10.1161/CIRCULATIONAHA.121.054824

SARS-CoV-2 Cardiac Involvement in Young Competitive Athletes

Running Title: *Moulson & Petek, et al.; SARS-CoV-2 Cardiac Involvement in Athletes*

Nathaniel Moulson, MD[1,2*]; Bradley J. Petek, MD[1,2*], Jonathan A. Drezner, MD[3]; Kimberly G. Harmon, MD[3]; Stephanie A. Kliethermes, PhD[4]; Manesh R. Patel, MD[5]; Aaron L. Baggish, MD[1,2]; for the ORCCA Investigators

[1]Division of Cardiology; [2]Cardiovascular Performance Program, Massachusetts General Hospital, Boston MA; [3]Department of Family Medicine and Center for Sports Cardiology, University of Washington, Seattle, WA; [4]Department of Orthopedics and Rehabilitation, University of Wisconsin Madison, Madison, WI; [5]Division of Cardiology, Duke Heart Center, and Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC

*Co-first Authors

A complete list of the members of the Outcomes Registry for Cardiac Conditions in Athletes (ORCCA) Study Group are listed in the Appendix at the end of this article.

Address for Correspondence:
Aaron L. Baggish, MD, FACC, FACSM
Cardiovascular Performance Program
Massachusetts General Hospital
Yawkey Suite 5B, 55 Fruit Street
Boston, MA 02114
Tel: 617-643-7117
Fax: 617-643-7222
Email: abaggish@partners.org

This work was presented as an abstract at the American Medical Society for Sports Medicine Annual Meeting, April 13-18, 2021.

Abstract

Background: Cardiac involvement among hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is common and associated with adverse outcomes. The objective of this study was to determine the prevalence and clinical implications of SARS-CoV-2 cardiac involvement in young competitive athletes.

Methods: In this prospective multicenter observational cohort study with data from 42 colleges/universities, we assessed the prevalence, clinical characteristics, and outcomes of SARS-CoV-2 cardiac involvement among collegiate athletes in the United States. Data were collected from September 1, 2020 to December 31, 2020. The primary outcome was the prevalence of definite, probable, or possible SARS-CoV-2 cardiac involvement based on imaging definitions adapted from the Updated Lake Louise Criteria. Secondary outcomes included the diagnostic yield of cardiac testing, predictors for cardiac involvement, and adverse cardiovascular events or hospitalizations.

Results: Among 19,378 athletes tested for SARS-CoV-2 infection, 3018 (mean age 20 years [SD,1 year]; 32% female) tested positive and underwent cardiac evaluation. A total of 2820 athletes underwent at least one element of cardiac 'triad' testing [12-lead electrocardiography (ECG), troponin, and/or transthoracic echocardiography(TTE)] followed by cardiac magnetic resonance (CMR) if clinically indicated. In contrast, primary screening CMR was performed in 198 athletes. Abnormal findings suggestive of SARS-CoV-2 cardiac involvement were detected by ECG (21/2999,0.7%), cardiac troponin (24/2719,0.9%), and TTE (24/2556,0.9%). Definite, probable, or possible SARS-COV-2 cardiac involvement was identified in 21/3018 (0.7%) athletes, including 15/2820 (0.5%) who underwent clinically indicated CMR (n=119) and 6/198 (3.0%) who underwent primary screening CMR. Accordingly, the diagnostic yield of CMR for SARS-COV-2 cardiac involvement was 4.2 times higher for a clinically indicated CMR (15/119,12.6%) versus a primary screening CMR (6/198,3.0%). After adjustment for race and sex, predictors of SARS-CoV-2 cardiac involvement included cardiopulmonary symptoms (OR:3.1,95% CI:1.2,7.7) or at least one abnormal triad test (OR:37.4,95% CI:13.3,105.3). Five (0.2%) athletes required hospitalization for non-cardiac complications of SARS-CoV-2. During clinical surveillance (median follow-up 113 days [IQR=90,146]), there was one (0.03%) adverse cardiac event likely unrelated to SARS-CoV-2 infection.

Conclusions: SARS-CoV-2 infection among young competitive athletes is associated with a low prevalence of cardiac involvement and a low risk of clinical events in short term follow-up.

Key Words: COVID-19; SARS-CoV-2; Myocarditis; Young Competitive Athletes; Screening; Return-to-Play

Non-standard Abbreviations and Acronyms

CMR= cardiac magnetic resonance
ECG= electrocardiography
LGE= late gadolinium enhancement
LVEF= left ventricular ejection fraction
NCAA= National Collegiate Athletic Association
ORCCA= Outcomes Registry for Cardiac Conditions in Athletes
PCR= polymerase chain reaction
RTP= return-to-play

TTE= transthoracic echocardiography
SARS-CoV-2= severe acute respiratory syndrome coronavirus 2

Clinical Perspective

What is new?

- The ORCCA registry was created to investigate the prevalence and clinical outcomes of cardiovascular disease, including cardiac involvement following SARS-CoV-2 infection, among young competitive athletes.
- Our data indicate a low prevalence of cardiac involvement (0.5-3.0%) following SARS-CoV-2 infection among young competitive athletes undergoing return-to-play cardiac testing.
- To date, no adverse cardiac events related to SARS-CoV-2 infection have been observed among more than 3000 collegiate athletes during short-term clinical surveillance.

What are the clinical implications?

- The present findings suggest that asymptomatic or mildly symptomatic athletes that have fully recovered from SARS-CoV-2 infection may return to sport without cardiac testing.
- Cardiac evaluation inclusive of 12-lead ECG, troponin, and transthoracic echocardiography (TTE) should be considered in athletes with moderate and/or cardiopulmonary symptoms during initial illness or upon return to exercise.
- Cardiac magnetic resonance imaging (CMR) is most useful in athletes with high pretest probability for SARS-CoV-2 cardiac involvement as defined by the presence of cardiopulmonary symptoms and/or abnormalities on cardiac testing (ECG, troponin, TTE), however, the significance of CMR findings in the absence of symptoms remains unknown.

Introduction

Cardiac involvement associated with adverse outcomes is common among hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[1] At present, limited data exist on the prevalence and clinical relevance of cardiac involvement in non-hospitalized, otherwise healthy populations, including young competitive athletes. Post-viral myocarditis is a well-documented cause of sudden cardiac death during exercise.[2-4] Accordingly, concern for SARS-CoV-2 myocarditis contributed to the cancellation of organized sports and led to the development of expert consensus recommendations for the cardiac evaluation of athletes after SARS-CoV-2 infection.[5-8]

Observational data among middle-aged people recovering from SARS-CoV-2 infection document high-rates of potential cardiac involvement (78%) as evidenced by elevated cardiac biomarkers and cardiac magnetic resonance imaging (CMR) abnormalities.[9] Single center observational cohort studies of collegiate athletes undergoing return-to-play (RTP) cardiac testing inclusive of CMR report highly variable rates of SARS-CoV-2 cardiac involvement (1.4-56%) using heterogeneous, non-standardized definitions of disease.[10-13] A subsequent study in professional athletes undergoing RTP cardiac testing reported a lower prevalence of cardiac involvement (0.6%) when utilizing a testing strategy of 12-lead electrocardiography (ECG), blood cardiac troponin assay, and transthoracic echocardiography (TTE), followed by CMR when clinically indicated.[14] To date, the precise prevalence, clinical correlates, and outcomes of SARS-CoV-2 cardiac involvement in competitive athletes remains uncertain.

The Outcomes Registry for Cardiac Conditions in Athletes (ORCCA) was designed to address these issues. This registry collected data documenting cardiac diagnoses, non-cardiac

diagnoses, and attendant clinical outcomes among competitive collegiate athletes returning to organized athletics during the SARS-CoV-2 pandemic.

Methods

The data that support the findings of this study are available from the corresponding authors upon reasonable request. This was a prospective observational cohort study. The primary aim was to determine the prevalence of cardiac involvement in collegiate athletes diagnosed with SARS-CoV-2 infection. Secondary aims were to assess the diagnostic yield of cardiac testing, identify risk factors for cardiac involvement and determine the prevalence of adverse cardiac events or hospitalizations following SARS-CoV-2 infection in collegiate athletes. De-identified data were collected from participating institutions from September 1, 2020 to December 31, 2020, inclusive of all athletes with prior SARS-CoV-2 infection. All aspects of this study were approved by the Massachusetts General Brigham Institutional Review Board (Protocol #2020P002667).

Recruitment, Eligibility Criteria, and Data Collection

All National Collegiate Athletic Association (NCAA) institutions that implemented SARS-CoV-2 infection testing and performed cardiac pre-participation evaluations for athletes infected with SARS-CoV-2 were eligible. Athletes with confirmed SARS-CoV-2 infection by laboratory testing [polymerase chain reaction (PCR), antigen, or antibody] and who underwent local cardiovascular evaluation were included. Athletes were often tested for SARS-CoV-2 infection multiple times by participating institutions, and were included in this study if they had any positive SARS-CoV-2 test. Each athlete is only represented once in the registry based on the initial positive SARS-CoV-2 test. Evaluations included a clinical assessment and a range of

cardiac testing as determined by the institution including one or more of the following: 12-lead ECG, cardiac troponin assay, TTE, and CMR. 'Triad' testing refers to the combination of ECG, troponin, and TTE. Athletes were excluded if they had only a clinical assessment with no additional cardiac testing, or if they had not yet started their cardiac evaluation.

The Massachusetts General Hospital served as the central data collection center. Each participating institution submitted data via a standardized data capture tool and de-identified original clinical reports of the cardiovascular testing performed. Raw imaging data for both TTE and CMR were not available to the study investigators and diagnoses were therefore adjudicated using original clinical reports. Submitted data collection spreadsheets were reviewed for completeness and accuracy before being transcribed into a central REDCap database. Further details on recruitment and data collection methods are provided in the **Methods Supplement.**

Key Definitions

Symptom severity was categorized using reported symptoms from the initial infection and the presence of any recurring symptoms with return to exercise as initially proposed for collegiate athletes.[5] Prespecified symptom severity categories included: 1) asymptomatic, 2) mild, 3) moderate, and 4) cardiopulmonary.[5] Mild symptoms were defined as cough, fatigue, gastrointestinal symptoms (nausea, vomiting, and/or diarrhea), headache, anosmia, ageusia, rhinorrhea, sore throat, or nasopharyngeal congestion. Moderate symptoms were defined as the presence of COVID toes/fingers, chills, fever, or myalgias. Cardiopulmonary symptoms were defined as chest pain, shortness of breath, palpitations, or exercise intolerance. If an athlete had symptoms in multiple categories, they were assigned the most severe category based on their symptoms. ECGs were deemed normal or abnormal using the International Criteria for ECG interpretation in athletes.[15] Abnormal ECGs, TTE, and CMR reports were adjudicated as related

to SARS-CoV-2 infection or unrelated to SARS-CoV-2 infection using pre-specified definitions (**Supplemental Table I**). A troponin measurement was considered abnormal if it was >99% upper limits of normal per the local laboratory commercial assay standards. 'Borderline' abnormal triad testing was defined as any cardiac test that was considered abnormal by the local institution and led to CMR testing, but did not meet pre-specified study definitions after adjudication (**Supplemental Table I**). These included: 1) Detectable troponin level but not above the 99th percentile; 2) Non-specific ECG abnormalities not fulfilling the International Criteria; 3) TTE findings including abnormalities of unclear significance or those at the upper or lower limit of the normal range and felt to potentially represent pathology (i.e. left ventricular ejection fraction [LVEF] of 50%).

Study definitions were derived for both myocardial and pericardial involvement with imaging components adapted from the Updated Lake Louise imaging criteria (**Supplemental Table I**).[16] *Definite* myocardial involvement was defined as: 1) CMR T1 abnormality or presence of late gadolinium enhancement (LGE) + T2 abnormality, 2) CMR T2 abnormality + one or more supportive findings (LVEF <45%, small or greater pericardial effusion, pericardial enhancement, or troponin >99% upper limit of normal). *Probable* myocardial involvement was defined as: 1) CMR T1 abnormality or presence of LGE + one or more supportive finding (same as definite myocardial involvement). *Possible* myocardial involvement was defined as: 1) isolated CMR T1 abnormality or presence of LGE. SARS-CoV-2 pericardial involvement was defined as a small or greater pericardial effusion or pericardial enhancement on CMR. Any athlete meeting criteria for myocardial involvement of SARS-CoV-2 infection who also had pericardial involvement was labeled as definite, probable, or possible myopericardial involvement based on the definitions for myocardial involvement.

Outcomes for this study included adverse cardiovascular events (new clinically significant arrhythmias, clinical heart failure, or sudden cardiac arrest or death) or hospitalizations related to SARS-CoV-2. Follow-up time was defined as the date of symptom onset or date of positive SARS-CoV-2 test if asymptomatic (or if symptoms were not reported) to the date of last cardiovascular outcomes update from each institution.

Statistical Analysis

Patient characteristics, SARS-CoV-2 symptomology, and cardiac testing results were described using basic descriptive methods including frequency distributions, means and standard deviations (SD), and medians and interquartile ranges (IQR). 95% confidence intervals (CI) for all prevalence estimates were calculated via the exact binomial distribution. Due to the small number of observed SARS-CoV-2 cardiac cases and the known small sample bias with maximum likelihood estimation, the firth penalized logistic regression method was used to assess unadjusted associations with definite, probable and possible SARS-CoV-2 related cardiac involvement. A multivariable firth logistic regression model using backwards variable selection was built to identify independent predictors of SARS-CoV-2 myocardial/pericardial involvement. The final model was determined based on goodness of fit using the Akaike Information Criteria. Odds Ratios (OR) and 95% CIs are reported. Secondary analyses modeling only definite and probable SARS-CoV-2 related cardiac involvement were also conducted using the same approach. Statistical analyses were performed using SAS (Version 9.4, SAS Institutes, Cary, NC SAS Institutes, Cary, NC) and R: A Language and Environment for Statistical Computing (R Core Team, Vienna, Austria, year 2020, https://www.R-project.org/).

Results

Study Population

Among 19,378 athletes enrolled during the study period, 3384 (17.5%) tested positive for SARS-CoV-2 infection and 3018 (15.6%) met study inclusion criteria (**Supplemental Figure I**). Baseline characteristics for the cohort and for the subgroup with SARS-CoV-2 cardiac involvement are presented in **Table 1**. The cohort, comprised of athletes from 42 colleges/universities, includes representation from 26 distinct sporting disciplines including American-style football (36%), baseball (9%), cross country/track and field (8%), lacrosse (6%), and basketball (6%) (**Supplemental Table II**). The majority of athletes were asymptomatic (33%) or had mild symptom burden (29%), most commonly accounted for by loss of taste or smell (40%), headache (39%), and sore throat (31%) during the acute phase of SARS-CoV-2 infection (**Figure 1**). Cardiopulmonary symptoms (chest pain, shortness of breath, palpitations, or exercise intolerance) during the acute illness or upon return to exercise were reported by 13% of athletes. The most commonly employed cardiovascular testing protocol was triad testing (74%) **(Table 1)**. A total of 198 athletes underwent CMR performed as part of the primary cardiovascular screening protocol irrespective of symptom burden or the results of other testing and 119 underwent CMR for clinical indications (**Supplemental Table III**). The time from initial diagnosis of SARS-CoV-2 infection to the completion of each component of cardiac triad testing and CMR is shown in **Figure 2**. Abnormal triad testing possibly related to SARS-CoV-2 cardiac involvement were detected by TTE (24/2556, 0.9%), 12-lead ECG (21/2999, 0.7%), and cardiac troponin testing (24/2719, 0.9%), including 5 athletes tested with high-sensitivity troponin-I and the other 19 athletes tested with conventional troponin-I or troponin-T assays. Of athletes with abnormal triad testing possibly related to SARS-CoV-2, 65 athletes had a single

abnormal triad test, 2 athletes had two abnormal triad tests (12-lead ECG and TTE), and no athlete had abnormalities on all 3 triad tests.

Cardiac Involvement following SARS-CoV-2 Infection

A total of 21 athletes (0.7% [95% CI:0.4,1.1]) had definite, probable, or possible SARS-CoV-2 cardiac involvement (**Table 2**). This included 6/198 (3.0% [95% CI:1.1,6.5]) athletes identified by primary screening CMR of which 3 (1.5% [95% CI:0.3,4.4]) had definite or probable cardiac involvement (**Figure 3A)** and 15/2820 (0.5% [95% CI:0.3,0.9]) athletes identified by either one or more elements of cardiac triad testing, or moderate or greater symptoms, followed by clinically indicated CMR of which 12 (0.4% [95% CI:0.2,0.7]) had definite or probable cardiac involvement (**Figure 3B**). For athletes in the clinically indicated CMR cohort with at least one abnormal triad test (n=34), 6 (17.7% [95% CI:6.8, 34.5]) had definite or probable cardiac involvement.

In the overall cohort, 137/3018 athletes (4.5% [95% CI: 3.8, 5.3]) who underwent any form of cardiac screening had abnormal testing (**Figure 4**). Eighty-one (2.7% [95% CI:2.1,3.3]) had abnormal cardiac testing possibly related to SARS-CoV-2 infection and 56 (1.9% [95% CI:1.4,2.4]) had cardiac abnormalities unrelated to SARS-CoV-2 infection (a combination of known and new cardiac findings). Among athletes with one or more abnormal triad test potentially related to SARS-CoV-2 (n=67), 37 underwent CMR while the remaining 30 were ultimately deemed to have isolated testing abnormalities unrelated to SAR-CoV-2 (**Supplemental Table IV**). Of the 37 athletes who underwent CMR for an abnormal triad test, only 2 (5.4%) had multiple abnormal tests (**Figure 4**). Fourteen athletes had normal triad testing but were found to have CMR abnormalities potentially related to SARS-CoV-2.

Predictors of SARS-CoV-2 Cardiac Involvement

Significant univariable predictors of definite, probable, or possible cardiac involvement included White-Hispanic race (OR:7.6, 95% CI:2.2,26.1), basketball participation (OR:5.1, 95% CI:1.8,14.5), cardiopulmonary symptoms during acute infection or on resumption of exercise (OR:4.2, 95% CI:1.4,12.4), and one or more abnormal triad test (OR:48.2, 95% CI:18.5,125.6) potentially related to SARS-CoV-2 infection (**Supplemental Table V**). On multivariable analysis, after adjusting for sex and race, cardiopulmonary symptoms (OR:3.1, 95% CI:1.2,7.8) and any abnormal triad test (OR:37.4, 95% CI:13.3,105.3) were predictive of cardiac involvement (**Supplemental Table VI**).

Clinical Outcomes

No adverse cardiac events (median follow-up period=130 [IQR 97,160] days) were reported in athletes with definite, probable, or possible SARS-CoV-2 cardiac involvement (n=21). Among the entire cohort of SARS-CoV-2 positive athletes (n=3018, median follow-up period=113 [IQR 90,146] days), we observed one adverse cardiac event (successfully resuscitated sudden cardiac arrest). This athlete underwent CMR 17 days following SARS-CoV-2 infection symptom onset without findings suggestive of acute cardiac involvement rendering the etiology of this event uncertain and likely unrelated to SARS-CoV-2. Ten athletes were either hospitalized (n=5) or treated in the emergency department (n=5) for non-cardiac complications of SARS-CoV-2 infection. Non-cardiac SARS-CoV-2 complications included submassive pulmonary embolism (n=1), symptomatic large pleural effusion (n=1), and palmar desquamation secondary to mild multisystem inflammatory syndrome (n=1).

Discussion

We report data characterizing collegiate athletes undergoing cardiovascular evaluation after SARS-CoV-2 infection with the following key findings. First, cardiac evaluation conducted in accordance with current recommendations[5, 7], which suggest risk stratification based on SARS-CoV-2 symptom burden to determine the role of triad testing and CMR, had a diagnostic yield for definite, probable, or possible cardiac involvement of 0.5% (95% CI:0.3,0.9). Second, the prevalence of definite, probable or possible SARS-CoV-2 cardiac involvement, derived from the first multicenter cohort of competitive athletes undergoing screening CMR was 3.0% (95% CI:1.1,6.5). Our data suggest these represent the lower and upper estimates (0.5-3.0%) of cardiac involvement following SARS-CoV-2 in young otherwise healthy individuals. Third, clinical predictors of SARS-CoV-2 cardiac involvement include cardiopulmonary symptoms during acute infection or upon return to exercise and any abnormality on triad testing suggestive of SARS-CoV-2 cardiac involvement. In this cohort, a step-wise approach that used the presence of moderate severity or cardiopulmonary symptoms or any abnormal triad test to trigger a diagnostic CMR would have identified 9 of 11 (81.8%) athletes diagnosed with definite or probable myocardial or myopericardial involvement. Finally, no athlete diagnosed with definite, probable, or possible cardiac involvement had an adverse cardiac event through the available follow-up period.

The prevalence and clinical implications of cardiac sequalae following SARS-CoV-2 infection among people not requiring hospitalization have yet to be determined. Defining disease prevalence is of paramount importance to understand diagnostic testing performance and inform recommendations for population-based screening. Among a German cohort recovering from SARS-CoV-2 (mean age 49 years, 33% hospitalized for symptoms of SARS-CoV-2), 78% were

reported to have cardiac involvement as defined by abnormalities on CMR.[9] Recent single center cross-sectional studies of collegiate athletes undergoing screening CMR following SARS-CoV-2 infection have documented highly variable prevalence estimates of cardiac involvement ranging from 1.4 to 56%.[10-13] The basis for this heterogeneity is multifactorial with contributions from variable study designs, limited sample sizes, and inconsistent definitions of cardiac involvement. Findings from the present study, leveraging multicenter CMR data and the use of strict and conservative definitions that adhere to contemporary clinical imaging criteria, suggest that SARS-CoV-2 cardiac involvement among collegiate athletes is less common than previously reported. This finding is similar to the prevalence rate of cardiac involvement recently reported among professional athletes (0.6%) who were assessed using triad testing followed by clinically indicated CMR.[14]

CMR has emerged as the non-invasive reference standard for confirming myocarditis among patients with disease specific symptoms or other cardiac testing suggestive of this diagnosis. Numerous factors including the paucity of normative CMR data in athletes, interreader interpretation variability, financial cost, and access to testing underlie uncertainties about the use of CMR as a primary screening tool. Our data highlight important tradeoffs pertaining to use of CMR as a screening modality versus its use to confirm cardiac involvement. Among athletes undergoing clinically indicated CMR based on symptom burden or an abnormal triad test (n=119), 12.6% (95% CI:7.2,17.9) were diagnosed with definite, probable, or possible cardiac involvement. This diagnostic yield was four-fold higher than that observed when CMR was used as part of primary screening protocol (6/198, 3.0% [95% CI:1.1,6.5]). However, 3/6 of athletes with definite, probable, or possible cardiac involvement undergoing screening CMR were asymptomatic or had mild symptoms and normal triad testing. Additionally, CMR detected

isolated late gadolinium enhancement or abnormal T1 data, age indeterminant markers of myocardial fibrosis or abnormal tissue architecture, in a small number of athletes with no other features suggestive of acute SARS-CoV-2 cardiac involvement. While we strongly suspect that these findings were unrelated to recent SARS-CoV-2 infection, we categorized these findings as "possible cardiac involvement" underscoring the need to better understand their prevalence and clinical significance among young competitive athletes. In aggregate, these issues illustrate the inherent tradeoff between a CMR-inclusive screening protocol that may enhance sensitivity and a clinically-driven approach that maximizes specificity.

Autopsy series have established myocarditis as an important cause of sudden death during exercise.[2-4] Prior to the SARS-CoV-2 pandemic, myocarditis was routinely diagnosed among patients presenting with post-viral cardiovascular symptoms, malignant arrhythmias, or myocardial dysfunction. Diagnostic CMR imaging criteria and sport eligibility recommendations were developed based on considerable experience with this clinical presentation.[16-18] It remains unclear whether isolated cardiac abnormalities detected through CMR-based screening harbor a risk similar to typical clinically diagnosed myocarditis and how often these findings occur in other viral infections. Our SARS-CoV-2 cardiac involvement prevalence estimate is similar to documented prevalence rates of myocarditis following influenza infection.[19] Although many collegiate athletes in this cohort did not undergo CMR as part of their return to play screening algorithm, we observed no adverse cardiac events in this group. While longer follow-up is of critical importance, our data suggest that the potential for subclinical cardiac involvement characterized by isolated CMR abnormalities is of low short-term clinical risk.

There are several limitations of this study. First, we acknowledge that screening protocol heterogeneity across participating institutions may have impacted our estimates of prevalence

and diagnostic yield. Nonetheless, this study examines the largest number of athletes who have undergone some form of cardiac testing following SARS-CoV-2 infection (n=3018) and the largest multicenter CMR-inclusive screening cohort (n=198) of competitive athletes to date. Second, diagnostic testing results reported for both TTE and CMR were extracted from the primary clinical reports provided by participating institutions. While this approach captures the actual clinical experience of our cohort, the unblinded clinical interpretation of the testing may have resulted in a degree of observer bias on the part of the interpreting physician. Unbiased imaging adjudication by a centralized core facility represents an important area of future work. Third, we acknowledge that there is currently no uniformly accepted definition of cardiac involvement attributable to SARS-CoV-2 infection. We therefore used fundamental components of the Updated Lake Louise Imaging Criteria[16] to generate de novo definitions of possible, probable, and definite cardiac involvement and presented full clinical profiles of athletes meeting these criteria. Future work is warranted to validate this approach. Finally, we acknowledge the relatively short duration of our clinical follow-up and underscore the need for on-going clinical surveillance of this cohort. However, the median 113 [IQR=90,146] days follow-up captured coincides with the period of highest risk of adverse events during exercise following acute myocardial injury.

Implications for 'Return-to-Play' SARS-CoV-2 Cardiac Testing

Findings from this study provide an opportunity to assess and refine consensus recommendations for pre-participation cardiac screening of athletes following SARS-CoV-2 infection[5, 7]. Given the low prevalence of cardiac involvement and the absence of adverse events during short term clinical surveillance related to SARS-CoV-2 infection among both collegiate and professional athletes[14], we propose the following considerations regarding future return-to-play cardiac

testing following SARS-CoV-2 infection. First, our data support that athletes with asymptomatic or mild symptom burden from acute SARS-CoV-2 infection do not require additional cardiac testing prior to resumption of organized athletics. Second, 'triad' testing in the form of a 12-lead ECG, cardiac troponin, and TTE should be considered among athletes following acute SARS-CoV-2 infection who experience moderate systemic and/or cardiopulmonary symptoms, with the presence of cardiopulmonary symptoms representing a particularly important marker of risk. Finally, our data suggest that the diagnostic yield of CMR will be optimized by confining its use to athletes presenting with increased clinical pretest probability of acquired myocardial pathology as defined by the presence of SARS-CoV-2-related cardiopulmonary symptoms and/or abnormalities on triad testing. These recommendations are generally consistent with the most recent return-to-play cardiac testing guidelines.

Conclusion

In a large prospective registry of collegiate athletes, SARS-COV-2 infection occurred in 17.5% of athletes. Clinical evaluation revealed a low prevalence (0.5-3.0%) of definite, probable, or possible SARS-CoV-2 cardiac involvement and a low risk of adverse cardiac events during short term follow-up. The clinical relevance of cardiac testing abnormalities following SARS-CoV-2 infection among athletes without other clinical features of myocardial involvement requires additional study. Future studies with extended clinical follow up and appropriate control populations including athletes without SARS-COV-2 infection are needed to better inform risk and the refinement of evidence-based screening strategies.

Acknowledgments

Special thanks to the collaborators for the ORCCA registry.

Sources of Funding

This work was funded in part by a grant from the American Medical Society for Sports Medicine (AMSSM) Foundation and AMSSM Collaborative Research Network (CRN).

Dr. Moulson is supported by the University of British Columbia Clinician Investigator Program

Disclosures

Dr. Patel Advisory Board: Amgen, Bayer, Janssen, Heartflow, Medscape: Grant funding: NHLBI, Bayer, Janssen, Heartflow, Idorsia. Dr. Patel's research is also supported by the Joel Cournette Foundation for research on athlete's hearts.

Dr. Baggish has received funding from the National Institute of Health/ National Heart, Lung, and Blood Institute, the National Football Players Association, and the American Heart Association and receives compensation for his role as team cardiologist from the US Olympic Committee / US Olympic Training Centers, US Soccer, US Rowing, the New England Patriots, the Boston Bruins, the New England Revolution, and Harvard University.

Supplemental Materials

Members of the ORCCA Study Group

Methods Supplement

Supplemental Figure Legends

Supplemental Figure I

Supplemental Tables I-VI

References 10, 15, 16

Appendix:

Members of the ORCCA Study Group:

Steering Committee:

Irfan M. Asif, MD, Aaron L. Baggish, MD, James Borchers, MD, Jonathan A. Drezner, MD, Katherine M. Edenfield, MD, Michael S. Emery, MD, MS, Kyle Goerl, MD, Brian Hainline, MD, Kimberly G. Harmon, MD, Jonathan H. Kim, MD, MSc, Stephanie Kliethermes, PhD, William E. Kraus, MD, Rachel Lampert, MD, Matthew Leiszler, MD, Benjamin D. Levine, MD, Matthew W. Martinez, MD, Nathaniel Moulson, MD, Francis G. O'Connor, MD, MPH, Manesh R. Patel, MD, Bradley J. Petek, MD, Dermot Phelan, MD, Lawrence D Rink, MD, Herman A Taylor, MD, MPH.

Investigators:

Carl Ade, PhD, Aryan Aiyer, MD, Jarrah Alfadhli, MD, Chloe Amaradio, Scott Anderson, ATC, Stephanie Arlis-Mayor, MD, Jonathan S. Aubry, MD, Andrea Austin, MSN, RN, Timothy Beaver, MD, Nicolas Benitez, Brant Berkstresser, Thomas M. Best, MD, PhD, Tiffany Bohon, MD, Jonathan P. Bonnet, MD, MPH, Elizabeth Boyington, James Bray, MD, Jenna Bryant, MD, Sean Carnahan, DO, Rachel Chamberlain, MD, Samantha Charters, ATC, Timothy W. Churchill, MD, Douglas Comeau, DO, Laura E Cook, MD, Deanna Corey, MD, Amy Costa, MD, Marshall Crowther, MD, Tarun Dalia, MD, Craig Davidson, MD, Kaitlin Davitt, MS, ATC, Annabelle De St. Maurice, MD, MPH, Peter N. Dean, MD, Katelyn DeZenzo, Courtney

Dimitris, Jeanne Doperak, DO, Calvin Duffaut, MD, Craig Fafara, Katherine Fahy, MD, Jason Ferderber, MD, Megan Finn, Angelo Galante, MD, Todd Gerlt, ATC, Amy Gest, MPA, Carla Gilson, ATC, Jeffrey Goldberger, MD, Joshua Goldman, MD, MBA, Erich Groezinger, MS, Jonathan R. Guin, MD, Heather Halseth, Joshua Hare, MD, Beth Harness, ATC, Nicolas Hatamiya, DO, Julie Haylett, RN, MSN, Neal Hazen, MBA, PT, ATC, LAT, Yeun Hiroi, BS, Amy Hockenbrock, MD, Amanda Honsvall, MD, Jennifer Hopp, MD, Julia Howard, ATC, Samantha Huba, Mustafa Husaini, MD, Lindsay Huston, MD, Calvin Hwang, MD, Laura Irvin, DO, Val Gene Iven, MD, Robert Jones, MD, Donald Joyce, MD, Kristine Karlson, MD, Christian Klein, MD, Chris Klenck, MD, Michele Kirk, MD, Jordan Knight, Laura Knippa, RN, Madeleine Knutson, ATC, Louis E. Kovacs, MD, Yumi Kuscher, Andrea Kussman, MD, Chrissy Landreth, Amy Leu, DO, Dylan Lothian, Maureen Lowery, MD, Andrew Lukjanczuk, MS, ATC, LAT, John M. MacKnight, MD, Lawrence M. Magee, MD, Marja-Liisa Magnuson, DO, MS, Aaron V. Mares, MD, Anne Marquez, Grant McKinley, MD, Megan Meier, MD, Christopher Miles, MD, Emily Miller, MD, Hannah Miller, MSEd, ATC, LAT, Raul Mitrani, MD, Robert J Myerburg, MD, Greg Mytyk, ATC, Andrew Narver, DO, Aurelia Nattiv, MD, Laika Nur, MD, Brooke E. Organ, MD, Meredith Pendergast, ATC, Frank A. Pettrone, MD, Sourav K. Poddar, MD, Diana Priestman, Ian Quinn, DO, Fred Reifsteck, MD, Morgan Restivo, James B. Robinson, MD, Ryan Roe, PAC, Thomas Rosamond, MD, Carrie Rubertino Shearer, Miguel Rueda, Takamasa Sakamoto, MEd, ATC, Brock Schnebel, MD, Ankit B. Shah, MD, MPH, Alan Shahtaji, DO, Kevin Shannon, MD, Polly Sheridan-Young, PA-C, Siobhan M. Statuta, MD, Mark Stovak, MD, Andrei Tarsici, Kenneth S. Taylor, MD, Kim Terrell, Matt Thomason, ATC, Jason Tso, MD, Daniel Vigil, MD, Francis Wang, MD, Jennifer Winningham, MS, ATC, LAT, Susanna T. Zorn, MD.

References

1. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, Jain SS, Burkhoff D, Kumaraiah D, Rabbani L, et al. COVID-19 and Cardiovascular Disease. *Circulation*. 2020;141:1648-1655.
2. Eckart RE, Scoville SL, Campbell CL, Shry EA, Stajduhar KC, Potter RN, Pearse LA and Virmani R. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Annals of internal medicine*. 2004;141:829-834.
3. Harmon KG, Asif IM, Maleszewski JJ, Owens DS, Prutkin JM, Salerno JC, Zigman ML, Ellenbogen R, Rao AL, Ackerman MJ, et al. Incidence, Cause, and Comparative Frequency of Sudden Cardiac Death in National Collegiate Athletic Association Athletes: A Decade in Review. *Circulation*. 2015;132:10-19.
4. Peterson DF, Kucera K, Thomas LC, Maleszewski J, Siebert D, Lopez-Anderson M, Zigman M, Schattenkerk J, Harmon KG and Drezner JA. Aetiology and incidence of sudden cardiac arrest and death in young competitive athletes in the USA: a 4-year prospective study. *Br J Sports Med*. 2020. doi: 10.1136/bjsports-2020-102666.
5. American Medical Society for Sports Medicine and the American College of Cardiology. Cardiac Considerations for College Student-Athletes during the COVID-19 Pandemic. 2020. https://www.amssm.org/Content/pdf-files/COVID19/NCAA-COVID-19-Algorithm-12-AUG-2020.pdf.
6. Baggish A, Drezner JA, Kim J, Martinez M and Prutkin JM. Resurgence of sport in the wake of COVID-19: cardiac considerations in competitive athletes. *British journal of sports medicine*. 2020;54:1130-1131.
7. Kim JH, Levine BD, Phelan D, Emery MS, Martinez MW, Chung EH, Thompson PD and Baggish AL. Coronavirus Disease 2019 and the Athletic Heart: Emerging Perspectives on Pathology, Risks, and Return to Play. *JAMA Cardiol*. 2021;6:219-227.
8. Phelan D, Kim JH and Chung EH. A Game Plan for the Resumption of Sport and Exercise After Coronavirus Disease 2019 (COVID-19) Infection. *JAMA Cardiology*. 2020;5:1085-1086.
9. Puntmann VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, Shchendrygina A, Escher F, Vasa-Nicotera M, Zeiher AM, et al. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). *JAMA Cardiology*. 2020;5:1265-1273.
10. Brito D, Meester S, Yanamala N, Patel HB, Balcik BJ, Casaclang-Verzosa G, Seetharam K, Riveros D, Beto RJ, Balla S, et al. High Prevalence of Pericardial Involvement in College Student Athletes Recovering From COVID-19. *JACC Cardiovasc Imaging*. 2021;14:541-555.
11. Clark DE, Parikh A, Dendy JM, Diamond AB, George-Durrett K, Fish FA, Slaughter JC, Fitch W, Hughes SG and Soslow JH. COVID-19 Myocardial Pathology Evaluation in AthleTEs with Cardiac Magnetic Resonance (COMPETE CMR). *Circulation*. 2021;143:609-612.
12. Rajpal S, Tong MS, Borchers J, Zareba KM, Obarski TP, Simonetti OP and Daniels CJ. Cardiovascular Magnetic Resonance Findings in Competitive Athletes Recovering From COVID-19 Infection. *JAMA Cardiology*. 2021;6:116-118.
13. Starekova J, Bluemke DA, Bradham WS, Eckhardt LL, Grist TM, Kusmirek JE, Purtell CS, Schiebler ML and Reeder SB. Evaluation for Myocarditis in Competitive Student Athletes Recovering From Coronavirus Disease 2019 With Cardiac Magnetic Resonance Imaging. *JAMA Cardiology*. 2021. doi:10.1001/jamacardio.2020.7444.

14. Martinez MW, Tucker AM, Bloom OJ, Green G, DiFiori JP, Solomon G, Phelan D, Kim JH, Meeuwisse W, Sills AK, et al. Prevalence of Inflammatory Heart Disease Among Professional Athletes With Prior COVID-19 Infection Who Received Systematic Return-to-Play Cardiac Screening. *JAMA Cardiol*. 2021. doi:10.1001/jamacardio.2021.0565.
15. Drezner JA, Sharma S, Baggish A, Papadakis M, Wilson MG, Prutkin JM, Gerche A, Ackerman MJ, Borjesson M, Salerno JC, et al. International criteria for electrocardiographic interpretation in athletes: Consensus statement. *Br J Sports Med*. 2017;51:704-731.
16. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, Kindermann I, Gutberlet M, Cooper LT, Liu P, et al. Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation: Expert Recommendations. *J Am Coll Cardiol*. 2018;72:3158-3176.
17. Maron BJ, Zipes DP and Kovacs RJ. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Preamble, Principles, and General Considerations: A Scientific Statement From the American Heart Association and American College of Cardiology. *J Am Coll Cardiol*. 2015;66:2343-2349.
18. Pelliccia A, Sharma S, Gati S, Back M, Borjesson M, Caselli S, Collet JP, Corrado D, Drezner JA, Halle M, et al. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *European heart journal*. 2021;42:17-96.
19. Datta R, Helou E, Tucker M, John B, Martinello RA and Malinis M. Detection of influenza myocarditis using national healthcare safety network surveillance definitions accounting for fever in older adults. *Infect Control Hosp Epidemiol*. 2018;39:1145-1147.

Table 1. Patient Characteristics for the Total Cohort and for Athletes with Definite, Probable, or Possible Myocardial and/or Pericardial SARS-CoV-2 Involvement

Patient Characteristics*	**Total Cohort (n=3018)**	**Myocardial/ Pericardial SARS-CoV-2 involvement (n=21)**
Female	957 (32)	10 (48)
Age, mean (SD)	20 (1)	20 (2)
BMI, male, mean (SD)	27 (5)	25 (2)
BMI, female, mean (SD)	23 (3)	25 (5)
White- Non-Hispanic	1922 (64)	10 (48)
Black	829 (27)	8 (38)
White-Hispanic	87 (3)	3 (14)
Mixed	62 (2)	0
Other[†]	80 (3)	0
Pre-Existing Conditions*		
Sickle Cell Trait	31 (1)	1 (5)
Diabetes	10 (0.4)	1 (5)
Hypertension	10 (0.4)	0
Hyperlipidemia	7 (0.3)	1 (5)
Asthma (Mild- intermittent)	154 (6)	0
Asthma (Mild-persistent or greater)	68 (2)	0
Immunosuppressive agent	5 (0.2)	0
Structural/Valvular Cardiac Disease	18 (0.6)	0
Electrical Cardiac Disease	14 (0.5)	0
Symptom Categories*		
Asymptomatic	887 (33)	5 (24)
Mild	789 (29)	4 (19)
Moderate	663 (25)	4 (19)
Cardiopulmonary	337 (13)	8 (38)
SARS-CoV-2 Positive Test		
PCR	2465 (82)	18 (86)
Antibody	263 (9)	2 (10)
Antigen	234 (8)	1 (5)
Unknown	56 (2)	0
Cardiovascular Testing Performed		
ECG + Troponin + TTE	2231 (74)	0
ECG + Troponin + TTE + CMR	188 (6)	18 (86)
ECG only	172 (6)	0
ECG + Troponin	159 (5)	0
ECG + Troponin + CMR	124 (4)	3 (14)
ECG + TTE	121 (4)	0
Other[‡]	23 (0.8)	0

Presented as n (%) unless noted otherwise.

Definition of abbreviations: BMI= body mass index, CMR = cardiac magnetic resonance imaging, ECG= electrocardiogram, PCR= polymerase chain reaction, TTE= transthoracic echocardiography

*Partial data for available for the following characteristics: age n=3006 (Total Cohort), sex n=3017 (Total Cohort), BMI n=2621 (Total Cohort) and n=20 (Myocardial/Pericardial SARS-CoV-2 involvement), race

n=2980 (Total Cohort), Pre-existing conditions n=2800 (Total cohort), Symptom Categories n=2676 (Total Cohort)

†Other category includes Asian, American-Indian, Native Hawaiian, Pacific Islander and self-selected other

‡Includes other combinations not listed above

Table 2. Clinical Characteristics and Cardiac Evaluations for Athletes with Myocardial and/or Pericardial Involvement from SARS-CoV-2 as Adjudicated by Cardiac Magnetic Resonance Imaging

Athlete No.	Sex	Race	Past Medical History	**Symptom Severity/Duration** - Initial Symptoms - Exertional Symptoms (SARS-CoV-2 Test)	ECG	Troponin (ng/ml)	TTE	CMR	Time from symptoms to CMR*	Certainty of Involvement
Athletes with Isolated Myocardial Involvement from SARS-CoV-2 (n=11)										
1	M	White	None	**Moderate/"few days"** - Headache, myalgias -Not applicable (Antibody)	Normal	Troponin I <0.01	LVEF 60-65%, no WMAs, no pericardio efusión	LVEF 58% **T1= LGE at the inferior (basal) segment** **T2= increased signal consistent with mild myocardial edema** No pericardial effusion	39 days	**Definite**
2	M	Black	None	**Mild/5 days** - Congestion, cough, loss of taste/smell, sore throat -Not applicable (PCR)	Normal	Troponin T < 0.01	**Abnormal** **LVEF 45-50%**, no WMAs, no pericardial effusion	**LVEF 41%** T1= LGE could not be assessed due to allergy **T2= global hyperintensity of the LV myocardium c/w edema** No pericardial effusion	42 days	**Definite**
3	M	Black	T1DM	Asymptomatic -Not applicable (PCR)	Normal	**Abnormal** **hsTroponin 20**	Not Performed	LVEF 57% T1= No LGE **T2= Increased signal in LV myocardium consistent with edema** No pericardial effusion	34 days	**Definite**
4	F	Hispanic/ Latino	None	**Mild/2 days** - Loss of taste/smell, sore throat -Unknown (PCR)	**Abnormal** LAE, RAE	Troponin I <0.01	LVEF 60%, no WMAs, no pericardial effusion	LVEF 50% **T1= abnormal mapping and LGE in inferior (basal, mid), inferolateral (basal), anterolateral (mid) segments** **T2= abnormal mapping in basal inferior segment** No comment on effusion	72 days	**Definite**
5	M	Black	None	Asymptomatic -None (PCR)	Normal	Troponin-T <0.01	LVEF 50%, no WMAs, no pericardial effusion	**LVEF 42%,** **T1= increased T1 mapping, no LGE** **T2= increased T2 mapping** Trace pericardial effusion	38 days	**Definite**
6	M	Black	None	**Cardiopulm/9 days** - Chills, congestion, fevers, loss of taste/smell, myalgias, sore throat - Exertional CP, DOE (PCR)	Normal	Troponin I <0.03	LVEF 53%, no WMAs, no pericardial effusion	LVEF 56% T1= normal T1 mapping. **LGE of the inferolateral (apical) segment** T2= normal T2 mapping without edema No comment on effusion	29 days	**Possible**

7	M	White	ADHD	Asymptomatic -None (Antibody)	**Abnormal** RAE, LAE	Troponin I <0.01	LVEF 60-65%, no WMAs, no pericardial effusion	LVEF 61%, **T1= LGE at inferior (basal), inferolateral (basal), inferoseptal (basal) segments** T2= no myocardial edema No pericardial effusion	36 days	**Possible**
8	M	Black	ADHD, Anxiety	**Mild/1 day** -Headache, sore throat -Exertional CP (PCR)	Normal	Troponin I <0.01	LVEF 60%, no WMAs, no pericardial effusion	LVEF 55% **T1= abnormal T1 with LGE in inferior (basal), inferolateral (basal) segments** T2= normal mapping Trivial pericardial effusion	68 days	**Possible**
9	F	Black	None	**Mild/3 days** - Loss of taste/smell -None (PCR)	Normal	Troponin I <0.01	LVEF 55%, no WMAs, no pericardial effusion	LVEF 54% **T1= abnormal ECV fractions mid segment, no LGE but myocardium appearance of "inhomogenous null"** T2= normal mapping No comment on effusion	74 days	**Possible**
10	M	Black	Sickle Cell Trait	**Cardiopulm/2 days** - Fever, vomiting, SOB - DOE (PCR)	Normal	Troponin-I <0.017	LVEF 50%, no WMAs, no pericardial effusion	LVEF 50% T1= mapping normal. **LGE present in inferior (mid), inferolateral (mid) segments** T2= mapping normal but degraded by motion artifact No comment on effusion	84 days	**Possible**
11	M	White	None	**Cardiopulm/5 days** Fever, headache, congestion, "lung pain" -None (PCR)	Normal	Troponin I <0.01	LVEF 65%, no WMAs, no pericardial effusion	LVEF 59% **T1= abnormal ECV fractions, LGE present in inferolateral (basal), inferior (basal) segments** T2= normal mapping Trivial pericardial effusion	56 days	**Possible**
Athletes Diagnosed with Myopericardial Involvement of SARS-CoV-2 (n=6)										
12	F	Hispanic	None	**Cardiopulm/14-20 days** - Cough, fever, SOB -Not applicable (PCR)	Normal	Troponin <0.01	**Abnormal** Stress TTE-exercise-induced WMA basal -mid inferior wall, small pericardial effusion	LVEF 54% **T1= Increase of native T1.** No LGE. **T2= Increase of T2 mapping** **Small pericardial effusion**	Unknown	**Definite**
13	F	White	N/A	**Cardiopulm/9 days** - Chest pain, loss of taste/smell, myalgias - Exertional CP (PCR)	**Abnormal** Prolonged QTc (481ms)	Troponin I <0.01	LVEF 65%, no WMAs, no pericardial effusion	**LVEF 45%** **T1= LGE in the inferior (mid) segment** **T2= associated edema present in this segment on FIESTA imaging** **Small pericardial effusion**	123 days	**Definite**

14	F	White	Pre-HTN, HLD	**Moderate/2-3 days** - Headache, loss of taste/smell, myalgias, pink eye -Not applicable (PCR)	Normal	Troponin T < 0.01	LVEF 60%, no WMAs, trivial pericardial effusion	LVEF 62.5% **T1= abnormal T1 mapping with LGE in anteroseptal (basal), inferior (basal), inferolateral (basal) segments** T2= no comment on T2 mapping **Small pericardial effusion**	18 days	**Probable**
15	M	Black	None	**Moderate/3-4 days** - Headache, myalgias -Not applicable (PCR)	**Abnormal** Black athlete repol pattern, TWI V5-V6, RAE	hsTroponin <6	Not Performed	LVEF 60% T1= normal mapping. **LGE of the anterolateral (mid, apical) segments.** T2= normal/no evidence of edema **Small pericardial effusion**	31 days	**Probable**
16	F	White	None	Asymptomatic -None (PCR)	Normal	Troponin I <0.01	LVEF 60%, no WMAs, trivial pericardial effusion	LVEF 55% **T1= abnormal ECV fractions in LGE areas of inferior (basal, mid), inferoseptal (basal), inferolateral (basal) segments** T2= mapping upper limits of normal **Small pericardial effusion**	41 days	**Probable**
17	F	White	None	**Moderate/2 days** Chills, fever, headache, loss of taste/smell, myalgias -None (PCR)	Normal	Troponin-I <0.03	LVEF 60-65%, no WMAs, trivial pericardial effusion	LVEF 58%, T1= mapping normal. **LGE present in inferolateral (mid) and anterolateral (mid) segments** T2= mapping normal **Small pericardial effusion**	22 days	**Probable**
Athletes Diagnosed with Isolated Acute Pericardial Involvement of SARS-CoV-2 (n=4)										
18	M	White	None	**Mild/4-7 days** Headache, loss of taste/smell -None (PCR)	Normal	hsTroponin I <6	**Abnormal** LVEF not reported WMA not reported small pericardial effusion	LVEF "normal" No myocardial inflammation, fibrosis, or edema present. **Medium-sized pericardial effusion**	20 days	**Definite**
19	F	White	None	**Cardiopulm/4-7 days** - Nasal congestion, fatigue, sore throat, myalgias - Exertional CP, DOE (PCR)	Normal	Troponin <0.01	LVEF 60-65%, no WMAs, no pericardial effusion	LVEF 65%, T1= no LGE present T2= normal mapping without edema **Small pericardial effusion**	71 days	**Definite**

20	F	Hispanic	None	Asymptomatic -None (PCR)	Normal	hsTroponin 21	Not Performed	LVEF 67%, T1= normal mapping. No LGE present. T2= normal mapping. **Small pericardial effusion**	26 days	**Definite**
21	F	White	None	**Cardiopulm/5 days** - Cough, fatigue, sore throat - Exertional CP (Antigen)	Normal	Troponin-I <0.01	**Abnormal** LVEF 55-60%, no WMAs, small pericardial effusion	LVEF 58%, T1= normal mapping. No LGE present. T2= normal mapping. **Small pericardial effusion**	83 days	**Definite**

Cardiopulm= cardiopulmonary symptoms, CMR= cardiac magnetic resonance imaging, CP = chest pain, DOE = dyspnea on exertion, ECG = electrocardiogram, F = female, hs = high sensitivity, LGE = late gadolinium enhancement, LVEF = left ventricular ejection fraction, M = male, MRI = magnetic resonance imaging, No= number, PCR= polymerase chain reaction, TTE = transthoracic echocardiography, WMA= wall motion abnormality

*If the patient was asymptomatic, time is listed as time from positive SARS-CoV-2 testing to cardiac MRI

Mean age 21 ±0.4 years (range 17-24), with athletes from sporting disciplines including: baseball, basketball, cheerleading, cross-country/track and field, football, lacrosse, soccer, softball, tennis, and volleyball.

Figure Legends

Figure 1. Prevalence of Initial Symptoms in Athletes with Symptomatic SARS-CoV-2 Infection

*Athletes with known initial symptoms

Red bars indicate 'Cardiopulmonary Symptoms.'

Figure 2. Time From Initial Infection to Cardiac Testing

CMR= cardiac magnetic resonance, ECG= electrocardiogram, Trop=troponin, TTE= transthoracic echocardiography. Midline= Median, Box= interquartile range (IQR), Whiskers= 95% confidence intervals

*Time from initial infection calculated as the longest time from date of initial symptom onset or date of positive SARS-CoV-2 to date of cardiac test. The total athletes with known timeframe were as follows: CMR (n=302), ECG (n=2765), Trop (n=2537), TTE (n=2406)

Figure 3. Results of Primary CMR versus Clinically Indicated CMR Screening Protocols

Figure 3A. Athletes Undergoing Primary CMR screening protocol

Figure 3B. Athletes Undergoing Clinically Indicated CMR screening protocol

Definition of abbreviations: CMR = cardiac magnetic resonance imaging, cTn = cardiac troponin, ECG= electrocardiogram, TTE = transthoracic echocardiogram

*Borderline Triad Testing as indication for CMR included: 1) Detectable troponin level but not above the 99th percentile; 2) Non-specific ECG abnormalities not fulfilling the International Criteria; 3) TTE findings including abnormalities of unclear significance or those at the upper or

lower limit of the normal range and felt to potentially represent pathology (i.e. left ventricular ejection fraction of 50%).

Figure 4. Cardiovascular Testing Results Among NCAA Athletes Following SARS-CoV-2 Infection

Definition of abbreviations: ASA = atrial septal aneurysm, ASD = atrial septal defect, CMR = cardiac magnetic resonance imaging, cTn = cardiac troponin, ECG = 12-lead electrocardiogram, HCM = hypertrophic cardiomyopathy, PFO = patent foramen ovale, TTE = transthoracic echocardiogram

*Borderline Triad Testing as indication for CMR included: 1) Detectable troponin level but not above the 99th percentile; 2) Non-specific ECG abnormalities not fulfilling the International Criteria; 3) TTE findings including abnormalities of unclear significance or those at the upper or lower limit of the normal range and felt to potentially represent pathology (i.e. left ventricular ejection fraction of 50%).

†New and known diagnoses.