantly to both morbidity and mortality.

The pathophysiology of COVID-19-related cardiovascular complications is complex and multifactorial. The proposed mechanisms include direct viral cardiotoxicity, systemic inflammation ("cytokine storm"), endothelial dysfunction, and a hypercoagulable state.[4] These processes can contribute to myocardial injury, plaque instability, microvascular dysfunction, and ultimately, a variety of cardiovascular events.[5] Preexisting cardiovascular conditions, such as hypertension, coronary artery disease, and heart failure, significantly increase the risk of severe COVID-19 and the development of cardiovascular complications.[6,7] Furthermore, established cardiovascular risk factors, including advanced age, diabetes mellitus, and obesity, also play a crucial role in modulating the severity of COVID-19 and its cardiovascular manifestations.[8,9] This complex interaction is further underscored by laboratory findings in patients with COVID-19, which frequently reveal elevated cardiac biomarkers, including troponin and brain natriuretic peptide (BNP).[10,11] These elevated biomarkers serve as indicators of cardiac stress and injury, offering critical insights into the pathophysiological mechanisms linking COVID-19 and cardiovascular health. The interplay of these factors creates a complex clinical picture, necessitating a deeper understanding of the underlying mechanisms to guide effective management strategies.

Cardiovascular complications associated with COVID-19 are diverse, encompassing a spectrum of conditions including myocardial injury, heart failure, vascular dysfunction, and thromboembolic events. 3 These complications can manifest acutely, during convalescence, and may persist for months or years after initial infection, posing a significant challenge for long-term health management.[12] In particular, cardiac arrhythmias, ranging from benign palpitations to life-threatening ventricular fibrillation, have emerged as a particularly prevalent and concerning manifestation of COVID-19 in the cardiovascular system.[13] Studies have reported a prevalence as high as 17% in hospitalized non-ICU patients and exceeding 44% in critically ill ICU patients.[3,14] This high prevalence underscores the importance of understanding the mechanisms underlying these rhythm disturbances.

While the clinical manifestations of COVID-19-related arrhythmias are increasingly recognized, the precise pathophysiological mechanisms that drive these rhythm disturbances remain incompletely elucidated. Several contributing factors have been proposed, including direct viral infection of cardiomyocytes, hypoxia secondary to respiratory involvement, systemic inflammation, autonomic dysfunction, electrolyte imbalances, and the pro-arrhythmic effects of certain medications used to treat COVID-19.[13,15] However, the relative contribution of each of these factors and their complex interactions require further investigation. This knowledge gap hinders the development of targeted therapies and preventive strategies to mitigate the risk of arrhythmias in patients with COVID-19.

This review aims to address this critical need by providing an update and comprehensive overview of current understanding of COVID-19-associated cardiovascular complications associated with COVID-19, with a particular focus on arrhythmia. This review explores the various proposed mechanisms that contribute to arrhythmogenesis in the context of COVID-19, including direct viral effects, the role of inflammation and the immune system, and the influence of other contributing factors such as hypoxia, autonomic dysfunction, and drug-induced prolongation of QT. By synthesizing the existing evidence, this review seeks to inform clinicians, researchers, and policymakers, ultimately contributing to the improved diagnosis, treatment, and prevention of this significant cardiovascular complication of COVID-19. In addition, this review offers a unique contribution by focusing specifically on the pathophysiological mechanisms of arrhythmias, providing a more detailed and mechanistic perspective. This focus is crucial to developing targeted interventions and mitigating the burden of chronic cardiovascular sequelae in COVID-19 survivors.

Aim

This review aims to explore the multifaceted impact of COVID-19 on the cardiovascular system, with a particular focus on the clinical complication and underlying pathophysiology of cardiac arrhythmias. The various types of arrhythmias in COVID-19 and their underlying mechanisms are also elaborated.

Material and methods

A comprehensive literature search was conducted in PubMed and Google Scholar from its inception to December 2024, including peer-reviewed articles published in English. For searching articles, the authors used the following keywords: "cardiovascular", "myocardial injury", "cardiac injury" "COVID-19", "coronavirus", "heart failure", "coagulable", "thrombosis", "embolism", "arrhythmia", "dysrhythmia", "myocardial infarction", "acute coronary syndrome", "myocarditis". The search included systematic reviews, meta-analyses, randomized controlled trials, observational studies, narrative reviews, case series, case reports, and clinical guidelines focusing on cardiovascular complications in COVID-19. Pre-print articles were excluded. The reference lists of identified articles were meticulously reviewed. Two authors were independently assigned to search for articles relevant to their respective topics. Any discrepancies be-

tween the two authors were resolved through discussion and consensus with a third author.

Analysis of the literature

Pathophysiology of cardiovascular damage in COVID-19

Patients with myocardial damage exhibit increased morbidity and mortality from COVID-19.[16] The precise mechanisms underlying cardiovascular damage in COVID-19 remain under investigation and likely involve multiple factors. Although some studies suggest direct viral cardiotoxicity, the virus can also induce a hyperinflammatory state through the release of inflammatory cytokines.[4] This can lead to vascular inflammation, plaque instability, myocardial inflammation, hypercoagulability, and direct myocardial depression. The systemic complications of COVID-19, such as sepsis and disseminated intravascular coagulation (DIC), can also contribute to cardiac damage.[5] The pathophysiological processes involved in cardiovascular damage during COVID-19 and their manifestation are illustrated in Figure 1.

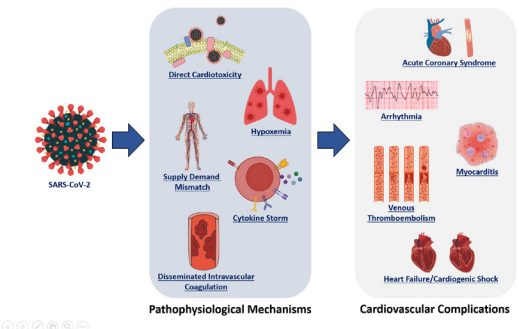

Fig. 1. Pathophysiological mechanisms underlying cardiovascular damage and their clinical manifestation in COVID-19. SARS-CoV-2 infection can induce direct cardiotoxicity, respiratory distress leading to hypoxemia, hemodynamic instability leading to a mismatch of oxygen and nutrient supply-demand, high levels of inflammatory molecules ('cytokine storm') and damage to the endothelium that contributes to hypercoagulable state such as disseminated intravascular coagulation (DIC), the pathological process during the infection period can cause a spectrum of cardiovascular complications, including acute myocardial infarction, arrhythmias, myocarditis, venous thromboembolism, and heart failure/cardiogenic shock

Cardiac biomarker in COVID-19

A modest increase in cardiac troponin levels (<2-3 times the upper limit of normal) can be attributed to pre-existing cardiac conditions or acute myocardial injury induced by COVID-19.[10] In critically ill patients with COVID-19 and deceased, significantly higher cardiac troponin levels (>5 times the upper limit of normal) are associated with severe respiratory failure, tachycardia, systemic hypoxemia, myocardial injury, endothelial dysfunction (which can lead to plaque rupture and acute coronary syndrome), Takotsubo cardiomyopathy, or multiorgan failure.[10,17] Severe inflammatory or respiratory conditions can lead to elevated levels of brain natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP).[11,18] These biomarkers are closely correlated with cardiac ventricular stress. Furthermore, elevated D-dimer levels are associated with an unfavorable prognosis for COVID-19.[19-21] The D-dimer reflects an activated coagulation state, a key characteristic of the disease. Serial D-dimer measurements can help guide prophylactic anticoagulation strategies for venous thromboembolism (VTE).[22]

Cardiovascular complication of COVID-19

Acute myocardial infarction

COVID-19 significantly increases the risk of acute myocardial infarction (AMI).[23] Systemic inflammations, a key feature of the disease, destabilize atherosclerotic plaques, making them more prone to rupture.[24] This, combined with a hypercoagulable state induced by the virus, increases the risk of blood clot formation within the coronary arteries.[25] Treatment of AMI in COVID-19 patients presents unique challenges. Although percutaneous coronary intervention (PCI) remains the preferred treatment for many STEMI cases, careful consideration is crucial, especially in patients with suspected or confirmed COVID-19.[26] Healthcare providers must balance the need for prompt revascularization with the potential for viral transmission and the need for adequate personal protective equipment.[27] In select cases, a conservative treatment approach can be considered, particularly in stable patients with non-ST elevation myocardial infarction.[26] This highlights the critical importance of a multidisciplinary approach and careful risk-benefit assessment when managing AMI in the context of COVID-19.

Arrhythmia

COVID-19 has been shown to significantly affect cardiac rhythm.[15] Although palpitations were reported in 7.3% of patients in one study, the true prevalence of arrhythmias remains uncertain due to limitations in data collection and the potential for under-reporting.[28] The mechanisms underlying COVID-19-associated arrhythmias are multifaceted. Direct viral injury to cardiomyocytes, pericardial inflammation, microvascular dysfunction, myocardial fibrosis, and the influence of pro-inflammatory cytokines can all contribute to the development of arrhythmias.[13] Viral interaction with the renin-angiotensin-aldosterone system can lead to electrolyte imbalances, potentially increasing arrhythmia susceptibility.[29] Furthermore, certain COVID-19 therapeutic agents of COVID-19, particularly chloroquine phosphate and hydroxychloroquine sulfate, can increase arrhythmia risk through QT interval.[30] In the management of stable patients with arrhythmias in

the context of COVID-19, clinical focus should initially be directed toward addressing the underlying respiratory distress and fever, rather than immediately implementing strategies to reduce heart rate.[31] Adherence to established treatment protocols is paramount, with amiodarone considered the preferred antiarrhythmic medication for the management of unstable patients or those experiencing heart failure.[31] For cases involving unstable atrial arrhythmias or dangerous ventricular arrhythmias, immediate cardiology consultation and strict adherence to advanced cardiac life support guidelines are essential.[28] The management of arrhythmias in COVID-19 requires a cautious and individualized approach, considering factors such as hemodynamic stability, potential drug interactions, and the presence of underlying conditions. Early recognition and appropriate management of these cardiac complications are crucial to optimize patient outcomes.

Myocarditis

Myocarditis, an inflammation of the heart muscle, is a concerning complication of COVID-19.[32] These findings echo observations from previous coronavirus outbreaks such as MERS-CoV, highlighting the potential for cardiac involvement in viral infections.[33] Myocarditis is associated with worse outcomes in patients with COVID-19, including an increased risk of death and long-term cardiac complications.[34] The clinical presentation of myocarditis in COVID-19 can range from mild symptoms to severe heart failure. Common symptoms include chest pain, shortness of breath, palpitations, and fatigue.[32] However, myocarditis can be asymptomatic in some cases, making early detection crucial. Studies have shown that a significant proportion of hospitalized COVID-19 patients exhibit elevated troponin levels, indicating myocardial injury.[35] Differentiating myocarditis from other conditions, such as acute coronary syndrome, can be challenging. Accurate diagnosis is based on a combination of clinical evaluation, electrocardiograms, echocardiography, and cardiac biomarker analysis. Early recognition and appropriate management are essential to improve patient outcomes.[3]

VTE

VTE is a significant complication of COVID-19.[36] COVID-19 presents a significant risk of VTE through multiple pathophysiological mechanisms, including systemic inflammatory response, coagulopathy, and multiple organ dysfunction syndrome.[37] Prospective studies have documented consistent abnormalities in coagulation parameters among patients with COVID-19, with elevated D-dimer levels emerging as a particularly significant biomarker.[38-40] Clinical research has established that D-dimer elevations exceeding 1 μg/mL correlate with an 18.4 times increased risk of in-hospital mortality among COVID-19 patients.[40] Clinical evidence supports the implementation of prophylactic anticoagulation therapy, with low molecular weight heparin demonstrating particular efficacy in reducing mortality rates among cases of severe COVID-19 cases.[41] The therapeutic benefits of anticoagulation are most evident in patients with D-dimer levels exceeding six times the established upper limit of normal.[42] These clinical observations underscore the critical importance of vigilant monitoring of coagulation parameters and the timely initiation of appropriate anticoagulation therapy, particularly in patients with severe COVID-19 manifestations or marked D-dimer elevations. Regular evaluation of thrombotic risk and proactive therapeutic intervention can significantly improve clinical outcomes in this high-risk patient population.[43]

Heart failure/cardiogenic shock

Heart failure (HF) and cardiogenic shock have been identified as the primary contributors to morbidity and mortality in COVID-19, and clinical studies documenting HF in approximately 23-33% of cases.[40,44] While the precise pathophysiological mechanisms of ventricular dysfunction in COVID-19 have not yet been fully elucidated, a subset of patients develops dilated cardiomyopathy, manifesting as diminished left ventricular systolic function and cardiogenic shock, despite no previous cardiac dysfunction.[45] The pathogenesis of COVID-19-associated HF encompasses multiple mechanisms, including direct myocardial injury, systemic inflammation, pulmonary hypertension, acute respiratory distress syndrome, renal dysfunction, fluid overload, and myocardial oxygen supply-demand mismatch.[28,46] Current therapeutic guidelines advocate for diuresis and standard heart failure protocols, maintaining angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) administration when no acute contraindications exist.[47] Patients presenting with new-onset systolic dysfunction require comprehensive cardiac evaluation, including cardiology consultation, echocardiographic assessment, and biomarker analysis.[31] In cases refractory to conventional therapies, extracorporeal membrane oxygenation (ECMO) may be considered, although preliminary data indicate poor outcomes with mortality rates over 80%.[48] The Extracorporeal Life Support Organization has issued guidelines restricting ECMO implementation to specialized centers for severe ARDS cases, emphasizing the necessity of multidisciplinary evaluation and recommending discontinuation if no recovery is evident after three weeks of support.[49]

Epidemiology of arrhythmias in COVID-19

Arrhythmias constitute the most common cardiac manifestation in patients with COVID-19, with clinical presentations ranging from palpitations to life-threatening

arrhythmias.[50] Patients with COVID-19 exhibit an increased risk of arrhythmias due to a confluence of factors, including pre-existing comorbidities, exposure to medication and the disease's progressive nature of the disease.[51] In a study encompassing 137 patients, 7.3% reported palpitations as a symptom.[52] Cardiac arrhythmias are highly prevalent in critically ill patients with COVID-19, occurring in approximately 19% to 36% of cases, depending on the presence of pre-existing cardiac abnormalities.[53] The most common tachyarrhythmias observed in patients with COVID-19 include atrial fibrillation, atrial flutter, and ventricular tachycardia/fibrillation.[54] The risk of arrhythmias in COVID-19 is multifactorial, encompassing hypoxia, myocarditis, myocardial strain, myocardial ischemia, medication effects, fluid and electrolyte imbalances, and systemic inflammatory responses.[13]

Pathophysiology of arrhythmia in COVID-19

SARS-CoV-2 can directly induce cardiomyocyte damage. The virus enters cells by binding to the ACE-2 receptor on the cell surface, a process facilitated by transmembrane serine protease 2 (TMPRSS2) through the cleavage of the viral spike protein.[55] At entry, the virus utilizes the NF-κB signaling pathway for replication. Activation of NF-κB can influence the expression of the pore-forming subunit of the fast transient outward potassium current, which can contribute to the development of arrhythmias.[56] Furthermore, activation of protein kinase C and oxidation of Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) can also contribute to arrhythmia in COVID-19. Histopathological findings in the myocardium may include irregularity, cytoplasmic darkening, minimal fibrosis, and mild hypertrophy.[57] These findings suggest ongoing myocarditis and can contribute to the development by inducing electrical abnormalities.[56]

Hypoxemia, a consequence of respiratory dysfunction in COVID-19, creates a relatively hypoxic environment within the myocardium.[58] Hypoxia can induce cardiomyocyte cell death and disrupt ion channel function, leading to alterations in the duration and / or repolarization of the action potential, increasing the risk of arrhythmias.[59]

Pro-inflammatory cytokines are significantly elevated in COVID-19 patients.[60] In particular, interleukin-6 (IL-6) plays a crucial role.[61] Acute exposure to IL-6 significantly increases the current density of L-type calcium channels and improves the amplitude and duration of calcium transients in ventricular cardiomyocytes. Chronic exposure to IL-6 can significantly disrupt intracellular calcium homeostasis. Furthermore, IL-6 can degrade the proteins that connect atrial myocytes, leading to atrial electrical remodeling of the atrium. Elevated IL-6 levels in patients with COVID-19 can therefore contribute to the development by altering cardiac electrophysiology.[56]

Hyperthermic states such as fever, a common symptom of COVID-19, can exacerbate the risk of arrhythmias.62 In individuals with preexisting cardiac conditions (e.g. dilated cardiomyopathy), fever may precipitate ventricular fibrillation.[63] Even in a structurally normal heart, fever can trigger tachyarrhythmias.[64] This may be partly attributed to the temperature-dependent effects on sodium channel function, potentially disrupting the ionic current migration of cardiomyocytes and attenuating the efficacy of antiarrhythmic medications.[56,64,65]

Table 1. Factors contributing to cardiac arrhythmias in COVID-19[26,28,69]

Contributing factor	Mechanism
Direct viral cardiotoxicity	Viral infection of cardiomyocytes leading to myocardial injury can contribute to the development by inducing electrical abnormalities
Drug-induced side effects and drug-drug interactions	Medications used to treat COVID-19, particularly chloroquine phosphate and hydroxychloroquine sulfate, may increase the risk of arrhythmias by prolonging the QT interval. This proarrhythmic effect is further amplified when coadministered with Azithromycin or Lopinavir/ Ritonavir
Hypoxia and pulmonary disease	Respiratory insufficiency can induce cardiomyocyte cell death and disrupt ion channel function, leading to alterations in the duration of the action potential and / or repolarization, predisposing to arrhythmias
Systemic inflammation	Chronic exposure to inflammatory cytokines during infection can degrade atrial myocytes, leading to atrial electrical remodelling and arrhythmias
Hyperthermia	Hyperthermic conditions (eg, fever) may have temperature-dependent effects on sodium channel function, potentially attenuating the efficacy of antiarrhythmic medications and inducing ventricular fibrillation
Autonomic imbalance	Sympathetic nervous system overactivity and vagal nerve dysfunction, potentially induced by the virus after acute stress, can disrupt cardiac rhythm
Electrolyte abnormalities	Virus interaction with the renin-angiotensin-aldosterone system can lead to electrolyte imbalances, potentially increasing arrhythmia susceptibility
Preexisting cardiovascular comorbidities	Individuals with underlying heart conditions, such as hypertension, coronary artery disease, and heart failure, are at a significantly higher risk of severe COVID-19 and may experience a higher incidence of arrhythmias

Treatment of COVID-19 involves the use of various medications, some of which can have adverse effects on cardiac function. The prolongation of the QT interval and Torsades de Pointes are potential side effects of chloroquine, hydroxychloroquine, favipiravir, lopinavir/ritonavir, azithromycin, moxifloxacin and, in certain cases, piperacillin-tazobactam.[66]

Other factors that contribute to cardiac arrhythmias in COVID-19 include autonomic imbalance (due to sympathetic nervous system overactivity and vagal nerve dysfunction), electrolyte abnormalities (due to virus interaction with the renin-angiotensin-aldosterone

system), and preexisting cardiovascular comorbidities (eg hypertension, coronary artery disease, and heart failure).[67] All of the contributing factors for arrhythmias in COVID-19 and their underlying mechanisms are summarized in Table 1.

Type of arrhythmias in COVID-19

Understanding arrhythmic complications in COVID-19 patients is constantly evolving. Observed cardiac arrhythmias in patients with COVID-19 include sinus tachycardia, sinus bradycardia, atrioventricular block, bundle branch block, atrial premature complexes, atrial fibrillation, supraventricular tachycardia, ventricular premature complexes, non-sustained ventricular tachycardia, polymorphic ventricular tachycardia (eg Torsades de Pointes), sustained ventricular tachycardia, ventricular fibrillation, and pulseless electrical activity.[29,67] The schematic picture of the various arrhythmias encountered in patients with COVID-19 is depicted in Figure 2.

Fig. 2. This schema depicts the diverse spectrum of arrhythmias observed in patients with COVID-19 (adapted from Manolis et al., Trends Cardiovasc Med 2020;30:451-60).[69] These arrhythmias arise from a complex interplay of factors, including direct cardiac effects of the virus, such as myocarditis and myocardial injury, systemic inflammation triggered by infection, the adverse (proarrhythmic) effects of COVID-19 therapies, drug-drug interactions, respiratory complications such as hypoxemia and hypercapnia, autonomic nervous system dysfunction, and electrolyte imbalances, the schema includes atrial fibrillation, atrioventricular block, long QT syndrome, pulseless electrical activity, sinus bradycardia, sudden cardiac death, sinus tachycardia, Torsades de Pointes, ventricular arrhythmias, ventricular fibrillation, and ventricular tachycardia

Bradycardia

Bradycardia can serve as a marker for the onset of a severe cytokine storm. In a retrospective case series of four patients, transient bradycardia was observed to persist for 1-14 days in patients with COVID-19, necessitating close monitoring.[68] The most common etiologies include severe hypoxia, inflammatory injury to the sinus node mediated by circulating cytokines, and an exaggerated response to medications.[67]

Sinus tachycardia

Sinus tachycardia, a supraventricular tachycardia, is a frequently reported rhythm disturbance in patients with COVID-19, with an incidence of approximately 72%.[56] This arrhythmia may be triggered by fever, hypoxemia/respiratory insufficiency, hemodynamic disturbances, anxiety/fear, pain, and various other physical and emotional stressors.[3,67]

Postural orthostatic tachycardia syndrome

Postural orthostatic tachycardia syndrome is a condition arising from autonomic dysfunction. The underlying mechanisms can involve peripheral neuropathy, elevated serum norepinephrine levels, baroreceptor dysfunction, or hypovolemia.[69] This syndrome has been reported to develop after acute stress, including viral illnesses, and has been observed in some patients recovering from COVID-19.[70] Symptoms typically include palpitations, dizziness, weakness, resting tachycardia, and worsening of symptoms with activity.[71]

Atrial fibrillation

Atrial fibrillation is the most common cardiac arrhythmia observed in patients with COVID-19, with a reported prevalence of up to 27%.[72] Potential causative mechanisms include systemic infection, direct viral injury to cardiomyocytes leading to peri-myocarditis and subsequent hypoxemia, increased susceptibility in the elderly and those with comorbidities, and sympathetic nervous system overactivity.[15,67]

Ventricular arrhythmias

In COVID-19 patients experiencing acute myocardial injury or myocarditis, serious ventricular arrhythmias can occur.[73-76] These arrhythmias may arise from a confluence of factors, including severe respiratory insufficiency, the systemic inflammatory response associated with the infection, the proarrhythmic effects of COVID-19 therapies, and potential drug interactions.[67] Furthermore, autonomic imbalance, hypoxemia, and electrolyte disturbances can exacerbate the risk of arrhythmia development.[77] Observed ventricular arrhythmias in this context range from premature ventricular complexes and non-sustained ventricular tachycardia to potentially life-threatening sustained ventricular tachycardia and ventricular fibrillation.[67]

Drug-induced QT prolongation and Torsades de Pointes
Ventricular arrhythmias, including Torsades de Pointes, have been reported in association with the use of certain medications that prolong the QT interval, particularly hydroxychloroquine.[15] Hydroxychloroquine exerts its proarrhythmic effect through the blockade of the potassium channel, thereby prolonging the QT interval and increasing susceptibility to Torsades de Pointes.[78] Individuals with congenital long QT syndrome are particularly susceptible to this effect, which can potentially lead to sudden cardiac arrest.[79,80] This risk is further amplified by the concomitant use of azithromycin or lopinavir/ritonavir due to drug-drug interactions.[66]

Role of vaccination in mitigating cardiovascular complications
COVID-19 vaccination has demonstrably reduced global morbidity and mortality. A modeling study estimated that vaccination prevented 14.4 to 19.8 million deaths worldwide within the first year, representing a 63% reduction in COVID-19 mortality.[81] These findings are corroborated by clinical data showing lower rates of acute hospitalization,[82] and reduced incidence of persistent symptoms in vaccinated individuals.[83-85] Furthermore, vaccination has proven effective in mitigating the risk of various cardiovascular complication, including myocardial injury, arrhythmias, and thromboembolic events.[86] Although initial concerns were raised regarding vaccine-associated myocarditis,[87,88] and the overall evidence supports a cardioprotective benefit.[89] Despite the benefit of vaccination, the emergence of novel SARS-CoV-2 variants, which may increase cardiovascular risk via reinfection, necessitates continued post-infection cardiovascular surveillance.[12,84,90] This surveillance is crucial to inform the need and timing of future booster vaccination campaigns. Although vaccination does not entirely eliminate the risk of cardiovascular events, it significantly reduces morbidity and mortality, underscoring its crucial role in public health strategies aimed at alleviating the burden of post-COVID-19 cardiac disease.

Study limitations
Current studies that examine the cardiovascular complications of COVID-19 face several methodological challenges. Studies show significant heterogeneity in patient selection, outcome measures, comparison groups, and research methodologies. Furthermore, many studies have limited sample sizes, which could introduce bias and limiting the generalizability of their findings. This underscores the need for further robust research with standardized methodologies to fully understand the complex relationship between COVID-19 and its cardiovascular sequelae.

Conclusion
COVID-19 is associated with a spectrum of cardiovascular complications. Among these, arrhythmias are the most common, ranging from palpitations to life-threatening arrhythmias. The causes of these arrhythmias in COVID-19 are complex and can include direct viral effects, systemic inflammatory responses, and proarrhythmic effects of certain medications. Treatment strategies for arrhythmias in COVID-19 patients, tailored to their underlying etiology, are highly advisable.

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Conflicts of interest
The authors declare that they have no conflict of interest.

Data availability
No data sets were generated or analyzed during the current study.

Ethics approval
Not applicable.

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