# IMPACT OF EXERCISE PRESCRIPTION IN LONG COVID - CARDIOVASCULAR SEQUELAE

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## Abstract

The COVID-19 infection, initially observed as Acute Respiratory Syndrome was identified to be caused by SARS-COV-2, presented with various long term extra pulmonary complications which included the cardiovascular sequelae that persisted beyond the acute phase which is referred to as Long COVID or Post-acute COVID Syndrome. This review aims to explore the impact and association of COVID-19 on an individual's cardiovascular health. This is crucial for a better understanding of whether long COVID could manifest with cardiac deconditioning, leading to impaired exercise performance among patients with long COVID and potentially resulting in long-term cardiovascular consequences.

**Keywords**: Cardiovascular Sequelae, Long COVID, Post-acute COVID Syndrome, Exercise Prescription

## Introduction

The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was primarily observed as viral pneumonia but it was also detected to cause many extra-pulmonary involvements like the cardiovascular, thromboembolic and cerebrovascular complications.[1] There is increasing evidence that suggests that beyond 30 days of the acute infection of COVID-19, people experience post-acute sequelae referred to as long COVID, which can involve not only pulmonary but also extra pulmonary manifestations.[2]The National Institute for Health and Care Excellence (NICE) has defined Long COVID or post-COVID syndrome as "signs and symptoms that develop during or after an infection consistent with COVID-19, which persist for more than 12 weeks and are not explained by an alternative diagnosis" [3]

Cardiac complications often appear within 15 days after the initiation of symptoms such as fever .[4] Slightly over one-fourth of hospitalized patients with COVID-19 developed cardiovascular disease (CVD) and arrhythmia which increase mortality by nearly 20 times and the need for ICU admission by 13.5 times. [5]
While cardiovascular complications have been observed during the acute phase of COVID-19, the matter of concern lies in the risk of cardiovascular disease, which extends well beyond the acute phase .[6] There is evidence linking Covid-19 to an increased risk of developing cardiovascular sequelae in the weeks after infection. Various studies imply a long-term effect on the cardiac health of patients who have recovered from acute COVID-19.

In spite of the exact mechanisms associating COVID-19 with the development of cardiovascular diseases in the post-acute phase is obscure. [7, 8] There is increasing evidence that many patients with

COVID-19 could experience a wide range of post-acute sequelae including cardiovascular complications. [9] Cardiovascular complications frequently observed in COVID-19 survivors include arrhythmias, inflammatory or ischemic heart diseases, myocarditis and thromboembolic disorders.[6,10]

Observations from the US Department of Veterans Affairs National Healthcare Databases (VHA) indicate that both hospitalized and non-hospitalized survivors of acute COVID-19 exhibit a high risk and burden of cardiovascular disease (CVD) over a 1-year period [11]
Various cardiac complications were observed regardless of age, gender, ethnicity, prior history of cardiovascular disease and cardiovascular risk factors prior to exposure to COVID-19 The potential long-term implications of these cardiovascular conditions has extended consequences for both patients and healthcare systems. This in turn, might impact economic productivity and life expectancy[6] Addressing the challenges posed by Long COVID necessitates a comprehensive and well-coordinated rehabilitative strategy within society.

## Probable Mechanisms of COVID-19's Effect on the Heart

The studies have demonstrated that, when compared to the liver and kidneys, the heart was the second most commonly affected organ by COVID-19 after the lungs.[5]
The irreversible damage to the respiratory system impairs lung function, potentially leading to systemic hypoxic stress. This could provoke an ischemic response, possibly resulting in ischemic heart disease or ischemic stroke [12,13] Furthermore, the persistent hyper-coagulopathy status following recovery from acute COVID-19 infection could elevate the risks of venous thromboembolic events [14]

Any typical viral infections are also associated with metabolic dysfunction, myocardial inflammation, and activation of the sympathetic nervous system. These factors collectively could predispose individuals to cardiac arrhythmias and acute myocarditis [4] It is known that after discharge of patients with a history of myocarditis they may develop myocardial scars, predisposing them to cardiac arrhythmias .[5]

SARS-CoV-2 infection known to trigger a cytokine storm, resulting in the production of various pro-inflammatory cytokines and chemokines can damage various organs in the cardiovascular system. [15,16] This inflammatory cytokine storm combined with a hyper-coagulopathy state due to the overstimulation of the sympathetic system may lead to complications associated with irreversible damage caused to the respiratory and cardiovascular systems. [17]

Meta-analyses have demonstrated that IL-6, which plays a critical role in cytokine release syndrome was observed to be elevated in approximately two-thirds of hospitalized patients with COVID-19. [5] Studies have emphasized the substantial role of IL-6 in pathophysiology of cytokine release syndrome in patients with severe clinical presentation of COVID-19 [5] The increased IL-6 levels can also potentially explain cardiac microvascular abnormalities in patients with COVID-19. [18]

Several studies have observed a delay between the initiation of symptoms and myocardial damage[4] The assumption that cardiomyocytes are directly affected by the viral invasion of SARS-CoV-2 could lead to the death of cardiac cells. Additionally, endothelial cell infection and endotheliitis, accompanied by transcriptional alterations of multiple cell types in heart tissue, could result in coagulopathy and micro-angiopathy. Moreover, the downregulation of ACE2 and dysregulation of the renin–angiotensin–aldosterone system, autonomic dysfunction, elevated levels of pro-inflammatory cytokines, and activation of TGF-β signalling could subsequently lead to fibrosis and

scarring of cardiac tissue, resulting in long-lasting issues.[6] Furthermore, tachyarrhythmia seen in COVID-19 infection could be due to electrolyte imbalances.[19] Additionally, medications used for COVID-19 treatment like the hydroxchloroquine and azithromycin, have been observed to have adverse effects on the cardiovascular system [20] It's noteworthy that some of the medications used in COVID-19 treatment could potentially contribute to cardiac toxicity.[4]
Investigations using cardiovascular MRI (magnetic resonance imaging) following acute COVID-19 infections conducted across different countries, such as a study conducted on Germans and another on young athletes in the United States revealed evidence of myocarditis, indicating myocardial involvement.[21]
Based on autopsy results of cardiac muscle tissue, the National Health Commission of the People's Republic of China reported myocyte necrosis and mononuclear cell infiltrates,[22] which aligns with case reports of Myocarditis. This suggests that myocarditis could be a major cause of acute cardiac injury in COVID-19 patients.[4]

Viral diseases can potentially destabilize atherosclerotic plaques through systemic inflammatory responses [23] much like the cytokine storm observed in COVID-19 which may have lead to plaque instability and myocardial infarction (MI). This is observed as a common cause of death among SARS/COVID-19 patients.[4]

The multifactorial causes of COVID-19-associated coagulopathy (CAC) can result in various manifestations. The Virchow's triad, which encompasses endothelial damage, alterations in blood flow, and the presence of pro-thrombotic components in circulation, appears to play a significant role in the development of CAC.[24]

## Role of Exercise for Individuals with Cardiovascular Complications

Individuals with cardiovascular disease may feel hesitant about engaging in exercise and may be unsure about what types and amounts are safe. Generally, exercise is considered safe for most patients with cardiovascular disease, and promoting moderate exercise is recommended for everyone. However, certain patients may require additional risk assessment or specific restrictions.[25]

Providing appropriate guidance, reassurance, and advice is crucial to help patients access the abundant benefits of exercise while minimizing associated risks. has been demonstrated to provide a protective influence against the prevalence of AF. Conversely, physical inactivity and a lack of exercise notably elevate the risk of AF and its associated risk factors. [25]

The consensus is strong regarding the benefits of consistent physical activity for cardiovascular health. Regular exercise is firmly linked to a reduction in cardiovascular mortality and the likelihood of developing cardiovascular disease. Those who engage in frequent physical activity typically exhibit lower blood pressure, heightened insulin sensitivity, and a better plasma lipoprotein profile. Animal studies on exercise demonstrate that repeated physical activity suppresses the progression of atherosclerosis and enhances the production of vasodilatory mediators such as nitric oxide and thus have positive effects on heart health.[26]

Significant meta-analyses have demonstrated an inverse relationship between increased exercise levels and the occurrence of cardiovascular events. Specifically, one of these analysis revealed a 14% reduction in the risk of incident coronary disease among those engaging in 150 minutes per week of moderate exercise activity.[25]

Physical inactivity is estimated to contribute to 7.2% of global all-cause mortality and 7.6% of cardiac mortality. [27] Consequently, enhancing exercise participation and minimizing sedentary behaviour are vital components of both primary and secondary prevention strategies aiming to alleviate the burden of cardiovascular disease and mortality.[25]

## Criteria for Exercise Prescription

The impact of exercise on cardiovascular health outcomes is dependent on the dose with individuals engaging in larger volumes of regular exercise experiencing more substantial benefits [28]. Current international cardiology guidelines recommend a minimum of 150 minutes per week of moderate-intensity or 75 minutes per week of vigorous-intensity aerobic exercise. [25] It is advisable that the majority of patients receive encouragement to engage in physical exercise aligned with the recommended levels for healthy individuals (such as 150 minutes of moderate-intensity aerobic exercise spread over 5 days, or 75 minutes of vigorous aerobic exercise across 3 days each week). Additionally, incorporating resistance training is recommended to enhance overall fitness, preserve muscle mass, and decrease body fat among cardiac patients [ 29]

Emphasis on an integrated strategy for personalized lifestyle interventions, incorporating a systematic application of the 'FITT' prescription for exercise training. This prescription provides guidance on the frequency, intensity, time, and type of exercise to be performed, along with the establishment of personalized exercise goals. While supervised in-hospital programs may be advantageous, particularly for high-risk patients, home-based and remote cardiac rehabilitation programs have demonstrated effectiveness and safety, with minimal adverse events [30,31]

The benefits of exercise can vary depending on factors like the type, duration, and intensity of physical activity. Therefore, tailored exercise plans may be necessary to maximize outcomes for patients with diverse capabilities. Engaging in physical activity of 150 minutes per week is associated with higher mental wellbeing scores,[32] suggesting a positive link between exercise and psychological health. Additionally, psychological wellbeing is deemed protective and correlates with a favourable risk factor profile, particularly crucial for individuals managing chronic diseases or recovering from cardiac events. Exercise-induced psychological wellbeing can aid patients in coping and bolster motivation to manage their health behaviours and conditions effectively. [25] Thus, personalized exercise prescriptions play a pivotal role in enhancing both physical and mental health outcomes, catering to individual needs and fostering holistic healthcare approaches.

A structured exercise program tailored to individual needs typically involves a personalized assessment of fitness, exercise instructions, lifestyle recommendations, and ongoing support representing a highly cost-effective intervention for secondary prevention of cardiovascular issues.[33]

This becomes especially critical given the anticipated rise in the cardiovascular risk factors following covid.(own) Exercise, available in various forms, proves to be a cost-effective and widely accessible method for both primary and secondary prevention. Strategies at both individual and population levels, coupled with recommendations promoting exercise and physical activity for overall health maintenance are becoming increasingly crucial.

## Conclusion

Exercise prescriptions have demonstrated notable enhancements in the quality of life and functional capacity among patients dealing with conditions such as Postural Orthostatic Tachycardia Syndrome

(POTS), Chronic Fatigue Syndrome (CFS), cardiac deconditioning, and even in addressing symptom severity associated with long COVID, as evidenced in a case series. This novel therapeutic exercise strategy offers potential benefits for managing the long COVID syndrome. [35]

Numerous long-term studies have demonstrated that higher levels of physical activity are connected with decreased overall mortality rates and may contribute to a modest increase in life expectancy. This effect is closely associated with a decrease in the likelihood of developing cardiovascular and respiratory illnesses.[36]

While further research is warranted to deepen our understanding it is prudent to consider exercise training for managing these patients, given the absence of contraindications. Exercise serves as a potent method for enhancing health, particularly in reducing cardiovascular morbidity and mortality, partly by influencing the prevalence of cardiac risk factors. Health organizations globally recommend regular, moderate exercise for individuals with or without cardiovascular disease. Despite apprehensions, moderate exercise seems to be both safe and beneficial for most individuals, including those with existing cardiovascular conditions. Ensuring proper screening of individuals at risk and customizing exercise recommendations can aid in enabling safe exercise participation.[25]

Tailoring exercise programs to individual needs and capabilities is essential. The ongoing research endeavours aim to refine these prescriptions for a more comprehensive and effective approach. The recommendation to incorporate exercise aligns with the broader principles of promoting physical activity for overall health. A detail assessment is required to ensure safety and appropriateness for each patient. The continuous pursuit of knowledge in this area is pivotal for refining guidelines and enhancing the well-being of individuals grappling with these complex conditions.

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