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.

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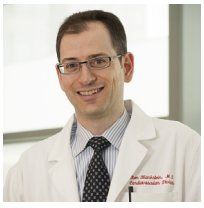

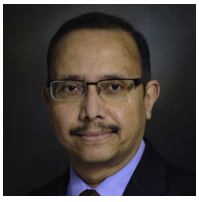

New Insights on COVID-19 and the Heart

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Cardiac imaging has played an important role in understanding the presence and extent of cardiac involvement in coronavirus disease-2019 (COVID-19) (1,2), as well as identifying patients who have a worse prognosis (3,4). Although the amount of scientific data that have emerged on this topic in <1 year has been astonishing, understanding the generalizability and clinical implications of the various reported studies has been challenging. A common limitation to most imaging studies has been that there is significant referral bias that determines which individuals undergo imaging. Moreover, differences in imaging techniques, study timing, and the severity of COVID-19 among participants have varied widely.

A cohort study of German patients who recovered from COVID-19 suggested that cardiac involvement by cardiac magnetic resonance (CMR) using late gadolinium enhancement as well as native T_1 and T_2 mapping was common and occurred in 78% of patients (5). In this cohort, imaging was performed at a median duration of 71 days after infection. The findings of this study led to wide concern regarding the potential implications of myocarditis, a condition that seems to be subclinical in many individuals and often not associated with any impairment in systolic function. Both scientists and laypersons asked whether a pandemic that causes myocardial fibrosis would lead to a future wave of patients with arrhythmias, heart muscle dysfunction, or even sudden cardiac death. This concern became even more amplified among athletes in whom myocarditis has long been recognized as a potential cause of sudden cardiac death.

However, the high burden of myocarditis has not been confirmed in other studies. While an assorted variety of CMR abnormalities are fairly common in patients recovering from COVID-19 (6), strong evidence for myocarditis has been much more scarce in both pathologic and imaging studies (7-9) in patients dying or recovering from COVID-19.

One of the first comprehensive study on student athletes (10) provided further insights on the impact of COVID-19 on athletes' hearts by presenting data on 48 student athletes from West Virginia University who recovered from COVID-19 and who were referred for CMR testing. Per institutional protocol, CMR was only performed in the presence of symptoms (n = 37) or abnormalities on electrocardiography (ECG) (n = 1) or echocardiography (n = 10). Among the 48 athletes who were referred to CMR, 27 (56%) had cardiac abnormalities, with 19 (40%) having late gadolinium enhancement of the pericardium, which commonly involved the pericardium overlying the lateral wall and which was often associated with small pockets of pericardial effusion. However, isolated myocardial involvement was less frequent (17%) and was nonspecific as it did not involve alterations in both T_1 and T_2 parameters. A more recent study of 145 student athletes with COVID-19, most of whom had mild or moderate symptoms during their disease, found that only 1.4% had evidence of myocarditis according to CMR performed at a median of 14 days after the positive test results (11). Similarly, a study of 12 professional elite athletes from Hungary (12) who recovered from severe COVID-19 after having mostly mild to moderate symptoms found no evidence of myocardial or pericardial disease according to CMR.

We believe these studies (11,12) are important because it highlights the potential of sophisticated imaging to detect wider sets of subclinical abnormalities than detected traditionally. For example, high prevalence of pericardial involvement among athletes

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who recovered from COVID-19. However, the exact etiology of this finding is unclear. The identification of late gadolinium enhancement of the pericardium suggests the possibility of direct viral involvement of the pericardium versus a secondary inflammatory effect resulting from the systemic multiorgan inflammatory response that these individuals sustained. From a clinical perspective, these findings imply that clinicians who evaluate patients who present with chest pain after recovering from COVID-19 should elicit for possible pericardial symptoms, such as discomfort that is positional or is worse with inspiration.

The study by Brito et al. also reinforces the concept that selective use of CMR imaging based on an algorithmic approach that first uses other more commonly available screening tests may improve the yield and efficiency of imaging-based testing. In the West Virginia study, CMR was only performed after initial screening with echocardiography and ECG. Although this approach is appropriate and plausible, it is noteworthy that only 5 athletes who tested positive for COVID-19 did not require further testing based on having a normal ECG and echocardiography. Regardless of the screening algorithm used, ultimately, the most challenging clinical question is how to incorporate CMR results, which may be subtle and have uncertain prognostic implications, into clinical decision-making, particularly among athletes who face a higher rate of sudden cardiac death.

A recent consensus statement published in *iJACC* (13) provided useful recommendations regarding screening of potential cardiac involvement in competitive athletes. This statement provides the following 2 key points: 1) in asymptomatic athletes and mildly symptomatic athletes, cardiovascular testing before return-to-play may not be necessary; and 2) until it has been established that complications of COVID-19 are rare in athletes who experience prolonged or more than mild symptoms, current recommendations suggest a prudent exclusion of complications with a combination of ECG, biomarkers, and echocardiography. With respect to pericarditis, the statement appropriately recommends that echocardiography is the first-line imaging in most cases, but CMR can further delineate pericardial enhancement or coexisting myocarditis.

When should CMR be considered for further evaluation of athletes who have recovered from COVID-19? The *iJACC* statement (13) on multimodality imaging of athletes after COVID-19 infection provides a few possible scenarios: 1) persistent symptoms without an alternative explanation; 2) sustained troponin elevation; 3) new or evolving ECG changes such as diffuse ST-segment elevations or new T-wave inversions; 4) regional wall motion abnormalities on echocardiography; 5) left or right ventricular dysfunction; and 6) more than trivial pericardial effusion.

Given the high prevalence of cardiac abnormalities on CMR among individuals who have recovered from COVID-19, future studies will need to determine the prognostic implications of these findings. Will abnormalities in T_1 or T_2 mapping offer any prognostic value among individuals who have normal ejection fraction and no late gadolinium enhancement? Will isolated pericardial enhancement in asymptomatic individuals have any prognostic implications? Is the frequency of CMR abnormalities higher in athletes compared with nonathletes who recovered from COVID-19? Will further risk stratification with exercise testing or external monitoring be helpful? Will future coronavirus strains have different cardiac manifestations? Our *iJACC* team, along with athletes, sport fans, clinicians, and scientists, all eagerly await the answers to these perplexing questions.

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