COVID-19 viral infection and myocarditis in athletes: the need for caution in interpreting cardiac magnetic resonance findings

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Common viral infections may cause a number of acute diseases that involve organ systems outside the respiratory tract, including inflammation of the heart muscle (myocarditis).[1] Diagnosis of myocarditis by cardiac magnetic resonance (CMR) traditionally relies on myocardial tissue characterisation abnormalities such as increased signal intensity on T2-weighted sequences (*oedema*), early gadolinium enhancement (*hyperaemia*) and late gadolinium enhancement (LGE) (*necrosis and/or fibrosis*).[1] Myocardial T1 and T2 mapping are recent techniques that allow a more accurate characterisation of myocardial tissue changes induced by inflammation.[2] According to the 2018 revised 'Lake Louise' criteria, diagnosis of myocarditis is fulfilled in the presence of relevant symptoms when at least one of the T1-based criteria plus at least one of the T2-based criteria are met.[3]

At the beginning of the COVID-19 pandemic, there was concern that heart muscle could be more frequently involved by SARS-CoV-2 infection than by other respiratory viruses. In athletes who recovered from COVID-19, a small study on 26 subjects reported 4 (15%) fulfilling Lake Louise criteria for myocarditis and 8 (31%) with isolated LGE,[4] while subsequent investigations with larger cohorts of athletes showed a much lower prevalence of myocardial involvement (online supplemental table).

In a recent study in the *British Journal of Sports Medicine*, Szabó *et al*[5] provided a new piece of evidence on the true incidence of myocardial tissue abnormalities at CMR in athletes who tested positive for SARS-CoV-2. The study had many methodological strengths: a large study population; a comprehensive and updated CMR tissue characterisation protocol, including T1 and T2 mapping; the availability of a subset of athletes with both pre-COVID and post-COVID CMR studies; and the inclusion of a cohort of controls without SARS-CoV-2 infection, either athletes or non-athletes. Overall, the study demonstrated that the large majority of athletes did not show any CMR abnormality, with the exclusion of junctional LGE. Particularly, morphofunctional ventricular findings (including strain analysis) and T1 and T2 mapping values did not differ between index COVID-19 athletes and control no-COVID-19 athletes and between preinfection and postinfection CMR studies in the same index COVID-19 athlete. Diagnosis of myocarditis according to the 2018 modified Lake Louise criteria was reached in just one out of 147 athletes; in 6 other athletes, there were myocardial tissue changes such as slightly elevated T1 and/or T2 mapping values or isolated LGE which were consistent with possible, but not definite, myocardial inflammation. Six of these seven athletes had either chest pain during the acute infection or long-COVID symptoms. Follow-up was uneventful in all athletes who returned to play after recovery.

According to previous investigations and the Szabó's study, great caution is needed in evaluating isolated CMR mapping abnormalities, to avoid the risk of overdiagnosis of pathologic findings like myocardial oedema or fibrosis.[5 6] The increasing experience with CMR imaging study has demonstrated that LGE is not an uncommon finding in the athlete. Junctional LGE is considered a non-pathological pattern that may be observed in up to 30% of athletes.[6] Bands of mid-myocardial/subepicardial LGE have also been reported in a minority of endurance athletes.[6] The current study reported two cases of isolated myocardial LGE and one of isolated pericardial LGE that were deemed as potentially COVID-19-related lesions. Although non-ischaemic LGE without myocardial oedema may be the result of a healed myocarditis, its relation with SARS-CoV-2 infection remains unproven in the absence of a history of clinically overt acute myocarditis during the course of the viral infection and ideally with a preinfection CMR for comparison. This explains the debated reliability of studies in which the presence of any CMR tissue characterisation abnormality, including focal junctional LGE, was 'tout-court' classified as signs of COVID-19 myocarditis. Moreover, because the evaluation of non-parametric criteria for myocarditis such as myocardial oedema and LGE is prone to subjectivity, the results of past and future studies not providing inclusion of controls, blind CMR interpretation and assessment of interobserver agreement should be interpreted with caution because of potential methodological biases.

Based on the results of the Szabó *et al*[5] and previous studies, systematic cardiovascular screening following SARS-CoV-2 infection and before return to play (RTP) does not seem justified, given the uncommon occurrence of heart lesions, particularly in athletes with mild or no symptoms (the large majority). In these athletes, the likelihood of developing a COVID-19 clinically relevant myocardial lesion at risk of sudden cardiac death during sport appears negligible.

Most proposed protocols of cardiovascular evaluation before RTP are based on a triad of cardiac tests, including basal ECG, troponin and echocardiography.[7] However, the sensitivity of this protocol for demonstration of inflammatory myocardial lesions after the athlete's recovery is inherently low. Both ECG and troponin normalise early during the myocarditis course and the presence of a postinflammatory left ventricular scar is usually undetectable by ECG and echocardiography. Indeed, non-ischaemic myocardial fibrosis can only be identified by contrast-enhanced CMR, because it is segmental and characteristically involves the outer layer of the ventricular wall, while sparing the subendocardial myocardium that mostly contributes to regional contractility.[8] In a different clinical context, there is compelling evidence that the most sensitive predictor of non-ischaemic myocardial scar at CMR is an exercise-induced ventricular arrhythmia with premature ventricular beats, either multifocal or with a right-bundle-branch-block morphology (figure 1).[8] Accordingly, to increase the sensitivity for detection of postinflammatory scar, a maximal exercise testing and/or a 24-hour Holter ECG monitoring (with a sport session) should be included in the cardiovascular protocol of screening the subset of athletes with relevant symptoms

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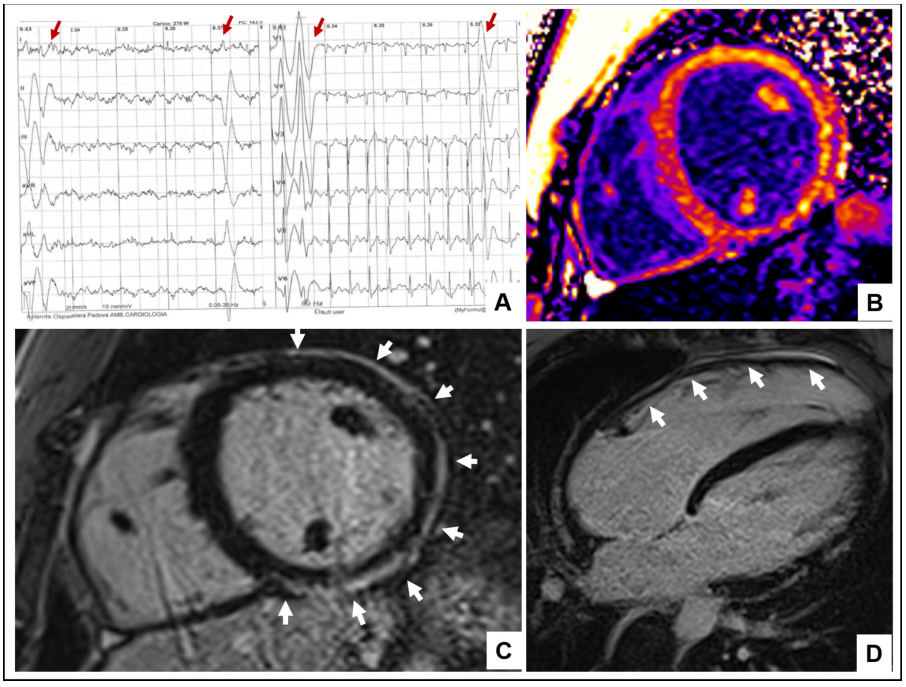

Figure 1 A professional athlete in his 20s underwent cardiac magnetic resonance for premature ventricular beats with right bundle branch block/superior axis morphology at high workload during exercise testing (A, red arrows) 2 months after gastrointestinal viral infection. Resting ECG and echocardiography were normal. Native T1 mapping short-axis sequence showed increased signal in the entire left ventricular free wall indicating myocardial oedema (B). Postcontrast sequences revealed a subepicardial stria of late gadolinium enhancement with a 'ring-like' pattern, involving the anterior, lateral and inferior left ventricular walls in their basal and medium portions (white arrows; (C) 4-chamber view; (D) short-axis view) indicating myocardial necrosis and/or fibrosis. Based on negative genetic testing a diagnosis of probable postinflammatory myocardial scar was made.

who undergo RTP clinical evaluation after recovery of COVID-19 infection.[9]

In conclusion, Szabó *et al*[5] should be commended for further clarifying the role of CMR in the diagnosis of myocardial inflammation in athletes with COVID-19 viral infection and showing that a CMR-based diagnosis of myocarditis is actually very uncommon. Diagnoses of COVID-19-related myocarditis in athletes based on CMR findings that do not meet rigorous diagnostic criteria (2018 revised Lake Louise), are not associated with clinical manifestations, or lack a previous CMR study for comparison should be evaluated with great caution. The risk of myocardial inflammation in SARS-CoV-2 infection appears not distinctively higher compared with other viruses and may depend on the severity of the infection. Currently used screening protocols to test athletes before RTP have low sensitivity for detection of myocardial fibrosis due to healed myocarditis from COVID-19. A maximal exercise test in athletes with cardiovascular symptoms after COVID-19 illness should be considered because the occurrence of exercise-induced ventricular arrhythmias has proven to be an accurate predictor of non-ischaemic myocardial scar.

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SUPPLEMENTAL FILE

Table – Main cardiac magnetic resonance studies evaluating the prevalence of myocardial abnormalities in athletes after SARS-Cov2 infection.

Reference	Athletes with CMR	CMR abnormalities
Rajpal et al. (1)	26	4 (15%) myocarditis 8 (30%) LGE w/o inflammation
Brito et al. (2)	48	19 (40%) pericardial LGE 1 (2%) myocardial LGE 7 (5%) reduced LV EF and/or GLS
Clark et al. (3)	59	1 (2%) myocarditis 1 (2%) pericarditis
Starekova et al. (4)	145	2 (1.4%) myocarditis
Martinez et al. (5)	27 of 789	3/27 (11%) myocarditis 2/27 (7%) pericarditis
Moulson et al. (6)	317 of 2820	21/317 CMR abnormalities (7% of those who underwent CMR for clinical indications, 0.7% of the overall sample)
Daniels et al. (7)	1598	2 clinical myocarditis subclinical probable myocarditis possible subclinical myocarditis
Szabo et al. (8)	147	1 myocarditis 1 pericarditis

CMR=cardiac magnetic resonance; GLS=global longitudinal strain; LGE=late gadolinium enhancement; LV EF=left ventricular ejection fraction

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