



## Long-Term Cardiovascular Sequelae of COVID-19 Infection: A Review

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### ABSTRACT

The rapid spread of the COVID-19 pandemic caused by the novel SARS-CoV-2 virus demonstrated that it is not just a disease of the lungs. Long COVID or Post-Acute Sequelae of SARS-CoV-2 infection (PASC) is a sequela that many post-viral survivors are experiencing. The severe and long-term effect on the cardiovascular system is one of the most worrying characteristics of PASC. The review provides the existing data regarding the long-term cardiovascular problems, including heart damage, dysautonomia, blood clots, and irregular heartbeat, that may occur after COVID-19. We speculate about the potential causes of these complications such as the virus remaining in the body, autoimmune response, blood vessel inflammation and persistent viral presence. The results have emphasized the need to be more clinically aware, monitor patients regularly and conduct more studies on the causes and management of these difficult long-term effects.

**Keywords:** Long COVID, PASC, SARS-CoV-2, Cardiovascular Disease, Myocarditis, Postural Orthostatic Tachycardia Syndrome (POTS), Myocardial Injury, Thrombosis.

### Introduction

As the acute stage of the world-wide COVID-19 pandemic passes, the cumulative health outcomes of the circumstances are becoming more apparent. It is now apparent that many patients, including those who had mild acute disease experience persistent symptoms months or weeks after their first infection. The condition is called Long COVID or PASC and it affects multiple organ systems, though it is primarily the cardiovascular system that is affected. The aim of the paper is to provide a comprehensive summary of the long-term cardiovascular outcomes of SARS-CoV-2 infection and describe the spectrum of conditions, their reasons, and the clinical issues posed by them.

### Long-term cardiovascular spectrum complications

- Myocardial Inflammation and Injury:

The heart muscle is inflamed and damaged. One of the complications that are familiar with the acute stage of COVID-19 is called myocarditis or inflammation of the heart muscle. But there is also evidence that this inflammation can persist. Myocardial inflammation and late gadolinium enhancement (indicating fibrosis and scarring) have been demonstrated on cardiac MRI studies in patients months post-recovery, even in patients who do not present. This recognized non-ischemic myocarditis could reduce the pumping capacity of the heart, resulting in low ejection fraction and, eventually, heart failure.

- Autonomic Nervous System dysfunction:

Postural Orthostatic Tachycardia Syndrome (POTS). Long COVID often becomes dysautonomia (POTS in particular) and is frequently disabling. The characteristics of this syndrome are a fast rise in the heart rate in the erect position, and any of the symptoms: dizziness, palpitations, fatigue, and cognitive impairment. The prevailing belief is that the fundamental mechanism involves autoantibodies that attach to G-protein-coupled receptors, thus disrupting the normal operations of the autonomic nervous system.

- Thromboembolic Incidents:

The infection caused by SARS-CoV-2 induces a significant pro-thrombotic condition due to inflammation of the endothelium (endotheliitis). Even after acute phase, there is a risk of blood clots. It has been found that up to six months after infection, there is a significantly increased risk of deep vein thrombosis (DVT), pulmonary embolism (PE), and arterial thromboses (such as strokes or heart attacks) in patients who are infected over uninfected individuals.

- Arrhythmias:

Long COVID groups typically experience palpitations and problems with the heart rhythm. They might be harmless sinus tachycardia or more serious such as atrial fibrillation (AFIB), ventricular tachycardia and other conduction disturbances. The etiology of these arrhythmias is probably heterogeneous and related to scarring of heart muscle, persistent inflammation, autonomic imbalance, and ischemia.

- Ischemic Heart Disease:

Inflammatory response of the body and endothelial damage may accelerate the atherosclerosis process and cause the acute coronary syndromes. It has been shown that there is an increased rate of ischemic heart disease, such as heart attack, one year after a COVID-19 infections.

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### Pathophysiological Mechanisms

A single factor does not cause the long-lasting cardiovascular harm but, instead, is a complex combination of several pathways:

- Direct Viral Invasion and Persistence:

ACE2 is highly concentrated in pericytes (support cells around blood vessels) despite the low concentration of ACE2 receptors in the cardiac myocytes. These cells may have their microvascular circulation disrupted by a viral invasion leading to ischemia and tissue damage. Viral persistence in multiple tissues, could be another reason of continued inflammation.

- Autoimmunity and Molecular Mimicry:

When the similarity is between viral antigens and the human proteins, it may cause the formation of autoantibodies that mistakenly attack the human body tissues such as the heart and the blood vessels.

- Lasting Endothelial Inflammation and Vascular Destruction:

Prolonged infection of endothelial cells causes extensive vascular inflammation that destabilizes the fragile vascular lining and provokes a pro-coagulant state long after the virus has disappeared.

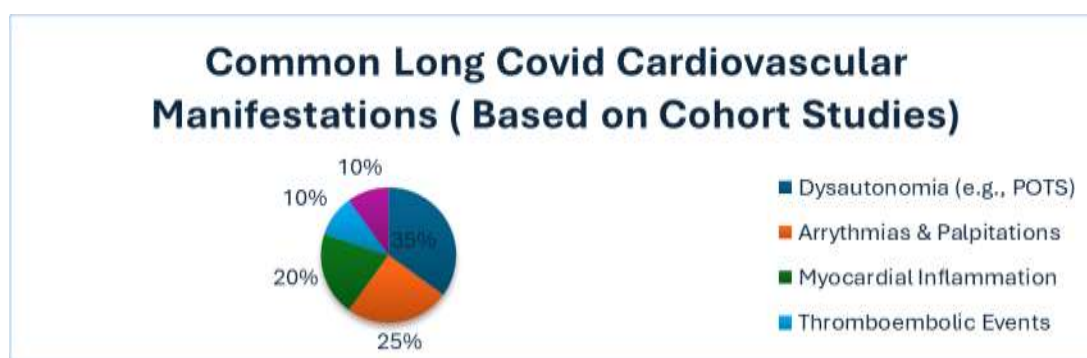
- Systemic Inflammation and Cytokine Storm Aftermath:

The severe inflammatory response that accompanies acute infection may have long-term effects on organ systems, leading to a condition of low-grade chronic inflammation that contributes to cardiovascular problems.

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### Breaking Down the Conceptualization of Reported Cardiovascular Manifestations in Long COVID.

The pie chart below represents a conceptual representation of the comparative prevalence of the different cardiovascular manifestations that have been reported in various Long COVID cohort studies and registries. It is important to note that the conditions are often comorbid in the same patient.




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### Conclusion and Future Directions

COVID-19 is having a major and increasing effect on the cardiovascular health of the population and long-term. The conditions listed above: heart injury, autonomic dysfunction, etc., could lead to long-term disability, poor quality of life, and increased risk of death. These issues are complex enough that they ought to be treated collaboratively with a team of specialists such as cardiologists, neurologists, immunologists, and rehabilitation specialists.

Going forward, it will be good to:

Create post-COVID cardiology clinics and have patients monitored and treated in a consistent manner. Develop evidence-based ways of screening people who are at risk. Begin extensive, life-long research on how these complications develop. Examine specific interventions, like immunomodulators to facilitate inflammation, or beta-blockers to improve patient outcomes for POTS.

The health care sector needs to remain observant to mitigate the long-lasting effects of SARS-CoV-2 on cardiac health.

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**References**


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1. Davis, H. E., McCorkell, L., Vogel, J. M., & Topol, E. J. (2023). Long COVID: major findings, mechanisms and recommendations. *Nature Reviews Microbiology*, 21(3), 133–146.
2. Puntmann, V. O., Carerj, M. L., Wieters, I., et al. (2022). Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered from Coronavirus Disease 2019 (COVID-19). *JAMA Cardiology*, 7(5), 555–557.
3. Raj, S. R., Arnold, A. C., Barboi, A., et al. (2021). Long-COVID postural tachycardia syndrome: an American Autonomic Society statement. *Clinical Autonomic Research*, 31(3), 365–368.
4. Fedorowski, A., Sutton, R., & van Dijk, J. G. (2021). Autoimmunity and Dysautonomia in Post-COVID Syndrome. *Nature Reviews Cardiology*, 18(5), 281–282.
5. Katsoularis, I., Fonseca-Rodríguez, O., Farrington, P., et al. (2022). Risks of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19: nationwide self-controlled cases series and matched cohort study. *BMJ*, 377, e069590.
6. heart rhythm, 19(8), 1234–1241. Seedahmed, M. I., & Virk, H. U. H. (2023). Arrhythmias in COVID-19. *Cardiology Clinics*, 41(3), 395–403.
7. Xie, Y., Xu, E., Bowe, B., & Al-Aly, Z. (2022). Long-term cardiovascular outcomes of COVID-19. *Nature Medicine*, 28(3), 583–590.
8. Evans, P. C., Rainger, G. E., Mason, J. C., et al. (2021). Endothelial dysfunction in COVID-19: a position paper of the ESC Working Group for Atherosclerosis and Vascular Biology, and the ESC Council of Basic Cardiovascular Science. *Cardiovascular Research*, 117(14), 2707–2714.
9. Wang, E. Y., Mao, T., Klein, J., et al. (2021). Diverse functional autoantibodies in patients with COVID-19. *Nature*, 595(7866), 283–288.
10. Swank, Z., Senussi, Y., Manickas-Hill, Z., et al. (2023). Persistent Circulating Severe Acute Respiratory Syndrome Coronavirus 2 Spike Is Associated With Post-acute Coronavirus Disease 2019 Sequelae. *Clinical Infectious Diseases*, 76(3), e487–e490.
11. Phetsouphanh, C., Darley, D. R., Wilson, D. B., et al. (2022). Immunological dysfunction persists for 8 months following initial mild-to-moderate SARS-CoV-2 infection. *Nature Immunology*, 23(2), 210–216.
12. Al-Aly, Z., Xie, Y., & Bowe, B. (2021). High-dimensional characterization of post-acute sequelae of COVID-19. *Nature*, 594(7862), 259–264.
13. Dennis, A., Wamil, M., Alberts, J., et al. (2021). Multiorgan impairment in low-risk individuals with post-COVID-19 syndrome: a prospective, community-based study. *BMJ Open*, 11(3), e048391.
14. Raveendran, A. V., Jayadevan, R., & Sashidharan, S. (2021). Long COVID: An overview. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 15(3), 869–875.
15. Castanares-Zapatero, D., Chalon, P., Kohn, L., et al. (2022). Pathophysiology and mechanism of long COVID: a comprehensive review. *Annals of Medicine*, 54(1), 1473–1487.