

## EDITORIAL

## Cardiac Involvement in Athletes Recovering From COVID-19

## A Reason for Hope

Satyam Sarma<sup>1</sup>, MD; Brendan M. Everett<sup>1</sup>, MD, MPH; Wendy S. Post<sup>1</sup>, MD, MS

**O**n March 12, 2020, the National Basketball Association suspended its 2020 season after 2 players tested positive for the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Fears of rapid viral spread, among not just athletes but spectators, were motivating concerns for halting play. Shortly thereafter, the National Collegiate Athletic Association canceled the 2020 March Madness national basketball championship. A significant factor in the decision to cancel sporting events was concerns of myocardial involvement and injury associated with coronavirus disease 2019 (COVID-19). Early observational studies described some degree of cardiac involvement in up to 78% of infected patients, ranging from troponin elevations to features of myocarditis and myopericarditis on cardiac magnetic resonance imaging (MRI).<sup>1</sup> The uncertain risks for myocarditis, a leading cause of sports-related sudden cardiac death, and heightened risks for transmission among athletes with limited ability to don personal protective equipment, factored heavily in the decision to halt play during the early months of the pandemic.

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The first 2 reported case series of athletes recovering from COVID-19 appeared to validate these concerns (Table).<sup>2,3</sup> Although these initial studies were relatively small, cardiac findings were common, occurring in ≈40% of athletes. In the first study,<sup>2</sup> 4 athletes out of 26 (15%)

had cardiac MRI findings suggestive of myocarditis on the basis of elevated T2 signal and presence of late gadolinium enhancement and 8 athletes had evidence for late gadolinium enhancement in isolation. No athlete had elevated serum troponin levels and T1 signals were similar between those with and without suspected myocarditis. In contrast, Brito et al<sup>3</sup> found that athletes with COVID-19 had primarily pericardial involvement by MRI with no cases of suspected myocarditis. Three athletes had abnormal echocardiograms with impaired global longitudinal strain or reduced ejection fraction (<50%). Only one athlete had elevated troponin levels.

These early studies highlighted the challenges in interpreting cardiac MRI in athletes and determining the clinical significance and specificity of findings suggestive of acute inflammatory changes. The absence of control athletes, small sample sizes, lack of previous baseline imaging, and uncertain pretest likelihood for myocardial involvement in patients with SARS-CoV-2 infection contributed to uncertainty in estimating myocarditis risk. Recent evidence suggests true COVID-19 myocarditis may in fact be uncommon, presenting pathologically in <5% of patients undergoing autopsy or referred for myocardial biopsies in a recent case series.<sup>4</sup> Subsequent studies of athletes recovering from COVID-19 have since demonstrated much lower rates of myocardial involvement than earlier studies, ranging from 0.6% to 3%, despite similar proportions of symptomatic athletes.<sup>5–8</sup>

In this issue of *Circulation*, Moulson and colleagues<sup>9</sup> report findings from a large, multicenter, prospectively

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Correspondence to: Satyam Sarma, MD, Institute for Exercise and Environmental Medicine, University of Texas Southwestern Medical Center, 7232 Greenville Ave, Dallas, TX 75231. Email Satyam.Sarma@UTSouthwestern.edu

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**Table. Summary of COVID-19 Athlete Studies**

Study	Sample size	MRI screening algorithm	Competition level	Symptomatic athletes, n (%)	Myocardial findings by MRI, n (%)	Myocarditis suspected, n (%)	Mean follow-up, d
Rajpal et al (2020) <sup>2</sup>	26	All inclusive	Collegiate	12 (27)	12 (46)	4 (15)	NA
Brito et al (2020) <sup>3</sup>	54	Selective (48 MRIs performed)	Collegiate	38 (70)	19 (40)	0 (0)	NA
Malek et al (2021) <sup>5</sup>	26	All inclusive	Professional	20 (77)	0 (0)	0 (0)	NA
Starekova et al (2021) <sup>6</sup>	145	All inclusive	Collegiate, high school	111 (77)	40 (28)	2 (1.4)	NA
Clark et al (2021) <sup>7</sup>	59 COVID+, 60 COVID-athletes	All inclusive	Collegiate	46 (78)	2 (3)	2 (3)	NA
Martinez et al (2021) <sup>8</sup>	789	Selective (30 MRIs performed)	Professional	460 (58)	5 (0.6)	5 (0.6)	180
Moulson et al (2021) <sup>9</sup>	3018	All inclusive (198 MRIs) + selective (119 MRIs)	Collegiate	1774 (59)	21 (0.7)	21 (0.7)	130

COVID-19 indicates coronavirus disease 2019; MRI, magnetic resonance imaging; and NA, not available.

collected observational registry (Outcomes Registry for Cardiac Conditions in Athletes) including data from COVID-19-positive collegiate athletes gathered during Fall 2020. In the largest study of COVID-19-positive athletes to date, the authors reviewed symptoms, cardiac screening studies, and cardiac MRI reports from 3018 athletes recovering from COVID-19. In 2820 athletes, MRI was obtained only if clinically indicated on the basis of abnormal screening cardiac testing (n=34) or presence of moderate or greater symptoms (n=85). A total of 119 MRIs was performed in this group. A smaller parallel cohort of 198 athletes underwent cardiac MRI regardless of symptoms or screening cardiac tests. Abnormal cardiac screening tests (eg, ECG, echocardiogram, serum troponin) were similarly uncommon (n=4) in this all-inclusive cardiac MRI group compared with the selective screening group. Criteria for myocardial involvement were prespecified on the basis of updated Lake Louise imaging myocarditis criteria, which were developed initially for patients with a clinical presentation consistent with myocarditis. Athletes undergoing cardiac MRI were categorized as definite, probable, or possible myocardial or pericardial involvement on the basis of myocardial late gadolinium enhancement, T1- and T2-weighted imaging, as well as signs of pericardial involvement. Using this framework, the authors observed low rates of cardiac involvement on cardiac MRI (0.5%) in 15 out of the 2820 athletes who underwent a selective screening algorithm on the basis of cardiac screening tests or symptoms. Of the 119 athletes who underwent cardiac MRI screening with this approach, 12.9% (n=15) had cardiac involvement, including 9 definite, 3 probable, and 3 possible cases of suspected myocardial involvement. In the all-inclusive MRI screening group, 3% of the 198 athletes had abnormal MRIs, with 1.5% (n=3) having either definite or probable cardiac involvement. Of note, 136 athletes in the all-inclusive arm had normal screening cardiac testing and mild to no symptoms. Four of these athletes were found to have either myocardial or pericardial involvement (2 definite, 1 probable). No athlete

with MRI abnormalities had clinical cardiac complications during the study follow-up period, although there was 1 case of cardiac arrest that was deemed to be unrelated to COVID-19. Ten athletes in the overall cohort experienced noncardiac COVID-19 complications, including pulmonary embolism and pleural effusion.

The authors, along with the Outcomes Registry for Cardiac Conditions in Athletes study group and steering committee, are to be commended for assembling this large, multicenter prospective registry. Information from this highly impactful study will provide essential information for millions of athletes, trainers, coaches, health care providers, and families in estimating risks of resuming sporting activities after COVID-19 and appropriate screening protocols. Team physicians and sports cardiologists will be able to engage in more meaningful shared decision-making discussions with athletes. Navigating the nuances of athlete testing is challenging and the use of probabilistic language to describe the likelihood of cardiac involvement is helpful in providing transparency in the shared decision-making process.

There are some important limitations and unanswered questions that arise from this study that should be noted. There was no core laboratory review of cardiac MRI, ECG, or echocardiogram images. Diagnostic reports were obtained from reporting schools and clinicians. This raises the potential for observer bias toward documenting abnormalities because athletes were known to carry a COVID-19 diagnosis. Blinded, independent review of cardiac MRI may help define the magnitude of this bias. In addition, there may be reader variability in interpretation of cardiac MRI. Second, the importance of cardiac screening tests compared with a symptom-based approach is uncertain. In the selective screening arm, 85 athletes had MRI because of moderate or greater symptoms, whereas 34 were referred because of abnormal cardiac screening tests. Almost half of the abnormal screening tests were deemed not to be related to COVID-19 pathology (30 out of 67) and the majority of athletes (65 out of 67) had abnormalities in only 1 element of cardiac testing.

Although the relative diagnostic yield for cardiac involvement by MRI was higher for athletes with abnormal cardiac testing (7 of 34 [21%]) compared with athletes who were symptomatic (8 of 85 [9%]), the larger number of athletes with cardiac involvement among those tested because of symptoms alone emphasizes the importance of careful screening for moderate to severe symptoms, particularly chest pain, dyspnea, and myalgias. Some additional limitations include that this registry is based on real-world data and did not mandate a standardized evaluation protocol across participating institutions.

In general, the findings from this study are remarkably consistent with previous studies that have taken either an all-inclusive MRI or a selective MRI approach on the basis of symptoms or abnormal screening cardiac testing (Table). In studies where cardiac MRI was performed inclusively in all athletes, rates of suspected myocarditis ranged from 0% to 15%, with 3 out of the 4 studies reporting rates between 0% and 3%. In the 2 studies where MRI was done selectively, rates of suspected myocarditis were 0% and 0.6%. There has not been a head-to-head comparison of selective screening versus all-inclusive cardiac MRI algorithms, but the nominally small differences between the 2 approaches and essentially 0 reported cases of cardiac complications suggest selective screening is a viable and cost-effective strategy. These findings support recommendations from the Return to Play algorithms and consensus statements for athletes after COVID-19,<sup>10,11</sup> which advocate for a multimodal assessment of pretest likelihood of myocardial injury before pursuing cardiac MRI. The algorithm relies on a symptom-driven approach such that the presence of moderate to severe symptoms with initial COVID-19, or persistent or recurrent symptoms, requires initial cardiac evaluation with ECG, serum troponin, and echocardiogram. Cardiac MRI is recommended for athletes with abnormalities on these initial cardiac screening tests that are likely COVID-19–related as well as those with persistent, unresolving symptoms. For colleges and universities with limited health care and financial resources, the Return to Play algorithms provide an effective, lower cost, and likely safe framework allowing athletes to resume sporting activities. It is important to note that the reassuring results of this study cannot be easily extrapolated to hospitalized patients with COVID-19 or older noncompetitive athletes.

The selective cardiac MRI approach also limits one of the primary challenges in interpreting cardiac MRI in highly trained athletes—findings of uncertain significance—particularly when the results are not definite myocardial abnormalities. As imaging technology and biomarker assays become increasingly more sensitive, assessment of pretest likelihood is critical in interpreting ambiguous findings. A major limitation in the field is the unknown frequency of MRI findings in athletes. Incorporation of a control group may help address this knowledge gap

but there is uncertainty as to determining the appropriate control group: the athletes themselves, other healthy athletes, athletes matched by sport, or athletes recovering from non-COVID-19 viral illness. Of the 7 published studies of athletes with COVID-19, the study by Clark et al.<sup>7</sup> has been the only one to include athlete and nonathlete controls. Of 60 athlete and 27 healthy controls, 13% of the healthy athletes and 8% of the healthy controls had evidence of mild increases in T1 and T2, compared with 39% of athletes with COVID-19. MRI myocarditis criteria are based on the presence of a “significant clinical” pretest suspicion.<sup>12</sup> For athletes with low pretest probability of myocarditis—those without abnormal cardiac screening tests and without at least moderate symptoms (eg, dyspnea, chest pain, lethargy, hypoxia)—the clinical significance of abnormal MRI findings suggestive of injury and inflammation is unknown and needs to be interpreted cautiously. Additional studies are needed to better understand the prevalence of MRI findings and distribution of signal measures in healthy athletes.

Reflecting on the events of 2020, for many, the resumption of sports provided much-needed relief from the stresses of a global pandemic. As Nelson Mandela said, “Sports has the power to change the world. It has the power to inspire. It has the power to unite people in a way that little else does.” The effort put forth by the sports cardiology community to develop safety measures and return to play protocols, and the work of athletic trainers, team physicians, and clinical providers, ensured athletes and training staff remained safe. That there has not been a single case of cardiac complication to date documented to be clearly related to COVID-19 is a testament to the effectiveness of collaborative care.

## ARTICLE INFORMATION

### Affiliations

University of Texas Southwestern Medical Center, Dallas (S.S.). Brigham and Women's Hospital, Boston, MA (B.M.E.). Johns Hopkins University School of Medicine, Baltimore, MD (W.S.P.).

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