Results From the Big Ten COVID-19 Cardiac Registry: Impact of SARS-COV-2 on Myocardial Involvement

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Abstract

Objective: COVID-19 has been associated with myocardial involvement in collegiate athletes. The first report from the Big Ten COVID-19 Cardiac Registry (Registry) was an ecological study that reported myocarditis in 37 of 1597 athletes (2.3%) based on local clinical diagnosis. Our objective was to assess the relationship between athlete and clinical characteristics and myocardial involvement. **Design:** Cross-sectional study. **Setting:** We analyzed data from 1218 COVID-19 positive Big Ten collegiate athletes who provided informed consent to participate in the Registry. **Participants:** 1218 athletes with a COVID-19–positive PCR test before June 1, 2021. **Assessment of Independent Variables:** Demographic and clinical characteristics of athletes were obtained from the medical record. **Main Outcome Measures:** Myocardial involvement was diagnosed based on local clinical, cardiac magnetic resonance (CMR), electrocardiography, troponin assay, and echocardiography. We assessed the association of clinical factors with myocardial involvement using logistic regression and estimated the area under the receiver operating characteristic (ROC) curve. **Results:** 25 of 1218 (2.0%) athletes met criteria for myocardial involvement. The logistic regression model used to predict myocardial involvement contained indicator variables for chest pain, new exercise intolerance, abnormal echocardiogram (echo), and abnormal troponin. The area under the ROC curve for these indicators was 0.714. The presence of any of these 4 factors in a collegiate athlete who tested positive for COVID-19 would capture 55.6% of cases. Among noncases without missing data, 86.9% would not be flagged for possible myocardial involvement. **Conclusion:** Myocardial involvement was infrequent. We predicted case status with good specificity but deficient sensitivity. A diagnostic approach for myocardial involvement based exclusively on symptoms would be less sensitive than one based on symptoms, echo, and troponin level evaluations. Abnormality of any of these evaluations would be an indication for CMR.

Key Words: cardiac symptoms, collegiate athletes, echocardiography, myocardial involvement, return to play

(*Clin J Sport Med* 2024;00:1–10)

INTRODUCTION

Myocarditis after viral infection is a well-known cause of sudden cardiac death in athletes.[1,2] Early in the COVID-19 pandemic, reports of heightened risk of myocarditis led to concerns about return to play after COVID-19 infection in collegiate athletes.[3–6] These concerns were amplified when published studies in athletes confirmed COVID-19–associated myocardial involvement.[7–10] Beginning in September 2020, the Big Ten Conference declared a policy of advanced cardiac testing after COVID-19 infection before return to play.[11]

Submitted for publication January 10, 2024; accepted June 3, 2024.

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The Jay and Jeanie Schottenstein Family Foundation provided funding to support the collection and management of data for the Big Ten COVID-19 Cardiac Registry and at the Ohio State University. The Rink Family Foundation provided funding to support the collection and management and analysis of data for the Big Ten COVID-19 Cardiac Registry. The PJ Schafer Cardiovascular Research Fund provided funding to support the collection and management of data at the University of Maryland. MPower at the University of Maryland supported data collection and analysis.

The authors report no conflicts of interest.

Results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. Results of the present study do not constitute endorsement by ACSM.

The dataset analyzed during the current study is not publicly available at this time because of active data collection.

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http://dx.doi.org/10.1097/JSM.0000000000001247

Testing included electrocardiogram (ECG), echocardiogram (echo), serum troponin level, and cardiac magnetic resonance (CMR) imaging.[11] Several cardiologists and sports medicine physicians formed the Big Ten COVID-19 Cardiac Registry (Registry). The objectives of the Registry were 4-fold: (1) Understand and minimize risk for athletes who have had COVID-19 infection; (2) Inform diagnostic testing decision-trees to minimize that risk; (3) Inform return-to-play decisions; and (4) Advance scientific discoveries of the cardiovascular and other health effects of COVID-19.[11]

The first report from the Registry was based on early institution-level results from 13 of the 14 Big Ten institutions. Among 1597 COVID-19–positive athletes, CMR-myocarditis was diagnosed in 37 of 1597 athletes (2.3%) based on the local reading according to updated 2018 Lake Louise criteria.[12,13] Institutional prevalence of myocarditis ranged from 0% to 7.6%. Ecological data are limited to counts of affected individuals, their diagnostic features and the population screened. Consequently, the initial report could not examine associations between individual-level characteristics and myocarditis.

We now present results based on individual-level data from 6 Big Ten institutions that continued to contribute data to the Registry. Consistent with the objectives of the registry, in the present study, we assess the relationship between athlete demographic/clinical characteristics and myocardial involvement.

METHODS

Study Participants

Participating Big Ten institutions obtained written informed consent to collect demographic and clinical information and imaging/laboratory study results for collegiate athletes after a positive PCR test for COVID-19 indicated by daily antigen screening. Local staff entered these data into the Registry REDCap data collection site. Indiana University, University of Iowa, University of Maryland, Ohio State University, Pennsylvania State University, and Rutgers University contributed data. Findings reported now are from athletes who underwent a cardiac evaluation before June 1, 2021. This period coincides with the time before vaccines were widely available and the Big Ten requirement for CMR was still in place. Institutional Review Boards from all participating institutions approved the Registry.

Demographic and clinical information, including COVID-related and cardiac symptoms, timing of testing, and return to play information, were collected from the athletes' sports and medical records. For the purposes of this article, a modification of return to play was any increase from the standard quarantine at the time of the athlete's illness. COVID-related symptoms comprised loss of taste or smell, fever or chills, cough, myalgia, rhinorrhea, pharyngitis, nausea, diarrhea, headache, fatigue, and shortness of breath at rest. Cardiac-related symptoms comprised chest pain, palpitations, tachycardia, syncope, dizziness, exercise intolerance, and shortness of breath with exercise.

Local assessments of CMR, ECG, and echo studies, and troponin levels from the first examination after the PCR positive test were also collected from the medical record. Troponin, ECG, and echo results >28 days after PCR-positive test were considered missing. Cardiac magnetic resonance imaging that occurred >100 days after PCR-positive test was considered missing. All echos were read in Intersocietal Accreditation Commission Echocardiography certified laboratories. Electrocardiographs were read using International Revised or Seattle criteria.[14,15]

Myocardial involvement was diagnosed based on local clinical, CMR, ECG, and echo interpretation. Myocardial involvement was identified on CMR using the updated Lake Louise criteria.[13] If only one T1 or T2 abnormality or late gadolinium enhancement was observed on CMR imaging, this was considered an abnormal CMR but not positive for myocardial involvement. Isolated delayed gadolinium enhancement at the right ventricular insertion site or trivial pericardial effusion was not considered abnormal.

Data Analysis

Missing and erroneous values in the data were queried with the person responsible for data entry at each institution. Distributions of athlete characteristics according to myocardial involvement status were compared and tested for statistical significance using Student t test or Wilcoxon rank sum test, and Fisher exact test as appropriate.

We assessed the association of clinical factors (listed above) with myocardial involvement using logistic regression. We added variables associated with myocardial involvement at $P \leq 0.05$ to the model all at once and then eliminated those with $P > 0.05$ to create our final model. We estimated the area under the receiver operating characteristic (ROC) curve using postestimation commands in Stata as a measure of the ability of a model to distinguish between diseased and undiseased. We created an indicator for having at least 1 factor that was included in the final logistic regression model and assessed the sensitivity and specificity of that variable for myocardial involvement.

All statistical analyses were performed with Stata Statistical Software: Release 17 (StatCorp LLC, College Station, TX), and statistical significance was set at $P \leq 0.05$.

RESULTS

This study presents data on 1218 athletes with a COVID-19–positive PCR test before June 1, 2021, from 6 participating institutions submitting data to the Big Ten COVID-19 Cardiac Registry. There were 288 athletes (23.7%) from Indiana University, 272 (22.3%) from Ohio State University, 229 (18.8%) from the University of Iowa, 188 (15.4%) from Rutgers University, 152 (12.5%) from the University of Maryland, and 89 (7.3%) from Pennsylvania State University (Table 1). Mean age was 19.8 (SD 1.5) years, 777 athletes (63.8%) were male, and 860 athletes (70.6%) were non-Hispanic White. More than a quarter of the population (28.8%) played football. Track was the next most common sport with 108 athletes (8.9%), followed by baseball (7.1%), rowing (7.0%), and soccer (6.1%). Four athletes (0.3%) were admitted to the hospital, and there were no sudden cardiac events in the cohort. Information on reasons for hospitalization was not available.

There were 986 (81.0%) athletes with CMR imaging, and 919 (75.5%) received the imaging within the 100-day timeframe. Average time to CMR among athletes who

TABLE 1. Characteristics of 1218 SARS-CoV-2 PCR+ Collegiate Athletes Overall and by Locally Diagnosed Myocardial Involvement*

	Total, N = 1218	Myocardial Involvement, n = 25	No Myocardial Involvement, n = 1193	*P*†
Site, n (%)				
Indiana	288 (23.7)	7 (2.4)	281 (97.6)	0.50
Iowa	229 (18.8)	6 (2.6)	223 (97.4)	
Maryland	152 (12.5)	2 (1.3)	150 (98.7)	
Ohio State	272 (22.3)	8 (2.9)	264 (97.1)	
Penn State	89 (7.3)	0	89 (100)	
Rutgers	188 (15.4)	2 (1.1)	186 (98.9)	
Age in years, mean (SD)	19.8 (1.5)	19.8 (1.6)	19.8 (1.5)	0.99
Weight in kg, mean (SD)	84.0 (22.5)	81.6 (17.3)	84.1 (22.6)	0.89
Height in cm, mean (SD)	178.9 (11.0)	176.2 (11.2)	179.0 (11.0)	0.21
Sex, n (%)				
Male	777 (63.8)	16 (2.1)	761 (97.9)	0.98
Female	441 (36.2)	9 (2.0)	432 (98.0)	
Year in school, n (%)				
1	322 (29.3)	7 (2.2)	315 (97.8)	0.99
2	299 (27.2)	7 (2.3)	292 (97.7)	
3	250 (22.8)	5 (2.0)	245 (98.0)	
4	174 (15.8)	4 (2.3)	170 (97.7)	
5	54 (4.9)	1 (1.8)	53 (98.2)	
Missing	119	1	118	
Race/ethnicity, n (%)				
Non-Hispanic White	860 (70.6)	15 (1.7)	845 (98.3)	0.13
Non-Hispanic Black	253 (20.8)	6 (2.4)	247 (97.6)	
Hispanic	45 (3.7)	3 (6.7)	42 (93.3)	
Asian	11 (0.9)	0	11 (100)	
American Indian/Alaska Native	8 (0.7)	1 (12.5)	7 (87.5)	
Native Hawaiian/Pacific Islander	8 (0.7)	0	8 (100)	
Other	33 (2.7)	0	33 (100)	
Training status, n (%)				
In season	339 (27.9)	8 (2.4)	331 (97.6)	0.29
In training	417 (34.3)	5 (1.2)	412 (98.8)	
Out of season	460 (37.8)	12 (2.6)	448 (97.4)	
Missing	2	0	2	
Received vaccine pre-COVID+, n (%)				
Yes	3 (0.3)	0	3 (100)	0.99
No	1180 (99.8)	25 (2.1)	1154 (97.9)	
Missing	36	0	36	
COVID symptoms, n (%)				
Any COVID symptom				0.05
Yes	860 (70.6)	13 (1.5)	847 (98.5)	
No	358 (29.4)	12 (3.4)	346 (96.7)	
Loss of taste/smell				0.18
Yes	359 (29.5)	4 (1.1)	355 (98.9)	
No	859 (70.5)	21 (2.4)	838 (97.6)	
Fever/chills				0.33
Yes	250 (20.5)	7 (2.8)	243 (97.2)	
No	968 (70.4)	18 (1.9)	950 (98.1)	

TABLE 1. Characteristics of 1218 SARS-CoV-2 PCR+ Collegiate Athletes Overall and by Locally Diagnosed Myocardial Involvement* *(Continued)*

	Total, N = 1218	Myocardial Involvement, n = 25	No Myocardial Involvement, n = 1193	P†
Cough				0.48
Yes	284 (23.3)	4 (1.4)	280 (98.6)	
No	934 (76.7)	21 (2.3)	913 (97.8)	
Myalgia				0.46
Yes	256 (21.0)	7 (2.7)	249 (97.3)	
No	962 (79.0)	18 (1.9)	944 (98.1)	
Rhinorrhea				0.45
Yes	239 (19.6)	3 (1.3)	236 (98.7)	
No	979 (80.4)	22 (2.3)	957 (98.7)	
Pharyngitis				0.99
Yes	247 (20.3)	5 (2.0)	242 (98.0)	
No	971 (79.7)	20 (2.0)	951 (97.9)	
Nausea				0.99
Yes	72 (5.9)	1 (1.4)	71 (98.6)	
No	1146 (94.1)	24 (2.1)	1122 (97.9)	
Diarrhea				0.99
Yes	38 (3.1)	0	38 (3.2)	
No	1180 (96.9)	25 (2.1)	1155 (97.9)	
Headache				0.65
Yes	313 (25.7)	5 (1.6)	308 (98.4)	
No	905 (74.3)	20 (2.2)	885 (97.8)	
Fatigue				0.46
Yes	259 (21.3)	7 (2.7)	252 (97.3)	
No	959 (78.7)	18 (1.9)	941 (98.1)	
Shortness of breath at rest				0.48
Yes	108 (8.9)	3 (2.8)	105 (97.2)	
No	1110 (91.1)	22 (2.0)	1088 (98.0)	
Number COVID symptoms, mean (SD)	2.0 (2.1)	1.8 (2.2)	2.0 (2.1)	0.61
Cardiac symptoms, n (%)				
Any cardiac symptom				0.17
Yes	204 (16.7)	7 (3.4)	197 (96.6)	
No	1014 (83.3)	18 (1.8)	996 (98.2)	
Chest pain				0.001
Yes	81 (6.7)	7 (8.6)	74 (91.4)	
No	1137 (93.4)	18 (1.6)	1119 (98.4)	
Palpitations				0.001
Yes	11 (0.9)	3 (27.3)	8 (72.7)	
No	1207 (99.1)	22 (1.8)	1185 (98.2)	
Tachycardia				0.15
Yes	8 (0.7)	1 (12.5)	7 (87.5)	
No	1210 (99.3)	24 (2.0)	1186 (98.0)	
Syncope				0.06
Yes	3 (0.3)	1 (33.3)	2 (66.7)	
No	1215 (99.8)	24 (2.0)	1191 (98.0)	
Dizziness				0.22
Yes	12 (1.0)	1 (8.3)	11 (91.7)	
No	1206 (99.0)	24 (20)	1182 (98.0)	

TABLE 1. Characteristics of 1218 SARS-CoV-2 PCR+ Collegiate Athletes Overall and by Locally Diagnosed Myocardial Involvement* *(Continued)*

	Total, N = 1218	Myocardial Involvement, n = 25	No Myocardial Involvement, n = 1193	*P*†
New exercise intolerance				0.01
Yes	8 (0.7)	2 (25.0)	6 (75.0)	
No	1210 (99.3)	23 (1.9)	1187 (98.1)	
Shortness of breath with exercise				0.06
Yes	73 (6.0)	4 (5.5)	69 (94.5)	
No	1145 (94.0)	21 (1.8)	1124 (98.2)	
No. of cardiac symptoms, mean (SD)	0.16 (0.51)	0.76 (1.6)	0.15 (0.45)	0.004
Any symptom (COVID or cardiac), n (%)				0.99
Yes	779 (69.2)	17 (2.2)	762 (97.8)	
No	347 (30.8)	8 (2.3)	339 (97.7)	
Admitted to hospital, n (%)	4 (0.3)	0	4 (0.3)	0.95
Troponin‡, n (%)				0.01
Abnormal	10 (1.2)	2 (20.0)	8 (80.0)	
Normal	845 (98.8)	14 (1.7)	831 (98.3)	
Imaging/testing local reads, n (%)				
CMR§				<0.001
Abnormal	53 (5.8)	25 (47.2)	28 (52.8)	
Normal	866 (94.2)	0	866 (100)	
ECG¶				0.01
Abnormal	74 (8.3)	5 (6.7)	69 (93.2)	
Normal	821 (91.7)	12 (1.5)	809 (98.5)	
Echo‖				0.02
Abnormal	29 (3.3)	3 (10.3)	26 (89.7)	
Normal	861 (96.7)	15 (1.7)	846 (98.3)	
History of cardiac disease, n (%)				0.06
Yes	45 (3.7)	3 (6.7)	42 (93.3)	
No	1173 (96.3)	22 (1.9)	1151 (98.1)	
Return to play modified, n (%)				<0.001
Yes	133 (10.9)	24 (18.1)	109 (82.0)	
No	1085 (89.1)	1 (0.1)	1084 (99.9)	

** Total column presents column percentages and myocardial involvement status columns present row percentages.*
† P-value for comparison between myocardial involvement and no myocardial involvement from χ^2 comparison of proportions, Fisher exact test, Student t test, or Wilcoxon rank sum test.
‡ n = 855.
§ n = 919.
¶ n = 890.
‖ n = 895.

received a CMR within 100 days was 28.5 (SD 18.4) days. Troponin testing was performed in 1084 athletes (89.0%) but only in 855 athletes (70.2%) within 28 days. Average time to troponin testing among athletes who received testing within 28 days was 15.7 (SD 4.9) days. Almost all athletes received ECG (1214 [99.7%]) but only 895 athletes (73.5%) received within 28 days of the positive PCR test. Average time to ECG among athletes who received an ECG within 28 days was 16.0 (SD 5.0) days. Similarly, 1215 athletes (99.7%) were studied with echocardiography but only 890 athletes (73.1%) were studied within 28 days. Average time to echo among athletes who received an echo within 28 days was 16.7 (SD 5.1) days. All 4 studies (ECG, echo, Troponin, and CMR) were performed in 655 athletes (53.8%) within the time frame for analysis.

Seventy-one percent of athletes reported a COVID-related symptom with loss of taste or smell (29.5%), headache (25.7%), and cough (23.3%) the most common (Table 1). Fewer athletes reported cardiac-related symptoms (16.7%), and of these, chest pain (6.7%) and shortness of breath with exercise (6.0%) were the most common. Of those with troponin testing within 28 days of a PCR positive test, 10 (1.2%) were abnormal. Among those with CMR imaging within 100 days, 53 (5.8%) were abnormal. Electrocardiography abnormalities were observed in 74 (8.3%) of the athletes with an ECG within 28 days, and 29 (3.3%) with an echo within 28 days were abnormal. One hundred thirty-three athletes (10.9%) had their return to play modified beyond the standard quarantine at the time of the athlete's illness, whereas 1085 (89.1%) did not have their return to play modified.

TABLE 2. Characteristics of 25 Individual Athletes PCR+ for SARS-CoV-2 and Affected by Myocardial Involvement According to CMR

Case	Any Cardiac Symptom	Chest Pain	Palpitations	Tachycardia	Syncope	Dizziness	New Exercise Intolerance	Shortness of Breath With Exercise	ECG	Echo	Troponin	CMR
1	−	−	−	−	−	−	−	−	Missing	Normal	Normal	Abnormal T2 and LGE*
2	−	−	−	−	−	−	−	−	Normal	Normal	Normal	Abnormal T2 and LGE
3	+	+	+	+	+	+	+	+	Nonspecific T-wave changes	Normal	Normal	Abnormal T1, T2 and LGE
4	−	−	−	−	−	−	−	−	Normal	Reduced EF† 44%, RV‡ function reduced	Normal	LGE and reduced left ventricular ejection fraction
5	−	−	−	−	−	−	−	−	Normal	Normal	Normal	Abnormal T2 and LGE
6	−	−	−	−	−	−	−	−	Normal	Normal	Normal	LGE. Pericardial effusion that regressed with evidence of inflammation in pericardial and epicardial areas
7	−	−	−	−	−	−	−	−	T-wave inversion in III, bidirectional aVR	Normal	Missing	Abnormal T1 and LGE
8	+	+	+	−	−	−	−	−	Missing	Missing	Missing	Abnormal T2 and LGE
9	−	−	−	−	−	−	−	−	Missing	Missing	Missing	Abnormal T2 and LGE
10	−	−	−	−	−	−	−	−	Missing	Missing	Missing	Abnormal T2 and LGE
11	−	−	−	−	−	−	−	−	Normal	Normal	Normal	Abnormal T2 and LGE
12	+	+	−	−	−	−	−	+	Normal	Normal	Abnormal	Abnormal T2 and LGE
13	−	−	−	−	−	−	−	−	Abnormal	Normal	Normal	Pericardial effusion and subepicardial and pericardial enhancement
14	−	−	−	−	−	−	−	−	Missing	Missing	Missing	Abnormal T2 and LGE
15	+	+	−	−	−	−	−	+	Missing	Normal	Normal	Abnormal T2 and LGE
16	−	−	−	−	−	−	−	−	Normal	Abnormal	Abnormal	LGE
17	+	+	−	−	−	−	−	−	Normal	Normal	Normal	LGE
18	−	−	−	−	−	−	−	−	Abnormal	Abnormal	Normal	Abnormal T1, T2 and LGE
19	−	−	−	−	−	−	−	−	Missing	Missing	Missing	Pericardial enhancement and globally depressed systolic function
20	−	−	−	−	−	−	−	−	Missing	Missing	Missing	Abnormal T2

TABLE 2. Characteristics of 25 Individual Athletes PCR+ for SARS-CoV-2 and Affected by Myocardial Involvement According to CMR *(Continued)*

Case	Any Cardiac Symptom	Chest Pain	Palpitations	Tachycardia	Syncope	Dizziness	New Exercise Intolerance	Shortness of Breath With Exercise	ECG	Echo	Troponin	CMR
21	–	–	–	–	–	–	–	–	Missing	Missing	Missing	LGE
22	+	+	–	–	–	–	+	+	Normal	Normal	Normal	Abnormal T2, pericardial enhancement
23	–	–	–	–	–	–	–	–	Normal	Normal	Normal	Abnormal T2, subepicardial enhancement
24	+	+	+	–	–	–	–	–	Normal	Normal	Missing	Abnormal T1, T2 and LGE
25	–	–	–	–	–	–	–	–	Normal	Normal	Normal	Abnormal T1 and LGE

** Late gadolinium enhancement.*
† Ejection fraction.
‡ Right ventricular.
EF, ejection fraction; LGE, late gadolinium enhancement; RV, right ventricular.
A total of 25 athletes from 6 Big Ten Universities were diagnosed with myocardial involvement. Of these 25 athletes, 7 experienced cardiac symptoms, 5 reported no cardiac symptoms but had abnormal ECG or troponin level, 6 had neither cardiac symptoms nor abnormal ECG or troponin level.

Twenty-five athletes (2.0%; 95% confidence interval [CI], 1.4%–3.0%) met criteria for myocardial involvement. Of the participants without cardiac symptoms, 8 were missing ECG, echo, or troponin testing.

Of the athletes with myocardial involvement in the present report, 18 (72.0%) were included in the original, ecological study. The newly reported cases included 7 athletes who were not counted among the cases in the earlier report either because they had not tested positive for COVID-19 by December 2020 (the earlier report's data file preparation date) or because they had not yet received a cardiac evaluation. Of the 19 athletes from the earlier report who were not included in this study, 8 were from institutions not submitting individual-specific data to the Registry. We were not able to obtain informed consent for use of individual-specific data from 11. Typically, these athletes had departed campus and did not respond to repeated attempts to contact.

Prevalence of myocardial involvement differed by site (range 0%–2.9%); there were no significant outliers (Table 1). Among athletes reporting chest pain, 8.6% were diagnosed with myocardial involvement compared with 1.6% of those without chest pain ($P = 0.001$). Among athletes reporting palpitations, 27.3% were diagnosed with myocardial involvement compared with 1.8% of those without palpitations ($P = 0.001$). Among athletes reporting new exercise intolerance, 25.0% were diagnosed with myocardial involvement compared with 1.9% of those without new exercise intolerance ($P = 0.01$). Athletes with myocardial involvement had a greater number of cardiac symptoms on average than those without myocardial involvement (0.76 [SD 1.6] vs 0.15 [SD 0.45] [$P = 0.004$]). None of the athletes with myocardial involvement were admitted to the hospital.

Abnormal cardiac study findings were associated with myocardial involvement (Table 1). Among athletes with abnormal troponin, 20.0% had myocardial involvement compared with 1.7% with normal troponin values ($P = 0.01$). Athletes with abnormal ECG (6.7% vs 1.5%, $P = 0.01$) and abnormal echo (10.3% vs 1.7%, $P = 0.02$) were more likely to be diagnosed with myocardial involvement compared with athletes without these abnormalities. Athletes with a history of cardiac disease were diagnosed more often with myocardial involvement compared with those without history of cardiac disease but not significantly so (6.7% vs 1.9%, $P = 0.06$).

Athletes whose return to play was modified were more likely to have been diagnosed with myocardial involvement relative to those whose return to play was not modified (18.1% vs 0.1%, $P < 0.001$).

Symptoms, routine test (ECG, echocardiography, and troponin level) results, and CMR findings for the 25 myocardial involvement cases in this report are presented in Table 2. A symptoms-based approach would have identified only 7 of 12 athletes (58%) affected by myocardial involvement with symptoms or findings on ECG, echo, or troponin and 7 of 25 (28%) of all those affected by myocardial involvement.

The final logistic regression model used to predict myocardial involvement status contained indicator variables for chest pain, new exercise intolerance, abnormal echo, and abnormal troponin. The area under the ROC curve was 0.714 (95% CI, 0.581–0.846) for the 804 athletes with complete data for all 4 factors (Figure 1). The presence of any of these 4 factors (occurrence of chest pain, new exercise intolerance, abnormal echo, or abnormal troponin) in a collegiate athlete who tested positive for COVID-19 would capture 10 of 18 (55.6%) of myocardial involvement cases with tests completed (Table 3). Among noncases without missing data, 108 of 822 (13.1%) would be flagged for possible myocardial involvement. The positive predictive value of the presence of any of these 4 factors in a collegiate athlete who tested positive for COVID-19 to identify myocardial involvement cases was 8.5% (10/118). Because the sensitivity of each factor is low, treating the athletes with missing information as negative results in sensitivity = 10/25 (40%) and specificity = 1085/1193 (91%).

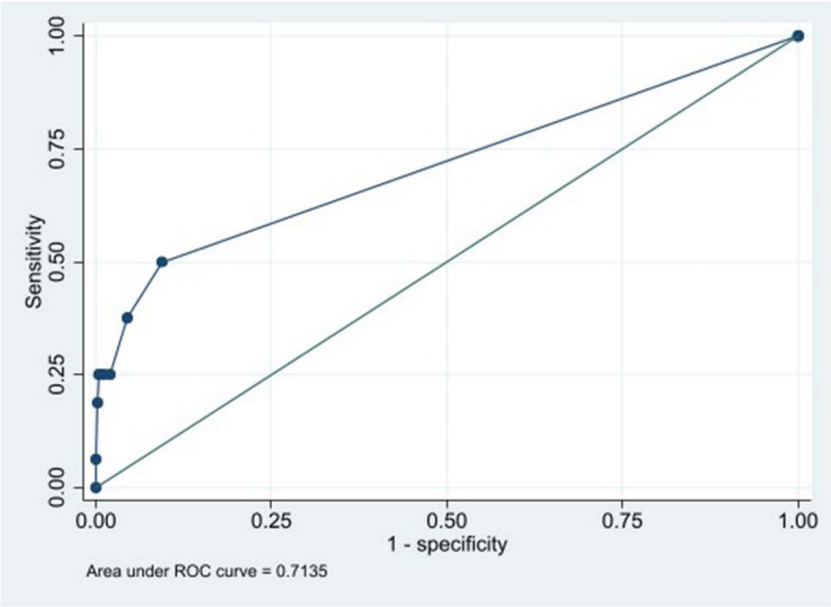

Figure 1. ROC curve for diagnosis of myocarditis in 804 SARS-CoV-2 athletes with complete information according to chest pain, new exercise intolerance, abnormal echo, and elevated troponin. ROC curve is based on 804 SARS-CoV-2 PCR+ athletes from 6 Big Ten Universities, 16 of whom have been diagnosed with myocarditis. Each dot on the curve represents a probability cutoff to distinguish cases from noncases based on different combinations of the 4 factors. The dot at approximately 50% sensitivity is represented by Table 3 (probability cut point >0.5).

DISCUSSION

In this study of Big Ten collegiate athletes with COVID-19, the majority (75.5%) of whom had CMR testing within 100 days of a PCR positive for SARS-CoV-2, prevalence of myocardial involvement was 2.0% (95% CI, 1.4%–3.0%). This is similar to the estimate reported in the ecological study (2.3%, 95% CI, 1.6%–3.2%) and consistent with results from the Outcomes Registry for Cardiac Conditions in Athletes (ORCCA) study of National Collegiate Athletic Association institutions.[9,12] Among athletes with CMR as part of the regular evaluation (198/3018), Moulson and colleagues reported 3.0% prevalence, and among 145 COVID-19–positive athletes who received CMR at the University of Wisconsin prevalence was 1.4%.[9,16]

Cardiac magnetic resonance diagnostic criteria for myocarditis based on the updated Lake Louise Criteria were intended for symptomatic patients; in the setting of mild or absent symptoms in athletic populations, these criteria are controversial.[17–19] In the current study, only 28% of cases had cardiac clinical symptoms.

Characteristics associated with myocardial involvement included presence of COVID-19 symptoms, cardiac symptoms (chest pain, palpitations, new exercise intolerance and shortness of breath with exercise), abnormal troponin levels, abnormal ECG or imaging (echo and CMR), and history of cardiac disease. Although these factors are consistent with findings from the ORCCA study,[9] the sensitivity of any one factor to detect myocardial involvement alone is small (Table 1). As opposed to the lack of any association with individual noncardiac COVID symptoms, the average number of cardiac symptoms was 5 times higher among our cases than the unaffected. Athletes reporting cardiac symptoms are a higher yield group for CMR findings, consistent with pre-COVID pandemic recommendations from the Society for Cardiovascular Magnetic Resonance that could be broadened.[18]

There is reason to be concerned with reliance on competitive athletes to report symptoms that may remove them from training and competition.[20,21] A symptoms-based approach would be less sensitive than one including ECG, echocardiography, and troponin assessments. The American College of Cardiology expert consensus document recommends ECG, echocardiography, and troponin level evaluation before CMR.[22] Kim et al,[23] on behalf of ORCCA, advocated CMR testing in collegiate athletes with moderate to high pretest probability of myocarditis, defined as a clinical syndrome consistent with myocarditis and abnormal troponin, ECG, or echocardiography. The recommendations from Kim et al in 2021, the American College of Cardiology in 2022 and Moulson et al in 2023 (representing or heavily informed by ORCCA) agree that CMR should be reserved for athletes with a clinical myocarditis syndrome.[22–24] Based on results from the Big Ten study in which 986 of 1218 athletes underwent CMR (vs 317/3018 in the ORCCA study), we recommend troponin and echocardiography for all and CMR testing among collegiate athletes with abnormal troponin or echocardiography or report of chest pain or new exercise intolerance.

Return to play decisions were made at the institutional level and were influenced by the current COVID-19 policy, availability of CMR, sport, and season. Other athletic conferences have published their approaches to diagnosis and management of the elite athletes infected with SARS-CoV-2, but information on return to play is not as readily available.[23,24]

The standards for return to play in the United States seem to be sufficient to prevent sudden cardiac death whether athletes are symptomatic or asymptomatic and with or without non-CMR objective correlates (ie, ECG, echo, or troponin level).[25] Still, the long-term clinical significance in asymptomatic athletes of CMR abnormalities that would be diagnostic of myocarditis in symptomatic athletes is not yet known. Cardiac

TABLE 3. Cross-tabulation of Myocardial Involvement Status With Chest Pain, New Exercise Intolerance, and Abnormal Echo and Elevated Troponin

	Myocardial Involvement	No Myocardial Involvement	Total
Positive (at least 1)	10	108	118
Negative (none)	8	714	722
Missing information*	7	371	378
Total	25	1193	1218

** Echo results or troponin level not available and neither chest pain nor new exercise intolerance reported.*
1218 SARS-CoV-2 PCR+ athletes from 6 Big Ten Universities with and without myocardial involvement cardiac evaluation results. Athletes who had at least 1 positive indicator (chest pain, new exercise intolerance, abnormal echo or elevated troponin) are in row 1 (positive), athletes with no positive indicator are in row 2 (negative), and athletes with missing echo or troponin results who reported no symptoms are in row 3 (missing). Treating the athletes with missing information as negative, sensitivity = 10/25 (40%) and specificity = 1085/1193 (91%).

magnetic resonance is validated for identifying cases of myocarditis.[26,27] Long-term follow-up of all athletes who present with CMR abnormalities is important to determine whether there are adverse consequences later in life.

Our best sensitivity and specificity for discriminating between athletes with and without myocardial involvement was achieved using report of chest pain, new exercise intolerance, abnormal echo, and abnormal troponin (Figure 1 and Table 3). Reliance on the presence of any of these factors to order CMR studies would capture all symptomatic and 60% of the asymptomatic cases in this study. The positive predictive value of the 4 factors is only 8.5%. Clinicians who have access to routine diagnostic facilities could recommend CMR for COVID-positive athletes who have chest pain, new exercise intolerance, abnormal echo, or abnormal troponin. We extend the findings from ORCCA by identifying 2 informative cardiopulmonary symptoms, chest pain and new exercise intolerance.

Prediction of myocardial involvement might be improved through earlier ECG, echo, and troponin testing. The present study began shortly after the start of the COVID pandemic in the United States when strict quarantine was a priority; cardiac tests were delayed beyond what would be appropriate now.

Athletes who were Hispanic and American Indian or Alaska Native were more likely to have the specific CMR abnormalities, but these differences were not statistically significant. No significant differences in the prevalence of myocardial involvement were observed by sex, age, sport, height, or weight.

Athletes with myocardial involvement were more likely to have their return to play modified than the unaffected. Still, return to play times for athletes affected by myocardial involvement were much less than the 3 or 6 months recommended in previous guidelines, opening the possibility that COVID-associated myocardial involvement is different from myocardial involvement of other etiologies and that time away from play could be reconsidered.

This study contributed to the objectives of the Registry by estimating the prevalence of myocarditis in collegiate athletes, identifying athlete characteristics associated with cardiac involvement, and providing guidance on criteria for CMR screening. Limitations of the current study include delays to testing and variability in local image interpretation. Now that quarantine is no longer an obstacle to cardiac evaluations, a careful medical history and ECG, echocardiography, and troponin testing should be performed as close to the appearance of cardiac symptoms or early in the course of acute infection as possible. Big Ten Conference athletes infected with SARS-CoV-2 are a highly selected patient population; our findings may not generalize readily to the larger COVID-19 patient population, notably the infirm or elderly and less elite athletes who are not as fit but who may both be more likely to report symptoms and more likely to suffer severe consequences of myocardial involvement. Results of this study focusing on collegiate athletes should also not be directly applied to high school athletes in sports. However, a conservative approach and thorough clinical evaluation by a cardiologist should be implemented in adolescent athletes suspected of having myocardial involvement. The present, prevalence study is cross-sectional and longitudinal studies would improve understanding of the sequelae of myocardial involvement. Our analyses are based on normal or abnormal categorical classification and more detailed, core laboratory ECG or echocardiography interpretation might improve prediction.

CONCLUSIONS

In this study of Big Ten collegiate athletes with COVID-19, myocardial involvement prevalence was 2.0%. Using data available from the clinical evaluation and initial cardiac testing, we were able to predict involvement with good but not excellent accuracy (ROC area under the curve = 0.714). There is a need for more sensitive (but sufficiently specific) tests to identify patients for whom CMR would be appropriate; an approach based exclusively on symptoms would be less sensitive than one based on symptoms, echo, and troponin level evaluations.

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