When to consider cardiac MRI in the evaluation of the competitive athlete after SARS-CoV-2 infection

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Uncertainty regarding the prevalence and clinical implications of myocarditis in athletes after SARS-CoV-2 infection prompted sports medicine and sports cardiology physicians to develop new return-to-play protocols early in the pandemic.[1 2] Concern that exercise may exacerbate the severity of cardiac injury and increase the risk of arrhythmic death in those with viral-related myocarditis led to recommendations for more intensive cardiac testing in athletes following SARS-CoV-2 infection, usually, in the USA, with some combination of a resting 12-lead ECG, troponin and transthoracic echocardiogram (so-called 'triad' testing). Based solely on expert opinion and rapidly evolving clinical experience, these initial recommendations emphasised the need to gather high-quality data to guide future recommendations.[1 2] Early-case series documenting local experiences with cardiac MRI (CMR) in asymptomatic and mildly symptomatic athletes reported high frequencies of cardiac injury.[3] These data factored heavily in decisions about restarting sports and even led one sports conference within the National Collegiate Athletic Association to mandate all athletes, whether symptomatic or not, be screened with a CMR.

Recently accrued registry data, now including >5000 professional and collegiate US athletes, provide some clarity regarding the prevalence of cardiac injury (both myocarditis and pericarditis) and the risk of adverse cardiovascular outcomes in athletes following SARS-CoV-2 infection.[4–6] Data from the Outcomes Registry for Cardiac Conditions in Athletes (n=3018) and a professional athlete cohort (n=789) document a low prevalence of cardiac involvement (0.6%–0.7%) in athletes who mostly underwent cardiac triad testing followed by CMR only when clinically indicated.[4 5] These studies identified moderate symptom severity during the acute phase of infection and/or the presence of cardiopulmonary symptoms as key risk factors for underlying cardiac inflammation.[4 5] In contrast, the Big Ten registry which reported on collegiate athletes who underwent mandatory screening CMR (n=1597) reported a 2.3% prevalence of myocardial involvement.[6] Accordingly, our aim is to examine the controversies and provide an expert perspective on the optimal use of CMR in the evaluation of athletes following SARS-CoV-2 infection.

CMR AND THE CLINICAL DIAGNOSIS OF MYOCARDITIS

CMR is a powerful diagnostic tool for the evaluation of myocarditis when *clinically indicated*. CMR is the only non-invasive imaging modality that can accurately measure myocardial function and provide tissue characterisation capable of detecting manifestations of myocarditis including necrosis/fibrosis/scar (using late gadolinium enhancement) and oedema/hyperaemia/capillary leak (using parametric mapping-derived T1 and T2 relaxation times).[7] The European Society of Cardiology and the American Heart Association recommend a diagnostic algorithm for myocarditis predicated on both a clinical presentation suggestive of disease and concomitant abnormal diagnostic testing including data derived from CMR.[8 9] Symptoms suggestive of myocarditis include acute/new-onset chest pain, dyspnoea, palpitations and syncope. Diagnostic criteria include ECG or rhythm abnormalities, elevated troponin, structural or functional abnormalities on cardiac imaging and abnormal tissue characterisation on CMR. Clinically suspected myocarditis is defined by the presence of ≥1 clinical symptom and ≥1 diagnostic criterion, or, in the absence of symptoms, ≥2 diagnostic criteria.[8] Importantly, CMR-derived tissue characterisation abnormalities, in the absence of symptoms or other diagnostic abnormalities, *do not* fulfil the contemporary definition of clinical myocarditis.

CMR TO SCREEN FOR INFLAMMATORY HEART DISEASE

Effective screening tools are characterised by a balance between sensitivity and specificity that produces acceptable accuracy, manageable cost and adequate availability. To date, the use of CMR as a primary screening modality for inflammatory heart disease has not been rigorously studied. Theoretical consideration of CMR as a screening tool raises numerous concerns. There are inherent technical imaging challenges related to tissue characterisation and inconsistencies in clinical interpretation may arise from interpreter bias or inexperience. Specifically, techniques for parametric mapping, image acquisition and evaluation are vendor specific with heterogeneity across commercially available pulse sequences requiring imaging sites to derive their own normal reference ranges. Ideally, T1 and T2 times should be considered abnormal only when >2 SDs above the site-specific reference range. The degree to which these important technical details were considered in prior SARS-CoV-2 athlete studies is unclear and likely inadequate. Accurate CMR use is also highly dependent on acquisition and interpreter expertise. In small single-centre COVID-19 athlete studies, the prevalence of reported myocarditis ranged from 0% to 15%.[3 10] Similarly, the prevalence of CMR-defined inflammatory heart disease in the Big Ten registry ranged from 0% to 7.6% among the participating 13 universities, with three sites reporting no myocarditis among 189 athletes.[6] This marked heterogeneity is most likely not explained by underlying pathobiology but rather site-by-site technical

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Table 1 Proposed use of cardiac MRI (CMR) in athletes after SARS-CoV-2 infection

CMR indicated:	Clinical symptoms suspicious for SARS-CoV-2-related cardiac injury (eg, chest pain, significant exercise intolerance without clear pulmonary aetiology, new palpitations or syncope) and ≥1 abnormal cardiac test (abnormal ECG, troponin, transthoracic echocardiogram or ventricular arrhythmias on monitoring or stress testing) **OR** New clinical symptoms concerning for SARS-CoV-2-related cardiac injury (eg, chest pain, significant exercise intolerance without clear pulmonary aetiology, new palpitations or syncope) on return to exercise after initial normal cardiac testing
CMR can be considered:	High clinical suspicion for SARS-CoV-2-related cardiac injury (eg, chest pain, significant exercise intolerance without clear pulmonary aetiology, new palpitations or syncope) despite normal cardiac testing **OR** Moderate systemic non-cardiac symptoms related to SARS-CoV-2 (eg, prolonged fever >48 hours, prolonged severe myalgias >48 hours, severe lethargy) and ≥1 abnormal cardiac test
CMR not recommended:	Screening in asymptomatic or mildly ill* athletes unless as part of a research study

*Mild symptoms include upper respiratory tract (congestion, coryza, sore throat, headache), gastrointestinal (nausea, vomiting, diarrhoea), anosmia, ageusia, mild fatigue and fever/chills/myalgias <48 hours.

and interpretation variability. The lack of a blinded core-laboratory review with healthy and appropriate case–controls also represents a significant limitation, and it must be emphasised that normative CMR data among young competitive athletes are sparse.[6] Finally, CMR is expensive and frequently only available in tertiary care medical centres. Based on these considerations and the available evidence to date, devoting widespread CMR resources to screen athletes after SARS-CoV-2 infection is neither practical nor likely to improve clinical outcomes.

ADVERSE CARDIAC EVENTS FOLLOWING SARS-COV-2 IN ATHLETES

The reported prevalence of SARS-CoV-2 cardiac injury among athletes ranges from 0.6% to 0.7% using a symptom-driven assessment followed by clinically indicated CMR,[4 5] and 2.3%–3.0% when using CMR as the primary screening modality.[4 6] Regardless, disease prevalence must always be coupled with disease relevance. It is noteworthy and highly reassuring that none of the large cohort studies in US collegiate and professional athletes, despite ongoing surveillance, have reported a confirmed SARS-CoV-2-associated adverse cardiac event. Accordingly, we recommend using CMR only when there is clinical suspicion of myocarditis, and we recommend against the use of CMR as a primary screening tool (table 1).

The French writer Jean-Baptiste Alphonse Karr coined the phrase '*plus ça change, plus c'est la même chose*' (*the more things change, the more they remain the same*). Although many SARS-CoV-2 clinical uncertainties persist, the approach to cardiac testing following SARS-CoV-2 infection in athletes should rely on the clinical pretest probability of disease to determine the need for CMR. This approach is consistent with the proven strategy of using advanced diagnostic testing only when clinically indicated.

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