Long COVID syndrome or post-acute COVID-19 syndrome (PACS) encompasses a wide range of organ dysfunction. It is more common in hospitalized survivors, but, even those who have experienced mild acute COVID-19 have a wide range of frequent, persistent, and disabling symptoms. Cardiovascular complications, including myocardial injury, heart failure, arrhythmias, and coagulation disorders, can manifest not only during the acute phase of COVID-19 but also in long COVID or PACS syndrome. In this study, German scientists used cardiac magnetic resonance imaging (MRI) to investigate the prevalence and extent of cardiac abnormalities in patients diagnosed with long COVID syndrome.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped, positive-sense, single-stranded RNA virus. Its genome encodes four structural proteins, namely the spike (S), envelope (E), nucleocapsid (N), and membrane (M) proteins. Two host-cell factors are important for SARS-CoV-2 entry into many cell types: angiotensin-converting enzyme 2 (ACE2), which is bound by the S protein, and transmembrane protease, serine 2 (TMPRSS2), which cleaves S protein, allowing this binding to take place. ACE2 receptors are more highly expressed in the heart than in other organs, and in cardiomyocytes of patients with heart failure than in cardiomyocytes of healthy individuals.

A recent *in vitro* study utilized a model of human cardiac microtissue and demonstrated a high risk of cardiac dysfunction in heart tissues with persistent SARS-CoV-2 infection. Hypoxic conditions mimicking ischemic heart disease further deteriorated cardiac function and disrupted vascular network formation in a heart tissue model infected with SARS-CoV-2. The authors emphasized that an explosive increase in the number of patients infected with SARS-CoV-2 may result in an enormous increase in the number of patients with a potential risk for heart failure.
https://discovermednews.com/deterioration-heart-function-cardiac-model-sars-cov-2-infection/

About the Study and Results

This two-center retrospective study investigated the presence and extent of cardiac abnormalities in all patients referred for cardiac MRI due to clinical signs of long COVID syndrome within two years. The median interval between a positive reverse transcription polymerase chain reaction test for SARS-CoV-2 and cardiac MRI was four months.

The study included 129 patients diagnosed with long COVID syndrome, 51% were women, and the mean age was 41 years. The most common symptoms of long COVID were exertional dyspnea (reported in 23% of patients) and tachycardia/palpitations (reported in 22% of patients). Other symptoms included fatigue, exercise intolerance, and chest pain, lasting more than four weeks after the acute infection.

21% of patients diagnosed with long COVID syndrome had abnormal (<55%) ejection fraction, 19% had left ventricular dilation, 14% had pericardial effusion (>5 mm) and 5% had pleural effusion (>20 mm). There was no case of active myocarditis or an acute myocardial infarction.

Importantly, cardiac MRI showed that 30% of patients diagnosed with long COVID syndrome had non-ischemic, possibly post-inflammatory fibrosis. Post-ischemic fibrosis was found in 4% of long COVID patients, and structural heart disease in 9% of long COVID patients. 57% of patients diagnosed with long COVID syndrome had no cardiac MRI abnormalities, but 8% of patients with normal cardiac results had suspected pulmonary abnormalities (fibrosis/atelectasis).

Conclusion

This study showed signs of non-ischemic myocardial fibrosis in a significant portion of the cohort diagnosed with long COVID syndrome (30%). Post-ischemic fibrosis was found in 4% of patients diagnosed with long COVID syndrome.

A previous study by Cao et al. discovered that the SARS-CoV-2 spike protein promotes cardiac fibrosis in obese mice. They suggested that the spike protein causes myocardial contractile impairment by inducing long-term aberrancies in the cardiac transcriptional signatures of mitochondrial respiratory chain genes. (Mol. Metab. 2023, 74, 101756) https://www.sciencedirect.com/science/article/pii/S221287782300090X?via%3Dihub A recent study that investigated the effects of SARS-CoV-2 spike protein on cultured human cardiac fibroblasts (CFs) and the molecular mechanisms underlying cardiac fibrosis induced by SARS-CoV-2 found that SARS-CoV-2 S1 protein activates CFs and promotes cardiac fibrosis. More specifically, they discovered that the S1 subunit of the SARS-CoV-2 spike protein activates human CFs by priming the NOD-, LPR-, and pyrin-domain-containing protein 3 (NLRP3) inflammasomes through nuclear factor kappa-B (NF-κB) signaling in an ACE2-dependent way.
https://discovermednews.com/sars-cov-2-spike-protein-activates-human-cardiac-fibroblasts-and-promotes-cardiac-fibrosis/

The authors of this study noted that they focused only on patients referred for cardiac MRI and strictly relied on established international guidelines to detect myocardial inflammation.

They emphasized that this prevalence of myocardial fibrosis is particularly concerning because it exceeds the prevalence of this disease in the normal adult population. Furthermore, these results suggest that a history of myocarditis might be the reason for the persistent cardiovascular symptoms in patients diagnosed with long COVID syndrome.

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Journal Reference

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