COVID-19 myocarditis cardiac magnetic resonance findings in symptomatic patients

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Abstract

Background: Coronavirus disease 2019 (COVID-19) may cause myocardial damage.

Purpose: To evaluate the short-term and medium-term results, as well as the imaging features of COVID-19 cardiac involvement, using cardiac magnetic resonance (CMR).

Material and Methods: In this study, laboratory and CMR findings of 15 patients with COVID-19 between May 2020 and May 2021 were evaluated retrospectively. Late gadolinium enhancement (LGE) imaging was evaluated for myocarditis. Cardiac functions were quantitatively evaluated and compared to the control patient group. High-sensitivity cardiac troponin I (Hs-cTnI), C-reactive protein (CRP) exchange, and LGE were compared.

Results: Fifteen patients (7 women; mean age = 38 years) were evaluated. Six patients were treated at home, while nine patients were treated in the hospital. The patients were given remdesivir and hydroxychloroquine treatment. LGE was detected in 2 (33%) patients treated at home and 5 (55.5%) patients treated in the hospital. In hospitalized patients, levels of Hs-cTnI (mean = 7.8 pg/mL) and CRP (mean = 32.3 mg/L) were elevated. A high correlation was observed between the increase in Hs-cTnI value and LGE ($r = 0.63$; $P < 0.001$). A low correlation was observed between an increase in CRP and LGE ($r = 033$; $P < 0.001$). There was no statistically significant difference in ventricular functions between the COVID-19 and control groups ($P < 0.001$).

Conclusion: CMR abnormalities were found in a high percentage (46%) of patients with COVID-19. Myocardial abnormalities in patients with COVID-19 can be detected by CMR. For COVID-19 myocarditis, no specific diagnostic CMR imaging feature was observed.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has affected the entire world (1). It is thought that the virus acts on the cells through the angiotensin-converting enzyme 2 (ACE-2) (2). Furthermore, the infection has the greatest impact on the lungs. Cardiac involvement in myocarditis includes myocardial fibrosis, edema, and pericarditis (3). Due to the high content of ACE-2 in patients with heart disease, serious cardiac complications have been reported in patients with COVID-19 (3,4). Heart damage as a result of COVID-19 has been reported to cause direct myocarditis, cardiac stress due to respiratory failure, and indirect damage secondary to systemic cytokine release syndrome and their combination (5–7).

Among known viral infections, COVID-19 is the most common cause of myocarditis (1–8). Cardiovascular magnetic resonance (CMR) is the non-invasive gold standard for the assessment of myocardial tissue pathology and edema. CMR is a highly accurate diagnostic tool for myocarditis (7,8). The American Heart Association (AHA) recommends CMR to detect heart damage (9). Other imaging methods may be insufficient to detect chronic infections, particularly cardiac muscle, and pericardial infections (7–9). The imaging features that distinguish

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COVID-19 cardiac involvement from other myocarditis etiologies have not been described in the literature (7–10). To define the characteristics of COVID-19 myocarditis imaging, large series of patients are needed for studies.

The aim of the present study was to contribute to the literature by defining the CMR diagnostic criteria for myocarditis secondary to COVID-19 by examining the imaging features and measurable cardiac functional parameters of COVID-19 myocardial involvement.

Material and Methods

Study design and study population

This is a retrospective study conducted at a single center. The university's ethics committee gave their approval.

Patients who had CMR between May 2021 and May 2020 had their records searched for COVID-19. The presence of COVID-19 was detected in 17 patients whose diagnoses were confirmed by a reverse transcription-polymerase chain reaction (RT-PCR) swab test. However, all patients were considered cured after 10 days of isolation because they had no clinical findings. The study excluded one patient with coronary artery disease and one patient who had undergone cardiothoracic surgery. As a result, the CMR examinations of 15 patients who had COVID-19 and were considered recovered were reviewed retrospectively. A group of healthy controls (20 patients) with normal CMR examinations and similar age and gender distribution were determined from the database of our hospital.

CMR protocols

All examinations were planned with standardized image interpretation and post-processing in the cardiovascular magnetic resonance (CMR) 2020 update (11). CMR studies were performed on a 1.5-T scanner (Aera®; Siemens Healthineers, Erlangen, Germany). Patients were scanned with the electrocardiogram (ECG) triggering using a 16-channel surface phased array body coil. After standard localizer scan images, breath-hold cine images were acquired in two-chamber and four-chamber views for ventriculus. The slice thickness of each slice was 8 mm with an interslice gap of 2 mm. The left ventricle (LV) and right ventricle (RV) function parameters were calculated with Syngo software. LV / RV end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), and cardiac output (CO) were calculated from functional parameters, and LV mass and LV/RV ejection fraction (EF) values were evaluated.

We administered 0.2 mmol/kg intravenous injection of contrast agent (Magnevist; Schering, Berlin, Germany) into an antecubital vein for late gadolinium enhancement (LGE) imaging. A flow rate of 2 mL/s was used. A minimum of 10 min after contrast administration, a PSIR

(phase sensitive inversion recovery) sequence was performed to optimally null the signal of the remote myocardium calculated automatically. Two-dimensional (2D) LGE images were acquired in short-axis views covering the entire LV myocardium using three different LGE sequences: a segmented, single-slice, single breath-hold, 2D fast low-angle, shot-based, phase-sensitive inversion recovery sequence (FLASH-PSIR).

Imaging analysis

CMR examinations were evaluated by a radiologist with a cardiac imaging certificate. EF, stroke volume, cardiac index (CI), and cardiac output (CO) were calculated automatically over functional sequences. In multisectional two- and four-chamber images, the end-diastolic 17-segment wall thicknesses were measured manually as a full layer and a non-compacted layer. Contrast enhancement in LGE images was marked with the AHA 17 segment t model. The presence of myocardial fibrosis was analyzed as present or absent regardless of segment size.

CMR images were acquired from the image archive system. Myocardial edema was evaluated on short tau inversion recovery (STIR) and T2-weighted (T2W) imaging. A comparison was made with the muscle tissue included in the section for the presence of myocardial edema. STIR and T2W imaging signal increased two times more than muscle tissue was considered as myocardial edema. It was defined as the segment and involved the myocardial layer of increased signal on LGE images.

Laboratory analysis

Laboratory data were obtained from the patient information system of our hospital. The researchers measured high-sensitivity cardiac troponin I (Hs-cTnI), C-reactive protein (CRP), serum potassium, and serum calcium levels. Hs-cTnI levels >3 pg/mL were considered significant.

Statistical analysis

All statistical analyses were performed using SPSS version 24.0 (IBM statistics, Armonk, NY, USA). Categorical variables were expressed as number (percentage) and the continuous variables as mean $\pm$ standard deviation or median. The normality of the distribution was tested using the Shapiro–Wilk test. Comparison between the two groups was made using the unpaired Student's t test for normal distribution. The Mann–Whitney U test was used with continuous variables in non-normal distribution. The chi-square test was used to explore the statistical significance of CMR parameters in the COVID-19 and control groups. Comparisons between groups were performed using ordinary one-way

Table 1. Patient characteristics of COVID-19 cases and control groups, including demographics and baseline co-morbidities.

Patients	COVID-19 patients	Control group
Age (years)	15 ± 8	20 ± 12
Male	8	12
Hypertension	4	8
Diabetes mellitus	1	2

*Values are given as mean ± SD.

Table 2. Blood test results in hospitalized patients.

Blood test results	COVID-19 patients with LGE+	COVID-19 patients with LGE−
CRP (mg/dL)	33.3 (14–60)	22 (2–35)
Hs-cTnI (pg/mL)	7.8 (2–16)	2.5 (0.1–5.5)

Values are given as median (range).
CRP, C-reactive protein; Hs-cTnI, high-sensitivity cardiac troponin I; LGE, late gadolinium enhancement.

analysis of variance or Kruskal–Wallis tests. $P < 0.05$ was considered statistically significant.

Results

We examined 15 patients (8 men, 7 women; age range = 30–45 years; mean age = 38 years) who met our study criteria. Four patients had hypertension and one patient had diabetes mellitus (Table 1). Before COVID-19, there was no known systemic or coronary disease in the patient group, and six of the patients were treated at home, while nine were treated in the hospital due to respiratory distress. One hospitalized patient received mechanical ventilation for five days and non-invasive ventilation with positive airway pressure for 10 days. For an average of 4 days (range = 2–8 days), eight patients were subjected to non-invasive ventilation with positive airway pressure (Fig. 1). Furthermore, remdesivir and hydroxychloroquine were
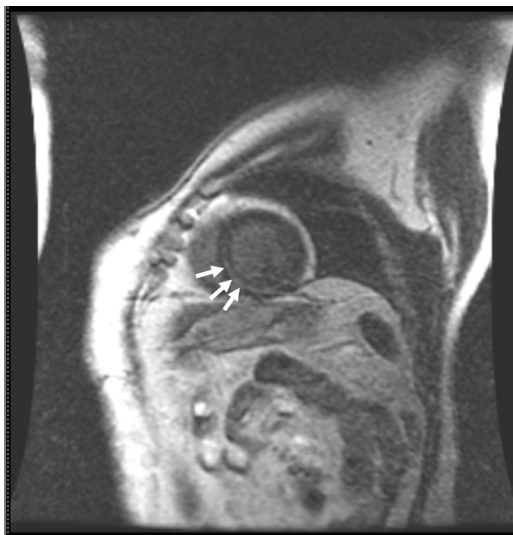

Fig. 1. A 48-year-old man with CMR imaging 45 days after COVID-19 diagnosis. He was treated in the hospital for severe dyspnea. Hs-cTnI level when he was in hospital was 15.4 pg/mL. His Hs-cTnI was 5 pg/mL on the day of CMR imaging. PSIR two-chamber image shows intramyocardial LGE (arrows).CMR, cardiac magnetic resonance; Hs-cTnI, high-sensitivity cardiac troponin I; LGE, late gadolinium enhancement.

administered to all patients. In addition, the patients received no steroid treatment.

The mean number of days between positive COVID-19 testing and CMR examination was 81 days (range = 61–105 days). Atypical chest pain (7 patients), palpitations (5 patients), and effort dyspnea (3 patients) were the most common complaints of COVID-19 at the cardiology polyclinic. There were also reports of shortness of breath (8 patients), general lassitude (5 patients), and diffuse muscle pain (2 patients). Before COVID-19 disease, none of the patients had a history of coronary disease drug use. In addition, the echocardiogram and echocardiography reports of the patients revealed no abnormalities.

Routine blood tests were used to assess Hs-cTnI, CRP, serum potassium, and serum calcium levels in all hospitalized patients. The mean Hs-cTnI value was 7.8 pg/mL (range = 2–16 pg/ml) higher than the reference values. Hs-cTnI values increased by >12 pg/mL in six hospitalized patients, and LGE was observed in the mean (Table 2). LGE was observed in an average of 5 segments (2-8 segments) in 6 hospitalized patients whose Hs-cTnI value increased excessively more than 12 pg/ml. A significant correlation was observed between the increase in Hs-cTnI value and the LGE ($r = 0.63$; $P < 0.001$). The CRP value was found to be high in all patients (mean = 33.3 mg/L; range = 14–60 mg/L). Moreover, a low correlation was observed between CRP value and LGE ($r = 0.33$; $P < 0.001$) (Table 2).

LGE was found in seven patients in total. LGE was found in one of the three patients with normal Hs-cTnI values who were treated at the hospital. In patients treated at home, Hs-cTnI was not measured (Fig. 2). LGE was observed in three and two segments in 2 (33%) patients who were treated at home without Hs-cTnI values.

The distribution of myocardial LGE was calculated as the number of segments in all patients in accordance with the American Heart Association 17-segment model and was used to define the extent of involvement. In the study, LGE consistent with myocarditis was observed in seven patients who did not fit into the vascular irrigation area (46%). Myocarditis was detected in 2 of 6 (33%) patients treated at home and 5 of 9 (55.5%) patients treated at the hospital. The average number of segments
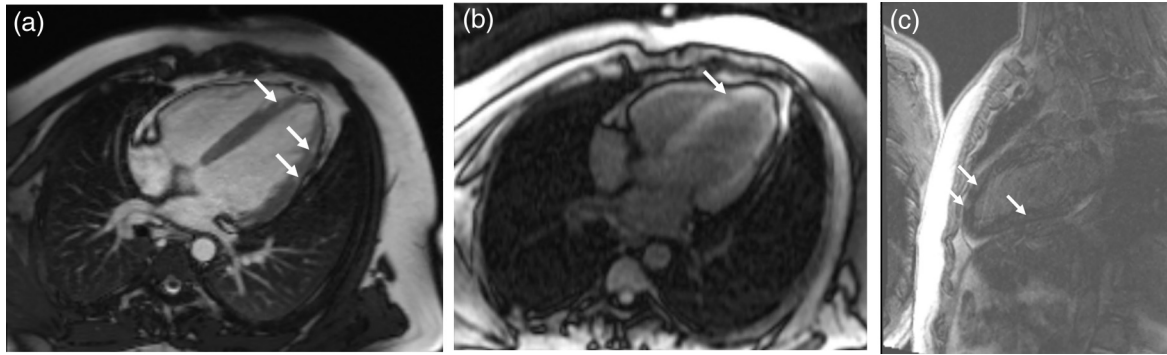
Fig. 2. A 62-year-old man was treated in his home for COVID-19. (a) Long-axis cine SSFP and (b) T1 sequences showed focal myocardial irregularity (arrows). (c) T1 PSIR short- and (d) long-axis images show focal myocarditis after COVID-19 (arrows).

involved is seven patients with COVID-19 secondary myocarditis. Three segments (1–6 segments) were discovered. Furthermore, LGE was observed in the inferior wall and interventricular septum of five patients, with a linear appearance in the medial of the myocardium (Fig. 3). In two patients, there was limited punctate LGE in the left ventricular free wall.

All patients had normal first-phase myocardial perfusion imaging. In SSFP cine images, wall movements were normal during the systole and diastole phases. STIR sequences also revealed no edema signal consistent with acute myopericarditis.

There was pericardial effusion in 2 (13%) patients. Extracardiac findings included pleural effusions in 4 (26%) patients, a Bosniak type 1 renal cyst, and a liver simple cyst in one. Eleven patients underwent computed tomography (CT) pulmonary angiography examination for a mean of 6 days (range= 2–26 days), with no pulmonary embolism detected. A non-contrast CT scan was performed on 12 patients who had been diagnosed with COVID-19. The evaluation was based on the Radiological Society of North America Expert Consensus

Statement on Reporting Chest CT Findings Related to COVID-19 criteria (12). All patients had moderate involvement of the parenchymal ground-glass type.

Functions were discovered in patients with LVEF (mean = 53%; range = 45%–68%) and RVEF (mean = 47%; range = 35%–51%). The left ventricular CI was 5.22 L/min/m^2, CO was 3.5 L/min, and the SV was 102 mL. The functions of the valves were within normal limits. In the control group, ventricular functions had a mean LVEF of 57% (range = 42%–65%) and a mean RVEF of 45% (range = 39%–61%) were discovered. Furthermore, the mean values for the left ventricle were CI 4.22, CO 3.8, and SV 85 mL. The ventricular functions of the two groups ($P < 0.001$) did not differ significantly (Table 3).

Discussion

In this study, 15 patients were examined who had no history of cardiac disease but reported cardiac symptoms after being infected with COVID-19. In 7 (46%) patients, CMR examination revealed LGE consistent with myocarditis. The LGE
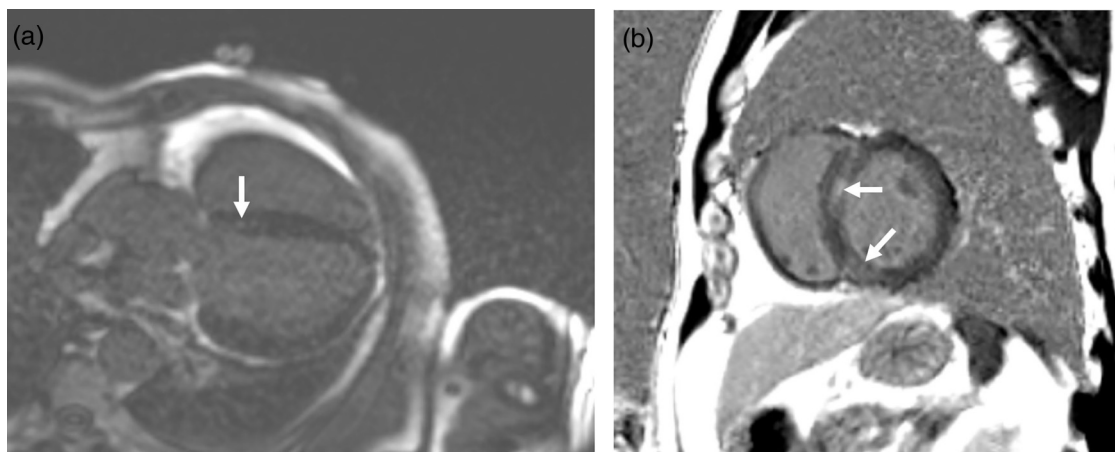

Fig. 3. 44 years old man with myocarditis 2 chamber (A) and 4 chamber(B) PSIR images show focal LGE interventricular septum (arrows).

Table 3. CMR imaging findings from the COVID-19 cases and control group, including the statistical comparisons.

CMR findings	COVID-19 patients with LGE+	COVID-19 patients with LGE−	Control group	P value
LVEF (%)	51 ± 16	54 ± 15	57 ± 15	<0.001
RVEF (%)	45 ± 12	51 ± 10	45 ± 12	<0.001
LVSV (mL)	95 ± 19	107 ± 21	85 ± 21	<0.001
LVCI (L/min/m^2)	5.4 ± 2.1	4.7 ± 2.1	4.22 ± 2.4	<0.001
LVC0 (L/min)	3.8 ± 1.5	3.4 ± 1.7	3.8 ± 2.2	<0.001
LGE (+)	7	8	0	<0.001

Values are given as mean ± SD unless otherwise indicated.
CMR, cardiac magnetic resonance; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; Hs-cTnI, High-sensitivity cardiac troponin I; LGE, late gadolinium enhancement; LVCI, left ventricular cardiac index; LVCO, left ventricular cardiac output; LVEF, left ventricular ejection fraction; LVSV, left ventricular stroke volume; RVEF, right ventricular ejection fraction.

pattern was inconsistent with vascular irrigation areas, and it had a non-specific distribution and appearance. There was a high correlation between Hs-cTnI and LGE. Detection of myocarditis was considered secondary to cardiac involvement of COVID-19. In addition, myocarditis may occur as a long-term permanent outcome in patients with COVID-19 (13,14). In our study, no thickening or contrast enhancement secondary to pericarditis was observed.

COVID-19 may cause multiorgan involvement, which has the potential to cause long-term social health problems. Many studies have reported cardiac involvement (15). These studies evaluate acute and chronic myopericarditis. LGE pattern and changes in heart function after COVID-19 are examined in patient groups in studies. Puntman et al. (13) evaluated 100 patients, while Ojha et al. (16) evaluated 199 patients with COVID-19 in prospective studies. These study results were consistent with those of the present study. Findings as a result of myocardial involvement were similar to the literature (1,3,15). In this study, selected patients admitted to the hospital with cardiac symptoms were examined. This may be the reason why the rate of post-COVID-19 myocarditis is higher than in some studies in the literature (17,18).

Clinically, long-term changes caused by cardiac involvement have yet to be reported. In our study, the right and left ventricular EF values were within normal limits, which was consistent with the literature (13–15,19). After COVID-19, there was no significant difference in cardiac functions when compared to the control groups. Furthermore, myocarditis was the only pathology that could be visualized radiologically (18). Cardiac involvement of the patients in our study was in its early stages. Hence, long-term studies should be conducted on patients. Quantitative CMR can be used to monitor cardiac involvement and its evolution (20). This study will be useful for inpatient follow-up.

The present study has some limitations. The first is the very small sample population. Second, only patients with COVID-19 who showed clinical signs of heart disease were examined. Therefore, our myocarditis rate can be interpreted as high. Before COVID-19, the patients had no CMR studies to compare. As analysis of images was not done blind to COVID-19 status there is a possibility of bias. The control group were known to have normal CMR. This lowered the threshold for observing statistically significant differences when comparing with cases of COVID-19 who were not known to have normal CMR. COVID-19 cases and controls were not matched for risk factors. This was another limitation of the study.

In conclusion, during COVID-19 infection, a high rate of myocardial damage (46%) was observed. Patients with significant short-term functional loss were not observed. The next step should be to examine the long-term myocardial damage and clinical effects of COVID-19 in large patient groups and to investigate the diagnostic CMR findings.

Declaration of conflicting interests

Funding

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References

1. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020;1:802–810.
2. Zhang H, Penninger JM, Li Y, et al. Angiotensin-converting enzyme 2(ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med 2020;46:586–590.
3. Long B, Brady WJ, Koyfman A, et al. Cardiovascular complications in COVID-19. Am J Emerg Med 2020;38:1504–1507.
4. Sanghvi SK, Schwarzman LS, Nazir NT. Cardiac MRI and myocardial injury in COVID-19: diagnosis, risk stratification and prognosis. Diagnostics (Basel) 2021;11:130.
5. Knockaert DC. Cardiac involvement in systemic inflammatory diseases. Eur Heart J 2007;28:1797–1804.
6. Friedrich MG, Sechtem U, Schulz-Menger J, et al. Cardiovascular magnetic resonance in myocarditis: a JACC white paper. J Am Coll Cardiol 2009;53:1475–1487.
7. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. J Am Coll Cardiol 2018;72:3158–3176.
8. Friedrich MG, Cooper LTJr. What we (don't) know about myocardial injury after COVID-19. Eur Heart J 2021;42:1879–1882.

9. Kociol Robb D, Cooper Leslie T, Fang JC, et al. Recognition and initial management of fulminant myocarditis. Circulation 2020;141:e69–e92.

10. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet 2020;395:1417–1418.

11. Kramer CM, Barkhausen J, Bucciarelli-Ducci C, et al. Standardized cardiovascular magnetic resonance imaging (CMR) protocols: 2020 update. J Cardiovasc Magn Reson 2020;22:17.

12. Simpson S, Kay FU, Abbara S, et al. Radiological Society of North America Expert Consensus Statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. Radiol Cardiothorac Imaging 2020;2:e200152.

13. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:1265–1273.

14. Wang H, Li R, Zhou Z, et al. Cardiac involvement in COVID-19 patients: mid-term follow up by cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2021;23:14.

15. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020;46:846–848.

16. Ojha V, Verma M, Pandey NN, et al. Cardiac magnetic resonance imaging in coronavirus disease 2019 (COVID-19): a systematic review of cardiac magnetic resonance imaging findings in 199 patients. J Thorac Imaging 2021;36:73–83.

17. Joy G, Artico J, Kurdi H, et al. Prospective case-control study of cardiovascular abnormalities 6 months following mild COVID-19 in healthcare workers. JACC Cardiovasc Imaging 2021;S1936–878X:356–359.

18. Kotecha T, Knight DS, Razvi Y, et al. Patterns of myocardial injury in recovered troponin-positive COVID-19 patients assessed by cardiovascular magnetic resonance. Eur Heart J 2021;42:1866–1878.

19. Huang L, Zhao P, Tang D, et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. JACC Cardiovasc Imaging 2020;13:2330–2339.

20. Clark DE, Parikh A, Dendy JM, et al. COVID-19 myocardial pathology evaluation in athletes with cardiac magnetic resonance (COMPETE CMR). Circulation 2021;143:609–612.