EDITORIAL

Return to Play for Athletes After COVID-19 Infection
The Fog Begins to Clear

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In October 2020, Kim and colleagues, representing the American College of Cardiology's Sports and Exercise Council, published recommendations[1] for the evaluation of athletes who had tested positive for COVID-19 to ensure safe return to play. The group recommended a tiered approach based on the presence of symptoms, followed by electrocardiography (ECG), injury biomarkers, and echocardiography. Abnormalities were then to be further characterized by the selective use of cardiac magnetic resonance (CMR) imaging. The recommendations were based on expert opinion of experienced sports cardiologists, because there were at the time only modest data to inform such a document. A report[2] on 26 college athletes who were asymptomatic or had only mild symptoms found CMR evidence of myocarditis in 4 (15%). Both the Kim et al report[1] and our Editorial[3] at the time called for larger data sets, so that recommendations could be refined and more informed by data.

Related article

In only 6 months since then, there has been a remarkable amount of information acquired, analyzed, and published regarding post–COVID-19 prevalence of cardiac abnormalities in athletes, as summarized in the **Table**.[2,4-11] In a recent study of 789 professional athletes, screening consisted of serum troponin testing, ECG, and echocardiography, regardless of symptoms.[8] Thirty of these athletes (3.8%) had abnormal test results resulting in referral for CMR imaging, with 3 diagnosed with myocarditis. Similarly, in a large cohort of 3018 college athletes from 42 universities,[9] a strategy using serum troponin tests, ECG, and echocardiography identified 15 athletes (0.5%) with possible cardiac involvement. In a subgroup of 198 athletes in that report[9] who underwent a primary CMR imaging–based screening strategy (ie, without selection by the other tests), a higher proportion of athletes demonstrated definite, probable, or possible cardiac involvement (n = 6 [3.0%]).

In the current issue of *JAMA Cardiology*, a study by Daniels et al[11] adds substantially to the extant information. As they note, starting in September 2020, the Big Ten athletic conference (involving 13 major universities) mandated comprehensive cardiac screening, including ECG, troponin testing, echocardiography, and CMR imaging for athletes in the aftermath of positive COVID-19 test results, regardless of prior symptomatic status. The authors report on a large sample of 2461 athletes, of whom 1597 (64.9%) had the complete comprehensive screening testing, including CMR imaging without prior selection. They found that 37 (2.3%) of these athletes demonstrated diagnostic criteria for myocarditis by CMR imaging, including 20 without cardiovascular symptoms and with normal ECG, echocardiography, and troponin test results, who would not have been identified without CMR imaging. While some of the prior studies involving smaller patient cohorts had also reported all athletes undergoing CMR imaging,[2,4,5] it was unclear what selection may have taken place before CMR imaging referral.

This mandated comprehensive testing in a large group of collegiate athletes provides the novel opportunity not previously available in large athlete cohorts (to our knowledge) to construct the data in their Figure 2,[11] which succinctly summarizes what would have been detected and missed by various screening strategies. In the report by Moulson et al,[9] among the 3018 athletes evaluated, almost 200 had screening that included CMR imaging without prior selection. The prevalence of cardiac abnormalities in that group was similar to that reported in the study by Daniels et al.[11]

Thus, the totality of data provides us with substantially more information to inform our thinking about screening and return to play than even just 6 months ago. We can be reasonably certain that the prevalence of signs on CMR imaging of myocarditis using the modified Lake Louise criteria is in the range of 1% to 3% in athletes following positive COVID-19 test results. Screening only on the basis of COVID-19 symptoms is insensitive. Sensitivity is improved by an algorithm combining the presence of symptoms as well as ECG, echocardiography, and troponin testing results. However, this approach will likely miss individuals who would be found to have CMR imaging evidence of myocarditis. While much has been learned, questions remain.

First, what are the implications of finding evidence on CMR imaging of myocarditis in the absence of prior symptoms or abnormalities on cardiac testing? The findings from the studies illustrated in the Table and the study of Daniels et al[11] demonstrate the increased diagnostic yield of CMR imaging for detecting COVID-19 cardiac involvement. There are limitations, in that independent core laboratory image interpretations were not performed based on practicality and funding and few studies had control referents.[4,7] Moreover, the clinical significance of abnormalities of CMR imaging in young athletes in competitive sports remains unknown, as does the prevalence of such abnormalities in larger and more general cohorts of young athletes.[12] Additionally, it is unclear if abnormalities on CMR imaging after COVID-19 represent markers for increased risk of sudden death in athletes, supporting an indication to restrict activity, because myocarditis in athletes has historically been diagnosed in the setting of cardiovascular symptoms and not by screening individuals without symptoms with CMR imaging. On the other hand, the absence of symptoms in athletes with myocarditis is not neces-

Table. Published Studies of Cardiac Screening in Athletes With Positive COVID-19 Test Results

Characteristic	Study									Total
	Rajpal et al[2]	Vago et al[4]	Małek et al[5]	Starekova et al[6]	Clark et al[7]	Martinez et al[8]	Moulson et al[9]	Hendrickson et al[10]	Daniels et al[11]	
Publication date, mo and y	September 2020	December 2020	January 2021	January 2021	February 2021	March 2021	April 2021	May 2021	May 2021	NA
Athlete type	College	Professional and elite	Professional and elite	College	College	Professional	College	College	College	NA
No. of athletes with COVID-19 reported	26	12	26	145	59	789	3018	137	2461	6673
Women, No. (%)	11 (42)	10 (83)	21 (81)	37 (26)	37 (63)	12 (1.5)	957 (31.7)	44 (32.1)	812 (33.0)	1941 (29.1)
Men, No. (%)	15 (58)	2 (16)	5 (19)	108 (74)	22 (37)	777 (98.5)	2061 (68.3)	93 (67.9)	1649 (67.0)	4732 (70.9)
Asymptomatic, No. (%)	14 (54)	2 (17)	6 (23)	24 (16.6)	13 (22)	329 (41.7)	887 (29.4)	25 (18.2)	NA	1300[a] (31.9)
CMR imaging performed, No. (%)[b]	26 (100)	12 (100)	26 (100)	145 (100)	59 (100)	27 (3.4)	317 (10.5)	5 (3.6)	1597 (64.8)	NA
Time to CMR imaging, mean (SD), median (interquartile range), or median (range), d	24 (10)[c]	17 (17-19)[d]	32 (22-62)[d]	15 (11-194)[e]	21 (13-37)[d]	19 (17)[c]	33 (18-63)[d]	22 (11)[c]	22 (10-77)[e]	NA
Prevalence of myocarditis by CMR imaging, No./total No. tested (%)	4/26 (15)	0/12	0/26	2/145 (1.4)	2/59 (3)	3/27 (11)	15/317 (4.7)	0/5	37/1597 (2.3)	63/2214 (2.8)[f]
Prevalence myocarditis diagnosed in full cohort, No./total No. tested (%)	4/26 (15)	0/12	0/26	2/145 (1.4)	2/59 (3.4)	3/789 (0.4)	15/3018 (0.5)	0/137	37/2461 (1.5)	63/6673 (0.94)[g]
Prevalence of nonmyocarditis findings on CMR imaging, No./total No. tested (%)[h]	8/26 (31)	0/12	5/26 (19)	2/145 (1.4)	1/59 (1.7)	2/27 (7.4)	10/317 (3.1)	0/5	81/1597 (5.1)	NA

Abbreviations: CMR, cardiac magnetic resonance imaging; NA, not available or not applicable.

[a] Of 4075 participants.

[b] Number and percentage of total athletes positive for COVID-19 reported in the study who underwent CMR.

[c] Mean (SD).

[d] Median (interquartile range).

[e] Median (range).

[f] 95% CI, 2.2% to 3.6%.

[g] 95% CI, 0.7% to 1.2%.

[h] Prevalence of cardiac findings excluding myocarditis, including pericardial enhancement consistent with pericarditis. Most studies did not include isolated late gadolinium enhancement of the inferior right ventricular insertion site as an abnormal finding.

sarily reassuring, because more than 50% of affected individuals in an autopsy series[13] of proven myocarditis in athletes were asymptomatic prior to death. Further complicating this picture is that none of the athletes screened by ECG, echocardiography, and serum troponin testing but not CMR imaging, as reported by Moulson et al[9] or Martinez et al,[8] had cardiovascular events to suggest that this more basic approach is ineffective in preventing sudden death, although the number of cases is small.

Do the new data suggest that CMR imaging should be the primary screening modality? While the Big Ten schools and other select universities may have resources and expertise to routinely include CMR imaging in screening athletes, the practicality when applied to other populations is challenging. There are almost 500 000 college athletes and an estimated 8 million high school athletes competing annually in the US. The data from 2 of the available studies[9,11] suggest that 15% to 30% of athletes tested positive for COVID-19 during the months of analysis, implying a very large number of screening CMR imaging studies in this country alone during pandemic conditions. While access to and the technical capabilities of CMR imaging have evolved substantially, access to CMR imaging throughout the US remains limited, is associated with high cost, requires substantial expertise for high-quality acquisition and interpretation, and can have extensive interpretative variability.[12] Even within the cohort of academic institutions represented by the study of Daniels et al,[11] the presence of abnormalities on CMR imaging was highly variable, ranging from 0% to 7.6% of athletes at each institution with myocarditis by CMR imaging.[11] A primary CMR imaging screening strategy would place a major burden on any health care system and athletic program.

Moreover, as vaccinations proceed apace and individuals with COVID-19 become less frequent and/or ill, we can reasonably anticipate that the pretest probability of finding signs of myocarditis will become lower with time. This will inevitably raise the specter of the effect of Bayes theorem, and screening will result in an increasingly lower yield and a higher number of false-positive and misleading results, as discussed recently by Kim et al.[14]

Hence, the rapid evolution of data in this area continues to support the idea that the more practical and more widely available approach of testing with ECG, echocardiography, and serum troponin likely improves specificity and decreases burden of potentially unwarranted athletic restriction. The data in the article by Daniels et al[11] elevate our ability to intelligently discuss the issues with athletes, their families, coaches, performance coaches, trainers, sports scientists, and institutions, among the many stakeholders involved in the well-being of athletes within the universe of organized sports. We can now say with more certainty that an evaluation strategy as noted will identify many but not all potential cases of cardiac involvement after COVID-19. It can be discussed with stakeholders that a more intensive CMR imaging strategy will identify another 1 to 2 cases in every 100 individuals screened, resulting in restriction of activity, but whether that affects clinical course is uncertain. As discussed in a related context by Baggish et al,[15] we can move away from a dichotomous view that one approach is right and one is wrong to a more nuanced approach, which in this case involves discussion with and input from all stakeholders and not just health care professionals.

Although we often call for more data, we are likely at a point now in which more data might get us closer to the true incidence of signs on CMR imaging of myocarditis with narrower confidence intervals for athletes in the aftermath of COVID-19, but we will still face the same conceptual hurdles of pretest probability of the individuals tested and sensitivity and specificity of the testing modalities, and the practical will always need to be balanced against the perfect. We certainly at this point know a lot more than we did just 6 months ago. We can applaud the sports cardiology community for the remarkable progress in such a short period, bringing all of these data to light and enabling a far more informed and data-driven approach to our efforts to ensure a safe return to play for young athletes.

ARTICLE INFORMATION

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Published Online: May 27, 2021. doi:10.1001/jamacardio.2021.2079

Conflict of Interest Disclosures: None reported.

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