

Long COVID-19: A Primer for Cardiovascular Health Professionals, on Behalf of the CCS Rapid Response Team.

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8 2021 6 6 2021 37 8 383274 1260 1262 4 3 2021 23 5 2021 06 06 2021 07 06 2021 10 09 2021 © 2021 Canadian Cardiovascular Society. Published by Elsevier Inc. All rights reserved. 2021 Canadian Cardiovascular Society Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website. Elsevier hereby grants permission to make all its COVID-19-related research

that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. It is now widely recognized that COVID-19 illness can be associated with significant intermediate and potentially longer-term physical limitations. The term, "long COVID-19" is used to define any patient with persistent symptoms after acute COVID-19 infection (ie, after 4 weeks). It is postulated that cardiac injury might be linked to symptoms that persist after resolution of acute infection, as part of this syndrome. The Canadian Cardiovascular Society Rapid Response Team has generated this document to provide guidance to health care providers on the optimal management of patients with suspected cardiac complications of long COVID-19.

Il est désormais largement reconnu que la COVID-19 peut être associée à d'importantes limitations physiques à moyen terme et, potentiellement, à plus long terme. Le terme « COVID-19 longue » est utilisé pour décrire tout patient présentant des symptômes persistants après une infection aiguë par le virus de la COVID-19 (soit au-delà de quatre semaines). On suppose qu'une atteinte cardiaque pourrait être liée aux symptômes qui persistent après la disparition de l'infection aiguë, dans le cadre de ce syndrome. Le Groupe de travail sur la réaction rapide à la COVID-19 de la Société canadienne de cardiologie a produit le présent document afin de fournir des conseils aux professionnels de la santé sur la prise en charge optimale des patients chez qui l'on soupçonne des complications cardiaques causées par la COVID-19 longue.

An estimated 870,000 Canadians have been infected by SARS-CoV-2 as of March 2, 2021, including > 22,000 known deaths. Cardiac injury, defined as an elevation in serum troponin, has been documented in up to 45% of inpatients with COVID-19 ¹ and has been linked to worse outcomes. ² It is also postulated that this type of injury might be linked to symptoms that persist after resolution of acute infection, as part of the syndrome commonly referred to as "long COVID-19." The purpose of this document is to provide guidance to health care providers on the optimal management of patients with suspected cardiac complications of long COVID-19. It must be recognized that this is an evolving area with few data at present to guide management.

Several potential mechanisms for myocardial injury secondary to SARS-CoV-2 infection have been proposed, including: (1) myocarditis from either direct viral toxicity and/or bystander immune damage; (2) myocardial ischemia from microvascular thrombosis; and/or (3) COVID-19-related hypoxemia. More recently, histopathological data from 201 COVID-19 patients who underwent endomyocardial biopsy (N = 9) or autopsy (N = 192) suggest that myocarditis is present in only 4.5%, despite a high likelihood of referral bias. ³ However, it is unclear if any of these cardiac manifestations during acute COVID-19 leads to significant long-term consequences.

Small cohort studies using cardiac magnetic resonance imaging have reported conflicting results, ⁴ ⁵ further highlighting the need to better elucidate potential long-term cardiac sequelae of COVID-19, especially as it pertains to patient symptoms and functional impairments. Furthermore, no data presently exist to support or refute the cardiovascular effect of COVID-19 in patients with or without preexisting cardiac conditions.

It is now widely recognized that COVID-19 illness can be associated with significant intermediate and potentially longer-term physical limitations. Recent survey data from the Office for National Statistics in the United Kingdom showed that 21% of respondents with COVID-19 exhibit symptoms for longer than 5 weeks and 10% exhibit symptoms for > 12 weeks. Although definitions are evolving, the term, "long COVID-19" is commonly used to define any patient with persistent symptoms after acute COVID-19 (ie, after 4 weeks; Supplemental Table S1).

There is a lack of high-quality data on the prevalence of symptom subtypes in patients with long COVID-19. A review of evidence performed by the National Institute for Health and Care Excellence in the United Kingdom showed that fatigue and shortness of breath are commonly reported,

affecting up to 98% and 85% of patients respectively, among other multisystem symptoms. Chest pain or palpitations have been reported in 10%-44% of cases and are potentially more common at 4-12 weeks post COVID-19 infection.

A growing awareness of the long-term effect of COVID-19 infections has led to the formation of patient-initiated online support groups, government-sponsored information Web sites for patients (eg, www.yourcovidrecovery.nhs.uk) and more recently, ambulatory clinics specializing in the care of these patients. Generally, cardiac specialists have either been integrated into these clinics or have provided consultation on an ad hoc basis. Thus, the following recommendations are largely on the basis of expert opinion and the current collective experience.

Consultation with cardiac specialists is warranted for patients with diagnosed COVID-19 illness > 4 weeks ago and: (1) Persistent or new unexplained chest pain. A cardiac etiology is more likely with multiple cardiac risk factors, documented cardiac injury and/or new Q waves or ST-T wave abnormalities on electrocardiogram, during or after initial COVID-19 illness.

Shortness of breath. A cardiac etiology is more likely with elevated b-type natriuretic peptide level, left ventricular dysfunction on imaging, and/or radiographic evidence of pulmonary edema.

Frequent palpitations. A cardiac etiology is more likely if associated with presyncope or syncope and/or a significant arrhythmia is detected on Holter or other cardiac monitoring device. For patients with persistent sinus tachycardia, consider a cardiac etiology in the absence of systemic causes (eg, fever, anemia, and hypoxia).

Postural light headedness. A cardiovascular etiology is more likely if orthostatic hypotension is documented.

The Canadian Cardiovascular Society Rapid Response Team has placed an emphasis on physical examination and noninvasive assessment using local expertise and periodic surveillance, especially among those with preexisting cardiac conditions or multisystem disease (Table 1).
Table 1 Symptom guided investigations for possible cardiac complications of long COVID-19

BNP, b-type natriuretic peptide; ECG, electrocardiography; NT-proBNP, N-terminal pro hormone brain natriuretic peptide.

Although there are no specific recommendations for managing cardiac symptoms in long COVID-19 patients, there is considerable support for maintaining guideline-based goal-directed therapy in patients with preexisting cardiovascular disease. Patients with new cardiac findings or symptoms should be managed using contemporary treatments, similar to patients without a history of COVID-19 infection (Supplemental Table S2).

After careful investigations to identify and treat cardiac and/or pulmonary causes of patient symptoms, many might remain symptomatic with chronic fatigue and tiredness. Although in some individuals these symptoms might be attributed to the slow nature of their recovery after a critical illness, in others it might result from deconditioning and other unrecognized factors. There is no clear relationship between chronicity of symptoms and severity of initial COVID-19 illness. Long COVID-19 patients often report less energy than preillness, and everyday situations requiring physical, cognitive, and/or emotional stamina might be exhausting in a waxing and waning pattern.

In many patients, a tailored return to exercise can be a useful adjunctive therapy. This requires a multidisciplinary team rehabilitation service consisting of nurses, physiotherapists, physiatrists, exercise specialists, neurologists, psychiatrists, respirologists, rehabilitation experts, and cardiologists to coordinate an individualized plan including in-person and electronic supports. Additional considerations should include baseline health, premorbid function, biomechanical assessments, exercise prescription, and a holistic patient review; much of which could be delivered

via telemedicine. The long COVID-19 patient care map illustrated in Figure 1 enables a cycle of “learn-teach and modify” to further refine interventions. Figure 1 Long COVID-19 patient care map.

Return to exercise is often regarded as an important milestone of recovering from COVID-19, resulting in post exertional malaise. Many with this syndrome experience a cycle of “push and crash” (Supplemental Figure S1).

The symptoms of post exertional malaise resemble myalgic encephalitis or chronic fatigue syndrome, and typically occur 24-72 hours post trigger, potentially lasting for several days. The opposite of “push and crash” is pacing. This further emphasizes the importance of early involvement of a multidisciplinary approach to prevent and support “push and crash” candidates to a path of pacing with reduced suffering, and improved sense of control and well-being.

Pacing involves: finding the individual's envelope, paying attention to the level of triggers, which might be physical, emotional, or cognitive; the individual adapting to their envelope; learning to control triggers; and expanding their envelope with gradual progression and adaptation.

The management strategies proposed for long COVID-19 have not yet been evaluated in clinical trials. However, these recommendations appear reasonable in light of current knowledge and experience. Future work on COVID-19 should continue to assess knowledge gaps and evaluate the long-term cardiovascular effects and potential effect on patient wellness and survival. Furthermore, long-term outcomes should also be studied in asymptomatic, recovered COVID-19 patients to determine any potential links to latent cardiovascular disease.

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