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Editorial commentary: Screening cardiac magnetic resonance imaging for athletes after COVID-19: Is it time to end the debate?



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Since the beginning of the coronavirus disease-2019 (COVID-19) pandemic, much has been learned regarding the effects of viral infection on the 'athletic heart'. Initially, the high prevalence of myocardial injury observed among hospitalized patients with COVID-19 [1] fueled significant apprehension regarding the safety of competitive sports for athletes recovered from SARS-CoV-2 infection and the likelihood of myocarditis. Indeed, numerous early consensus screening recommendations were put forth [2,3] that endorsed a conservative return-to-play (RTP) screening approach consisting of 'triad' [4] testing with 12-lead electrocardiography (ECG), cardiac troponin assessment, and echocardiography.

Some schools and collegiate athletic conferences chose to add more sensitive imaging with cardiac magnetic resonance imaging (CMR) in addition to 'triad' testing as part of their screening protocols. From these early experiences, numerous small observational case series were published that reported clinical profiles of athletes infected and results from testing with additive CMR [5,6]. Studies were primarily single-center and limited by lack of controls, no independent blinded review of CMRs, non-standardized CMR protocols, and small subject numbers. In the first published case series of US collegiate athletes ($N = 26$), individuals were asymptomatic or only mildly ill [5]. However, 4 of 26 (15%) athletes met modified CMR Lake Louise Criteria [7] for myocarditis and 8 (31%) had evidence of late gadolinium enhancement (LGE) without edema [5]. A second case series of 54 US collegiate student-athletes did not reveal any cases of myocarditis, but 40% with pericardial enhancement and/or pericardial effusion [6]. To date, in no other published study of athletes with COVID-19, including those leveraging a CMR-based screening strategy, has the same degree of pericardial involvement been reported.

Eventually, data from large registries, which included diverse populations of professional ($N = 789$) [8] and collegiate athletes ($N = 3,018$), [4] demonstrated a low prevalence of clinical myocarditis in athletes (~0.6–0.7%) [4,8] with the vast majority of athletes absent screening CMR. In the ORCCA registry, while 198 athletes had a mandated screening CMR and the prevalence of cardiac abnormalities increased to 3% in this sub-cohort, the diagnostic yield was 4-times higher if the CMR was a clinically-directed study [4]. Most importantly, to date, there have been no

acute adverse cardiac events reported as a direct consequence of COVID-19 infection in the athletes included in these large registries [4,8]. The most recent registry data come from the Big Ten Conference which included $N = 1,597$ athletes (vast majority asymptomatic or only mildly-ill) who all underwent CMR screening in combination with 'triad' testing [9]. Abnormalities on CMR consistent with myocarditis [7] were reported in 2.3% of athletes. However, there was marked heterogeneity in myocarditis prevalence (0–7.6%) from the 13 institutions included in this registry [9]. Most of these cases were deemed 'sub-clinical' myocarditis ($N = 28$) given lack of symptoms but detection by CMR [9]. In terms of clinically apparent myocarditis ($N = 9$, 0.6%), [9] the data were remarkably comparable to ORCCA and the professional athlete registries [4,8].

In this issue of *Trends in Cardiovascular Medicine*, Patel et al. concisely summarize and analyze trends within the current literature reporting myocardial involvement in athletes after COVID-19 infection as detected by CMR. They report on 9 studies, 4 with a CMR-based screening approach. The authors keenly note the extreme heterogeneity in all of these studies with myocarditis diagnosed in 0 to 15.38% of the athletes. Study designs were inconsistent, including the timing of CMR and non-standardized data collection techniques. As previously highlighted, lack of controls and case control subjects were also significant limitations in these studies.

The authors appropriately emphasize the fact that isolated abnormal CMR tissue characterization does not satisfy the diagnosis of myocarditis [10]. In addition, the modified Lake Louise Criteria are based on pre-test probability of clinical myocarditis and have not been validated as a screening tool in low-risk cases. [7]. As also commented on, athletes can demonstrate normally elevated cardiac biomarkers after intense exercise; isolated LGE may be present, particularly at hinge points in the interventricular septum; and normal CMR reference ranges for athletes are lacking. Thus, in the absence of pre-test probability, what is the clinical relevance of an 'abnormal' CMR finding? What would CMR demonstrate immediately after a non-COVID respiratory viral infection? The authors conclude that because of critical limitations present in the data available, it is not possible to determine the true inci-

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dence of clinically relevant myocarditis, as detected by CMR, after COVID-19 infection in athletes.

This report is another important contribution to the literature that establishes the inadequacy of current evidence supporting CMR as an *effective screening tool* for athletes after COVID-19 infection. It is important to stress the critical limitation of the lack of blinded, core-lab independent reviews of prior CMR data. For example, in the Big 10 Registry, there is disclosure of the number of CMRs performed and cases of myocarditis per institution [9]. In assessing the 2 universities that performed the highest volume of CMRs, it is reported that 'University 3' performed 283 CMRs with 14 cases of myocarditis (4.9%), while 'University 10' performed 324 CMRs with only 1 case of myocarditis (0.3%) [9]. This extreme heterogeneity suggests significant interpretation bias. In addition, to date, there is absolutely no evidence that CMR screening has improved outcomes for athletes after COVID-19 infection. Rather, non-specific findings have led to downstream negative consequences such as unnecessary follow-up testing, undue patient anxiety, and unnecessary temporary medical disqualifications. We also cannot ignore the real-world considerations of excessive costs and inappropriate healthcare resource allocation for CMR screening of healthy athletes.

Use of CMR in the evaluation of athletes after COVID-19 infection has an established role when it is clinically directed, particularly for those with high clinical pre-test probability (e.g. cardiopulmonary symptoms) and abnormal initial diagnostic testing suggestive of myocarditis. However, screening CMR in athletes with low clinical pre-test probability for myocarditis is likely to be low yield. We should acknowledge where uncertainties remain, particularly given the dynamic state of the COVID-19 pandemic. With emerging variants of SARS-CoV-2, including Omicron and others likely to follow, longitudinal follow-up will be required to assess the extent or severity of potential cardiac involvement. The clinical significance of abnormal findings as detected by CMR in low pre-test probability cases remains to be determined. Future research will require a core lab with blinded CMR interpretation and more tightly controlled analyses. Finally, ongoing COVID-19 registries of athletes are essential to accurately determine long-term cardiac and health outcomes.

As the sports cardiology community has struggled with the most appropriate and sensible RTP clinical evaluation for athletes recovered from COVID-19, we are reminded of a comparable narrative, the evolution of accurate ECG interpretation for asymptomatic athletes over the last two decades [11]. We should be mindful of this cautionary tale and not assume CMR, the most sensitive cardiac imaging test available, is an effective screening tool in the ab-

sence of rigorous scientific vetting. Limitations in preliminary CMR data, coupled with clinical myocarditis prevalence and RTP outcomes data in convalesced athletes from COVID-19, provide reassurance that the evaluation of athletes after COVID-19 should be based on pre-test clinical probability and not a universal CMR-based screening approach. In accordance with the accepted clinical approach for RTP for athletes recovered from *any* viral pathogen, it is time to move away from mandated intensive screening strategies.

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