

Supplemental Online Content

Starekova J, Bluemke DA, Bradham WS, et al. Evaluation for myocarditis in competitive student athletes recovering from coronavirus disease 2019 with cardiac magnetic resonance imaging. *JAMA Cardiol*. Published online January 14, 2021. doi:10.1001/jamacardio.2020.7444

eMethods

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eReferences.

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

MRI Protocol

The cardiac MRI protocol was designed to evaluate patients for myocarditis and is based on recommendations for standardized protocols from the Society for Cardiac Magnetic Resonance (SCMR)¹. Prior to GBCA administration, acquisitions included cardiac-gated double inversion recovery fat-saturated T2-weighted fast spin echo acquired in double oblique short axis (SA) plane, with whole coverage of left ventricle (LV); three slice (apex-, mid- and LV base) modified Look-Locker inversion recovery T1-, and multi-echo fast spin echo T2-mapping in double oblique SA plane (eTable 1). After administration of 0.2 mmol/kg of gadoterate meglumine (Dotarem®, Guerbet, Roissy, France), CINE cardiac-gated balanced steady state free precession (bSSFP) in double oblique SA plane (whole LV coverage), and in three standardized long axis (LA) planes (2-, 3-, and 4-chamber views) were acquired. At approximately 10-12 minutes after GBCA administration, cardiac-gated late gadolinium enhanced phase-sensitive inversion recovery (PSIR) T1-weighted images were acquired, in the same SA plane (whole LV coverage), and LA planes (eTable 1).

All imaging was performed on clinical 1.5T or 3T 70 cm wide bore clinical MRI systems (1.5T Optima MR450w, 1.5T Signa Artist, 3T Signa Architect, 3T Signa Premier, GE Healthcare, Waukesha, WI) using a 12-20 channel phased-array torso receive coil, using posterior elements embedded in the scanner table.

Evaluation of the LV and right ventricle (RV) was performed using a commercial cardiac MRI analysis package (cvi42® software, Circle Cardiovascular Imaging, Calgary, Alberta, Canada) to provide the following measurements: LV and RV ejection fraction (LVEF, RVEF), LV and RV stroke volume index (LVSVi, RVSVi), LV and RV end-diastolic volume (LVEDVi, RVEDVi), and LV mass index. Measurements of ventricular volumes and LV mass were performed in standard fashion using short axis cine images¹. For global assessment of T1 and T2 relaxation times, a single region of interest (ROI) was placed carefully within the mid portion of the ventricular septum on T1 and T2 maps, in areas free from artifacts or partial volume effects with the adjacent blood pool¹. Additional ROIs were drawn to assess T1 and T2 values within areas of abnormal T2 signal (on T2-weighted black blood images) and focal LGE¹.

Data Collection

In addition to MRI, demographic data and the following clinical data were collected: age, sex, type and date of COVID-19 testing; date of onset COVID-19 symptoms and detailed characteristics of these symptoms; record of hospitalization, if any; date of cardiac MRI; athlete's sport; systolic and diastolic blood pressure at rest (mmHg); height (m) and weight (kg). Body mass index (BMI, kg/m²) and body surface area (BSA, m²) were calculated². Clinical symptoms were categorized as mild (headache, cough, fatigue, congestion, sore throat, myalgias, body aches, loss of smell and taste, nausea and vomiting), moderate (fever and chills, chest pain and mild dyspnea) and severe (severe dyspnea, hypoxia, symptoms requiring hospitalization). Additional diagnostic tests included TTE, serum troponin-I (normal range 0.0-0.03 ng/mL), B-type natriuretic peptide (BNP, normal range 0-99 pg/mL), C-reactive protein (CRP, normal range 0.0-1.0 mg/dL), erythrocyte sedimentation rate (ESR, normal range 0-20 mm/hr), and chest radiograph (if performed). All ECG were compared to baseline ECG, performed as part of pre-participation evaluation and interpreted using modified interpretation criteria for athletes³. Any changes in ECG from baseline are reported.

Statistical Analysis

Descriptive data analysis and statistical analyses were performed using GraphPad Prism 8.1 (v8.1, GraphPad Software, Inc., San Diego, California) and Excel (v16.30, Microsoft, Redmond, Washington). Continuous data are presented as mean ± standard deviation (SD), and categorical data as absolute numbers and percentages. 95% confidence interval for prevalence of MRI findings consistent with myocarditis was determined using the Wilson score without continuity correction⁴.

eTable 1. Cardiac MRI Protocol.

Parameter	T2w DIR-FSE 1.5T / 3T	T1 Map 1.5T / 3T	T2 Map 1.5T / 3T	Inject GBCA ^a	CINE IR (Scout)	CINE bSSFP 1.5T / 3T	T1w PSIR 1.5T / 3T ^b
TR (ms)	def	3.0 / 2.9	def		3.0 / 3.1	3.2 / 3.0	4.7 / 6.1
TE (ms)	102 / 102	1.0 / 1.2	4 values ~12-80ms		1.2 / 1.4	1.3 / 1.2	2.2 / 2.8
Flip angle	90 + refocusing	35	90 + refocusing		5	45	25 / 20
TI (ms)	n/a	8 values ~150ms-5s	n/a		n/a	n/a	determined by CINE IR
Slice thickness (mm)	8 / 7	8 / 7	7		10 / 7	8 / 7	8 / 7
Slice gap (mm)	0 / 0	n/a	n/a		n/a	0 / 0	0 / 0
Acquisition matrix	256x224	168x148	200x160		128x128	224x192 / 224x224	224x160
Slices	Full LV coverage in SA	3 SA slices	3 SA slices		1 SA slice	Full LV coverage in SA; 3 LA slices ^c	Full LV coverage in SA; 3 LA slices ^c

^a 0.2 mmol/kg of gadoterate meglumine (Dotarem®, Guerbet, Roissy, France)

^b Images were acquired ~10-12 minutes after administration of gadolinium based contrast agent (GBCA).

^c For long axis (LA), slices in 2-, 3- and 4-chamber view were acquired

Abbreviations: bSSFP, balanced steady state free precession; def, defined by RR interval; FOV, field of view; LA, long axis; LV, left ventricle; T2w DIR-FSE, T2-weighted double inversion recovery fat-saturated T2-weighted fast spin echo; T1w PSIR, T1-weighted phase sensitive inversion recovery (PSIR); SA, short axis; TE, echo time; TI, inversion time; TR, repetition time; n/a, not applicable

eTable 2: Clinical and quantitative cardiac MRI parameters of two athletes recovering from COVID-19 with MRI findings consistent with myocarditis.

	Patient 1^a Myopericarditis	Patient 2^a Myocarditis
Cardiac MRI		
LVEF (%)	51	58
LV mass index (g/m ²)	63	58
LVCI (L/min/m ²)	2.7	2.6
LVEDVi (mL/m ²)	116	122
LVESVi (mL/m ²)	56	51
LVSVi (mL/m ²)	60	71
RVEF (%)	49	52
RVCI (L/min/m ²)	2.6	2.7
RVEDVi (mL/m ²)	119	138
RVESVi (mL/m ²)	60	66
RVSVi (mL/m ²)	58	72
Native T1 septum (ms)	1156	1181
Native T1 LGE areas (ms)	1223	1250
Native T2 septum (ms)	45	n/a
Native T2 LGE areas (ms)	57	n/a
LGE / edema present	yes / yes	yes / yes
LGE findings	Predominantly distal LV inferolateral wall	Inferior basal LV wall; Inferior RV insertion
TTE		
Abnormal findings	Mild reduction in global LV strain (GLS -15.4%)	no
ECG		
Change to baseline	ST and T wave changes in anterolateral leads	no
Blood parameters		
Troponin-I (ng/mL)	0.03, 0.04, 0.09 ^b	0.01
BNP (pg/mL)	17	23
ESR (mm/hr)	0	5
CRP (mg/dL)	0.1	0.1
CoV-19 positive test - MRI (days)^c	11	19
CoV-19 symptoms	Initially asymptomatic; one episode of mild dyspnea reported on 1-month clinical follow-up	Fever, myalgias, cough, mild dyspnea, sore throat, congestion, diminished loss of taste

^a Gender, age, sex, sport and other characteristics (weight, height, BMI) are not included to protect patient privacy. Both patients were imaged on a 3T system

^b Troponin-I was normal one day prior to the cardiac MRI (0.03 ng/mL), however, increased to 0.04 ng/ml and 0.09ng/ml, two and four days after the cardiac MRI exam, respectively

^c Time between onset of symptoms in patient with COVID-19 and cardiac MRI

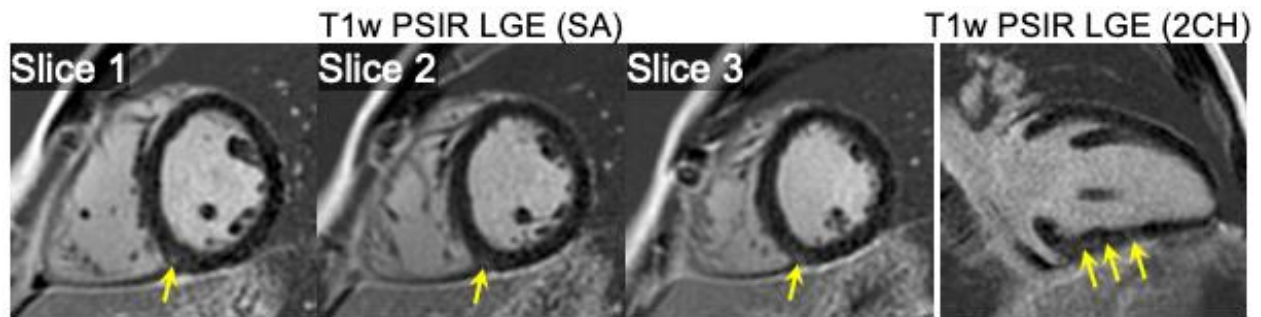
Abbreviations: BNP, B-type natriuretic peptide; CI, cardiac index; CRP, C-reactive protein; CoV-19, COVID-19; EDVi, end-diastolic volume index; EF, ejection fraction; ESR, erythrocyte sedimentation rate; ESVi, end-systolic volume index; GLS, global longitudinal strain; LGE, late gadolinium enhancement; LV, left ventricular; n/a, not available; TTE, transthoracic echocardiography; RV, right ventricular; SVi, stroke volume index

Reference values: BNP: ≤99 pg/mL; CRP: ≤1.0 mg/dL; ESR: males <15mm/h (for age group 0-50 years), females <20mm/h (for age group 0-50 years); Troponin-I: ≤0.03 ng/mL

eTable 3: Number of athletes with COVID-19 and documented specific symptoms during the course of their disease.

SARS-CoV-2 symptoms	All Athletes (n=145)	Male Athletes (n=108)	Female Athletes (n=37)
Nasal congestion	56 (38.6)	45 (41.7)	11 (29.7)
Headache	51 (35.2)	32 (29.6)	19 (51.4)
Sore throat	49 (33.8)	32 (29.6)	17 (45.9)
Loss of smell	47 (32.4)	39 (36.1)	8 (21.6)
Loss of taste	41 (28.3)	32 (29.6)	9 (24.3)
Cough	39 (26.9)	25 (23.1)	14 (37.8)
Fatigue	38 (26.2)	28 (25.9)	10 (27.0)
Myalgias	33 (22.8)	19 (17.6)	14 (37.8)
Fever, chills	30 (20.7)	19 (17.6)	11 (29.7)
Shortness of breath	9 (6.2)	6 (5.6)	3 (8.1)
Chest pain	7 (4.8)	4 (3.7)	3 (8.1)
Diarrhea	7 (4.8)	6 (5.6)	1 (2.7)
Nausea, Vomiting	6 (4.1)	4 (3.7)	2 (5.4)
Asymptomatic	24 (16.6)	17 (15.7)	7 (18.9)

Data are number (%).



eFigure. Nonspecific inferior-septal right ventricular insertion point late gadolinium enhancement.

Mild nonspecific focal enhancement at the inferior-septal right ventricular insertion point in one of the athletes (yellow arrows). No corresponding elevated T2-weighted signal or wall motion abnormalities were observed. Serum troponin-I was negative in this patient. Shown are T1-weighted phase sensitive inversion recovery images with late gadolinium enhancement (T1w PSIR LGE) in three contiguous short axis (SA) slices and the two-chamber view (2CH).

eReferences.

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