ORIGINAL RESEARCH

Myocardial Injury on CMR in Patients With COVID-19 and Suspected Cardiac Involvement

Mahesh K. Vidula, MD,[a] Justyna Rajewska-Tabor, MD, PhD,[b] J. Jane Cao, MD, MPH,[c] Yu Kang, MD,[a] Jason Craft, MD,[c] Winifred Mei, BS,[c] Preethi S. Chandrasekaran, MS,[d] Daniel E. Clark, MD, MPH,[e] Ana-Maria Poenar, MD,[f] Miroslawa Gorecka, MBBS,[f] Maan Malahfji, MD,[g] Eilidh Cowan, BS,[g] Jennifer M. Kwan, MD, PhD,[h] Samuel W. Reinhardt, MD,[h] Sarah Al-Tabatabaee, MS,[i] Patrick Doeblin, MD,[i] Adriana D.M. Villa, MD, PhD,[j] Ilya Karagodin, MD,[k] Nazia Alvi, DO,[k] Panagiota Christia, MD,[l] Nicholas Spetko, MD,[m] Mark Philip Cassar, MD,[n] Christine Park, MD,[o] Lakshmi Nambiar, MD,[o] Alper Turgut, BS,[p] Mahan Roosta Azad, MD,[q] Moritz Lambers, MD,[q] Timothy C. Wong, MD, MS,[r] Michael Salerno, MD, PhD, MS,[p] Jiwon Kim, MD,[o] Michael Elliott, MD,[s] Betty Raman, MBBS, DPHIL,[n] Stefan Neubauer, MD,[n] Connie W. Tsao, MD, MPH,[m] Gina LaRocca, MD,[l] Amit R. Patel, MD,[k] Amedeo Chiribiri, MD, PhD,[j] Sebastian Kelle, MD,[i] Lauren A. Baldassarre, MD,[h] Dipan J. Shah, MD,[g] Sean G. Hughes, MD,[e] Matthew S. Tong, DO,[d] Malgorzata Pyda, MD, PhD,[b] Orlando P. Simonetti, PhD,[d] Sven Plein, MD, PhD,[f] Yuchi Han, MD, MMSc[a,d]

ABSTRACT

BACKGROUND Myocardial injury in patients with COVID-19 and suspected cardiac involvement is not well understood.

OBJECTIVES The purpose of this study was to characterize myocardial injury in a multicenter cohort of patients with COVID-19 and suspected cardiac involvement referred for cardiac magnetic resonance (CMR).

METHODS This retrospective study consisted of 1,047 patients from 18 international sites with polymerase chain reaction–confirmed COVID-19 infection who underwent CMR. Myocardial injury was characterized as acute myocarditis, nonacute/nonischemic, acute ischemic, and nonacute/ischemic patterns on CMR.

RESULTS In this cohort, 20.9% of patients had nonischemic injury patterns (acute myocarditis: 7.9%; nonacute/nonischemic: 13.0%), and 6.7% of patients had ischemic injury patterns (acute ischemic: 1.9%; nonacute/ischemic: 4.8%). In a univariate analysis, variables associated with acute myocarditis patterns included chest discomfort (OR: 2.00; 95% CI: 1.17-3.40, $P = 0.01$), abnormal electrocardiogram (ECG) (OR: 1.90; 95% CI: 1.12-3.23; $P = 0.02$), natriuretic peptide elevation (OR: 2.99; 95% CI: 1.60-5.58; $P = 0.0006$), and troponin elevation (OR: 4.21; 95% CI: 2.41-7.36; $P < 0.0001$). Variables associated with acute ischemic patterns included chest discomfort (OR: 3.14; 95% CI: 1.04-9.49; $P = 0.04$), abnormal ECG (OR: 4.06; 95% CI: 1.10-14.92; $P = 0.04$), known coronary disease (OR: 33.30; 95% CI: 4.04-274.53; $P = 0.001$), hospitalization (OR: 4.98; 95% CI: 1.55-16.05; $P = 0.007$), natriuretic peptide elevation (OR: 4.19; 95% CI: 1.30-13.51; $P = 0.02$), and troponin elevation (OR: 25.27; 95% CI: 5.55-115.03; $P < 0.0001$). In a multivariate analysis, troponin elevation was strongly associated with acute myocarditis patterns (OR: 4.98; 95% CI: 1.76-14.05; $P = 0.003$).

CONCLUSIONS In this multicenter study of patients with COVID-19 with clinical suspicion for cardiac involvement referred for CMR, nonischemic and ischemic patterns were frequent when cardiac symptoms, ECG abnormalities, and cardiac biomarker elevations were present. (J Am Coll Cardiol Img 2023;16:609–624) © 2023 by the American College of Cardiology Foundation.

From the [a]Division of Cardiovascular Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; [b]Department of Magnetic Resonance, I Clinic of Cardiology, University of Medical Sciences, Poznan, Poland; [c]St. Francis Hospital, Roslyn, New York, USA; [d]Division of Cardiology, The Ohio State University, Columbus, Ohio, USA; [e]Division of Cardiology, Vanderbilt University Medical Center, Nashville, Tennessee, USA; [f]Biomedical Imaging Science Department, Leeds Institute of Cardiovascular

Since December 2019, the COVID-19 pandemic has spread rapidly across the world, with more than 600 million cases and 6.4 million deaths reported as of August 2022.[1] Although it is well known that COVID-19 results in significant pulmonary disease, several studies have shown that infection with SARS-CoV-2 is also associated with myocardial injury.[2-5] Prior studies have reported heterogeneous cardiac manifestations, including myocarditis,[6-10] myocardial infarction (MI),[11-13] arrhythmias,[2,14,15] stress cardiomyopathy,[7,16,17] and cardiogenic shock.[18] Although the precise pathophysiological mechanisms of myocardial injury remain unclear,[19] it is well established that myocardial injury in patients with COVID-19 is associated with increased morbidity.[20,21] It is therefore crucial to better understand the etiologies of myocardial injury in patients with COVID-19, to provide optimal treatment and monitoring for patients.

Cardiac magnetic resonance (CMR) is a powerful imaging technique for the assessment of cardiac function, morphology, and patterns of myocardial injury. CMR is especially helpful in differentiating between nonischemic and ischemic patterns, through late gadolinium enhancement (LGE) and tissue mapping sequences.[22,23] Previous studies examining CMR findings in patients with COVID-19 detected abnormalities consistent with myocardial inflammation and infarction, but these studies have been limited by small sample sizes and heterogeneous populations by selection and referral biases.[24-27]

Therefore, the objectives of this retrospective, multicenter study were to characterize myocardial injury by CMR in a large cohort of patients with COVID-19 to understand differences in CMR characteristics of myocardial injury in: 1) hospitalized vs ambulatory patients; 2) patients with and without known coronary artery disease (CAD); and 3) patients with and without laboratory evidence of myocardial injury, and investigate factors associated with acute myocarditis and acute ischemic patterns.

METHODS

STUDY POPULATION. We identified patients with polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection referred for CMR at 18 international sites from the United States, Poland, United Kingdom, and Germany (n = 1,051) (Supplemental Table 1). This cohort included all 6 Society for Cardiovascular Magnetic Resonance COVID-19 Registry sites, and 3 general Society for Cardiovascular Magnetic Resonance Registry sites. Each site was requested to contribute at least 20 patients. Athletes undergoing screening CMR as part of their return to play evaluation were excluded. Patients with pacemakers or defibrillators and patients who underwent CMR more than 30 days before their confirmatory SARS-CoV-2 test were excluded from the database (n = 4). This study received approval from each site's institutional review board for retrospective review of patient data and waiver of consent.

DATA COLLECTION. The data coordinating center (DCC) for this study was the University of Pennsylvania. Every site was required to attend a virtual information session, where instructions for collecting the required data were provided. The following clinical data were requested: demographics, time between PCR-confirmed diagnosis of COVID-19 and CMR, presenting symptoms, comorbidities, medications before COVID-19 infection, treatments received

and Metabolic Medicine, University of Leeds, Leeds, United Kingdom; [g]Houston Methodist Heart and Vascular Center, Houston, Texas, USA; [h]Cardiovascular Section, Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut, USA; [i]Department of Internal Medicine/Cardiology, German Heart Center Berlin, Berlin, Germany; [j]School of Biomedical Engineering and Imaging Sciences, Faculty of Life Sciences and Medicine, King's College London, London, United Kingdom; [k]Department of Medicine, Section of Cardiology, University of Chicago Medicine, Chicago, Illinois, USA; [l]Icahn School of Medicine at Mount Sinai, New York, New York, USA; [m]Cardiovascular Division, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA; [n]Division of Cardiovascular Medicine, Radcliffe Department of Medicine, National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC), University of Oxford, Oxford, United Kingdom; [o]Division of Cardiology, Department of Medicine, Weill Cornell Medicine, New York, New York, USA; [p]Cardiovascular Division, Department of Medicine, University of Virginia Health System, Charlottesville, Virginia, USA; [q]Department of Cardiology and Angiology, Contilia Heart and Vascular Centre Elisabeth-Krankenhaus, Essen, Germany; [r]Division of Cardiology, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA; and the [s]Sanger Heart and Vascular Institute, Atrium Health, Charlotte, North Carolina, USA.

for COVID-19, peak values for laboratory studies (including troponin and natriuretic peptides) at the time of COVID-19 presentation or CMR and whether these biomarkers were elevated based on locally defined thresholds, electrocardiogram (ECG) and echocardiogram findings before CMR, and known coronary anatomy (evaluated by coronary angiography or coronary computed tomography angiography) before CMR. The following CMR data were collected: indications for CMR, biventricular function and volumes, LGE presence and pattern, and tissue mapping characteristics. Sites were asked to characterize patterns of myocardial injury as nonischemic (acute myocarditis, nonacute nonischemic, or possible nonischemic) or ischemic (acute ischemic, nonacute ischemic, or possible ischemic). Acute myocarditis patterns required satisfying both of the main Modified Lake Louise criteria for nonischemic myocardial inflammation (1 T1-based criterion [elevated T1 mapping values or LGE] and 1 T2-based criterion [elevated T2 mapping values or abnormal T2-weighted signal]).[28] Patients with clinically suspected acute myocarditis (referred for CMR due to chest pain and an elevated troponin, or an elevated troponin alone) and nonstrict CMR criteria for an acute myocarditis pattern (either 1 T1-based or 1 T2-based criterion), were designated as meeting clinical criteria for acute myocarditis and nonstrict CMR criteria for an acute myocarditis pattern. Nonacute nonischemic patterns were defined as abnormal T1 mapping values or presence of LGE in a nonischemic pattern, with normal T2 mapping values, normal T2-weighted short-tau inversion recovery (T2STIR), or clinical history suggesting a nonacute process. Diagnosis of ischemic patterns required subendocardial or transmural delayed enhancement in a vascular distribution. Acute ischemic injury patterns were defined by clinical history, elevated T2 mapping values, or abnormal T2STIR. Nonacute ischemic injury patterns were defined as an ischemic LGE pattern without clinical history, elevated T2 mapping values, or abnormal T2STIR suggesting an acute clinical process. Patients with nonischemic or ischemic injury patterns in which acuity could not be established were designated as "possible non-ischemic pattern" or "possible ischemic pattern."

DATA ORGANIZATION. A deidentified datasheet was sent to the DCC by each participating site and was assessed for inconsistencies or incomplete data. Queries for clarification were sent to each site's coordinators by the DCC. Datasheets were subsequently compiled and evaluated for incongruous data: 1) if the ejection fraction (EF) field was incomplete, it was calculated from the provided end-systolic and

TABLE 1 Clinical Characteristics and CMR Findings of the Entire Cohort

	N	Mean ± SD or n (%)
Age, y	1,047	47.4 ± 16.5
Female	1,047	497 (47.5)
Race	913	
White		692 (75.8)
Black		136 (14.9)
Asian		41 (4.5)
Multiracial		5 (0.6)
Other		39 (4.3)
Hispanic	807	51 (6.3)
Hospitalized	1,040	377 (36.3)
Intubated	1,034	55 (5.3)
Presenting symptoms		
Dyspnea	846	468 (55.3)
Chest discomfort	820	237 (28.9)
Palpitations	754	92 (12.2)
Syncope	801	28 (3.5)
Shock	802	24 (3.0)
Fevers	782	394 (50.4)
Comorbidities		
Hypertension	988	322 (32.6)
Hyperlipidemia	965	264 (27.4)
Diabetes	977	147 (15.0)
Smoking	821	
Current		46 (5.6)
Former		129 (15.7)
Previously known at least moderate CAD	982	62 (6.3)
Previous myocardial infarction	979	32 (3.3)
Known coronary anatomy	364	
No apparent CAD		270 (74.2)
Obstructive disease		45 (12.4)
Nonobstructive disease		49 (13.5)
Pre-existing cardiomyopathy	961	
Dilated cardiomyopathy		46 (4.8)
Hypertrophic cardiomyopathy		7 (0.7)
Cardiac amyloidosis		1 (0.1)
Cardiac sarcoidosis		2 (0.2)
Prior myocarditis		4 (0.4)
Other		41 (4.3)
Pre-existing respiratory condition	952	
COPD/emphysema		37 (3.9)
Asthma		100 (10.5)
Interstitial lung disease		1 (0.1)
Obstructive sleep apnea		42 (4.4)
Other		15 (1.6)

Continued on the next page

end-diastolic volumes; and 2) patients who had PCR testing after the incident CMR or had no CMR functional parameters were excluded from analysis. Characterization of myocardial injury patterns were checked to ensure that they satisfied the previously described criteria, and queries for clarification were answered by each site's coordinators.

STATISTICAL ANALYSIS. Continuous data are shown as mean ± SD for normally distributed variables and analyzed using the nonpaired Student's *t*-test or

TABLE 1 Continued		
	N	Mean ± SD or n (%)
Pre-COVID-19 medications		
Diuretics	945	95 (10.1)
Beta blockers	970	214 (22.1)
ACEI/ARB	968	200 (20.7)
Statins or other cholesterol medications	971	224 (23.1)
Antiplatelet agents	966	111 (11.5)
Anticoagulation	967	71 (7.3)
Diabetes medications	946	123 (13.0)
Treatment for COVID-19		
Steroids	887	200 (22.6)
Remdesivir	893	95 (10.6)
Monoclonal antibodies	892	42 (4.7)
Therapeutic anticoagulation	898	80 (8.9)
Antiplatelet agents	897	37 (4.1)
Laboratory studies		
Troponin elevation	709	191 (26.9)
NT-proBNP or BNP elevation	584	193 (33.0)
C-reactive protein elevation	595	315 (52.9)
Erythrocyte sedimentation rate elevation	153	64 (41.8)
Lactate dehydrogenase elevation	245	157 (64.1)
D-dimer elevation	543	272 (50.1)

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BNP = B-type natriuretic peptide; CAD = coronary artery disease; CMR = cardiac magnetic resonance; COPD = chronic obstructive pulmonary disease; NT-proBNP = N-terminal pro-B-type natriuretic peptide.

analysis of variance. Categorical variables are shown as total counts with percentages and analyzed using the chi-square test or Fisher's exact test. Statistical significance was defined as $P < 0.05$.

Logistic regression was performed to assess the relationship between various parameters and acute myocarditis/acute ischemic patterns. In univariate models, the factors included in the analysis were age, sex, troponin elevation, natriuretic peptide elevation, ECG/echocardiogram abnormalities, symptoms (chest discomfort, palpitations, dyspnea, fatigue) at the time of CMR, hospitalization status, intubation status, and known CAD (obstructive or nonobstructive CAD). An abnormal ECG was defined as the presence of sinus tachycardia, atrial arrhythmias, ventricular arrhythmias, and/or ST-segment abnormalities. An abnormal echocardiogram was defined as the presence of left ventricular (LV) systolic/diastolic dysfunction, right ventricular (RV) dysfunction, pericardial effusion, and/or valvular abnormalities. Any factor with a $P \leq 0.10$ was included in the multivariate analysis, along with age and sex. All analyses were performed with SAS statistical software (version 9.4, SAS Institute).

RESULTS

CHARACTERISTICS OF THE OVERALL COHORT.
The final study cohort consisted of 1,047 patients who underwent CMR after a PCR-confirmed COVID-19 diagnosis (mean age 47.4 ± 16.5 years, 47.5% women, 75.8% White, 14.9% Black). Baseline clinical characteristics of the entire cohort are shown in Table 1. Comorbidities were most notable for hypertension (32.6%), hyperlipidemia (27.4%), diabetes (15.0%), preexisting cardiomyopathies (10.5%), and preexisting respiratory conditions (20.5%). Nearly all patients (1,046 of 1,047, 99.9%) underwent CMR after a positive COVID-19 result. One patient underwent CMR 3 days before their positive COVID-19 result, because of high suspicion for COVID-19 and myocardial involvement.

In this cohort, 377 of 1,040 (36.3%) patients were hospitalized for COVID-19, including 55 (14.6%) who were intubated. The most common presenting symptoms were dyspnea (55.3%), fever (50.4%), and chest discomfort (28.9%). Laboratory findings were notable for troponin elevation in 191 of 709 patients (26.9%) and elevated natriuretic peptides (N-terminal pro-B-type natriuretic peptide [NT-proBNP] or B-type natriuretic peptide [BNP]) in 193 of 584 patients (33.0%).

The most common indications for CMR were to evaluate for myocardial injury due to COVID-19 (72.1%) or suspected myocarditis (57.1%), further investigate symptoms (dyspnea [43.5%], chest discomfort [36.4%], fatigue [30.8%], and palpitations [28.4%]), assess abnormal findings on ECG (42.7%) and echocardiography (42.8%), and identify the etiology for a troponin elevation (13.8%) (Central Illustration). The mean time from a PCR-confirmed COVID-19 test to CMR was 131.9 ± 94.6 days.

Most CMRs were performed clinically (940 of 1,047; 89.8%), and the remaining were performed for research (107 of 1,047, 10.2%). Only 47 patients (4.5%) did not have a clear indication for CMR, of which 22 were clinical studies and 25 were research studies. Among patients without a clinical indication for CMR, there was 1 patient with an acute myocarditis pattern, and no patients with acute ischemic patterns (Supplemental Table 2). Similarly, myocardial injury patterns were rare in the research group, and no patients demonstrated acute myocarditis or acute ischemic patterns (Supplemental Table 2).

CMR findings for the entire cohort are shown in Table 2. The mean LVEF was 56.6% ± 11.1% and mean RVEF was 54.1% ± 9.4%. The mean LV end-diastolic volume index was 84.2 ± 24.0 mL/m² and the mean RV end-diastolic volume index was 82.3 ± 21.4 mL/m². LGE sequences were performed in 1,039 patients (99.2%) and LGE was present in 403 patients (38.8%), most commonly with midmyocardial (22.4%) and subepicardial (10.0%) patterns. In our cohort, 912

CENTRAL ILLUSTRATION CMR Patterns of Myocardial Injury in Patients With COVID-19 and Suspected Cardiovascular Involvement
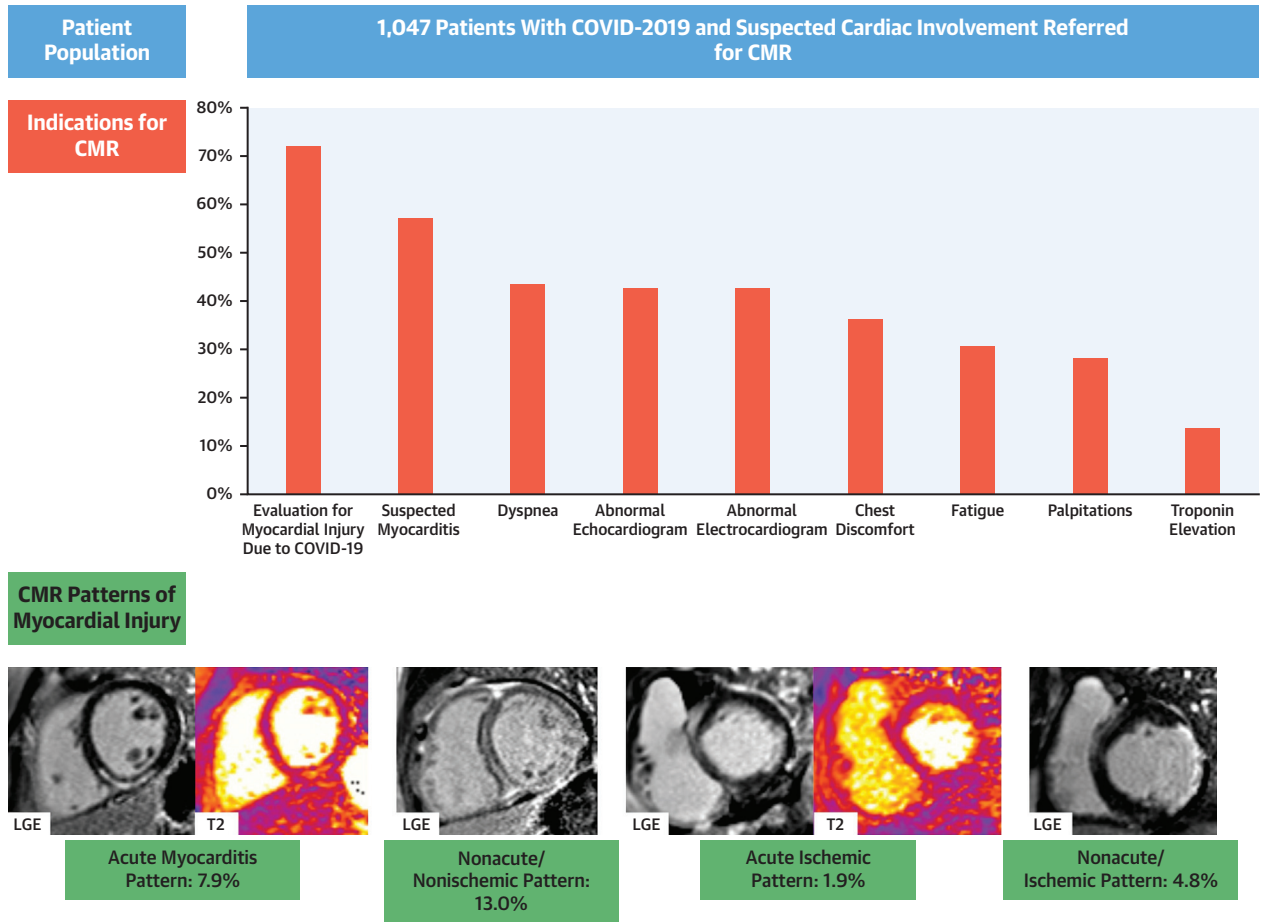
Vidula MK, et al. J Am Coll Cardiol Img. 2023;16(5):609–624.

In this retrospective study of 1,047 patients from 18 international sites with polymerase chain reaction–confirmed COVID-19 infection who underwent cardiac magnetic resonance (CMR) imaging, CMR was performed for a variety of indications **(graph)**. Representative images of the main nonischemic and ischemic patterns of myocardial injury are shown. LGE = late gadolinium enhancement.

patients (87.1%) had either T2 mapping (n = 756) or T2STIR (n = 480).

Overall, 309 patients (29.5%) had nonischemic patterns of myocardial injury, of which 83 patients (7.9%) had an acute myocarditis pattern, 15 (1.4%) met clinical criteria for acute myocarditis and nonstrict CMR criteria for an acute myocarditis pattern, 136 (13.0%) had a nonacute nonischemic pattern, and 75 (7.2%) had a possible nonischemic pattern. All 83 patients with acute myocarditis patterns fulfilled at least 1 T1 criterion (71 [85.5%] with LGE, 52 [62.7%] with elevated T1 mapping values) and 1 T2 criterion (75 [90.4%] with elevated T2 mapping values, 22 [26.5%] with abnormal

TABLE 2 CMR Characteristics of the Entire Cohort

	N	Mean ± SD or n (%)
Clinical presentations		
Chest discomfort	928	338 (36.4)
Palpitations	892	253 (28.4)
Dyspnea	932	405 (43.5)
Fatigue	832	256 (30.8)
Troponin elevation	842	116 (13.8)
Electrocardiogram findings	674	
Sinus tachycardia		82 (12.2)
Atrial arrhythmias		53 (7.9)
Ventricular arrhythmias		57 (8.5)
ST-segment abnormalities		96 (14.2)

TABLE 2 Continued		
	N	Mean ± SD or n (%)
Echocardiogram findings	615	
Left ventricular systolic dysfunction		173 (28.1)
Left ventricular diastolic dysfunction		32 (5.2)
Right ventricular dysfunction		20 (3.3)
Pericardial effusion		22 (3.6)
Valvular abnormalities		16 (2.6)
Evaluation for myocardial injury due to COVID-19	924	666 (72.1)
Suspected myocarditis	766	437 (57.1)
Vital signs before CMR		
Systolic blood pressure, mm Hg	791	127.6 ± 17.4
Diastolic blood pressure, mm Hg	791	76.0 ± 11.1
Heart rate, beats/min	930	76.8 ± 15.3
CMR findings		
Days to CMR	1,047	131.9 ± 94.6
Left ventricular ejection fraction, %	1,039	56.6 ± 11.1
Right ventricular ejection fraction, %	1,018	54.1 ± 9.5
Left ventricular end-diastolic volume, mL	1,041	165.5 ± 54.8
Left ventricular end-diastolic volume index, mL/m^2	1,039	84.2 ± 24.0
Left ventricular end-systolic volume, mL	1,039	75.2 ± 45.6
Left ventricular end-systolic volume index, mL/m^2	1,037	38.0 ± 21.4
Right ventricular end-diastolic volume, mL	1,018	162.0 ± 49.5
Right ventricular end-diastolic volume index, mL/m^2	1,017	82.3 ± 21.4
Right ventricular end-systolic volume, mL	1,018	76.0 ± 34.6
Right ventricular end-systolic volume index, mL/m^2	1,017	38.5 ± 15.6
Left ventricular mass, g	908	110.8 ± 38.4
Left ventricular mass index, g/m^2	907	56.5 ± 18.0
LGE present	1,039	403 (38.8)
LGE type	1,039	
Subepicardial		104 (10.0)
Midmyocardial		233 (22.4)
Subendocardial		66 (6.4)
Extracellular volume, %	728	27.5 ± 6.1
CMR patterns of myocardial injury (overall)	1,047	
Acute myocarditis pattern		83 (7.9)
Clinical criteria for acute myocarditis and nonstrict CMR criteria for acute myocarditis pattern		15 (1.4)
Nonacute nonischemic pattern		136 (13.0)
Possible nonischemic pattern		75 (7.2)
Acute ischemic pattern		20 (1.9)
Nonacute ischemic pattern		50 (4.8)
Possible ischemic pattern		6 (0.6)
CMR patterns of myocardial injury (single diagnoses)	1,047	
Acute myocarditis pattern		76 (7.3)
Clinical criteria for acute myocarditis and nonstrict CMR criteria for acute myocarditis		15 (1.4)
Nonacute nonischemic pattern		131 (12.5)
Possible nonischemic pattern		68 (6.5)
Acute ischemic pattern		15 (1.4)
Nonacute ischemic pattern		40 (3.8)
Possible ischemic pattern		2 (0.2)
CMR patterns of myocardial injury (dual diagnoses)	1,047	
Acute myocarditis pattern + acute ischemic pattern		2 (0.2)
Acute myocarditis pattern + nonacute ischemic pattern		3 (0.3)
Nonacute nonischemic pattern + acute ischemic pattern		1 (0.1)
Nonacute nonischemic pattern + nonacute ischemic pattern		4 (0.4)

CMR = cardiac magnetic resonance; LGE = late gadolinium enhancement.

T2STIR). A total of 76 patients (7.3%) had ischemic patterns of injury, of whom 20 (1.9%) had an acute ischemic pattern, 50 (4.8%) had a nonacute ischemic pattern, and 6 (0.6%) had a possible ischemic pattern. Representative images of CMRs with acute myocarditis and acute ischemic patterns are shown in **Figures 1 and 2**, respectively. Various nonischemic LGE patterns are shown in **Figure 3**.

In the overall cohort, 87 of 1,039 patients (8.4%) had midmyocardial or subepicardial LGE at the RV insertion point, of whom 15 were characterized with acute myocarditis patterns (with corresponding elevated T2 mapping values or abnormal T2STIR in that region), 20 with nonacute nonischemic patterns, 15 with possible nonischemic patterns, and 37 with no myocarditis patterns. Furthermore, the presence of any pattern of LGE was associated with increased biventricular volume (except for RV end-diastolic volume index) and reduced biventricular function (Supplemental Table 3). Nine patients had pericardial LGE, and 22 patients had pericardial effusions on echocardiography. The location of LGE in patients with a single diagnosis of acute myocarditis patterns is shown in Supplemental Table 4, and most patients had subepicardial and midmyocardial involvement of the inferolateral, inferior, and inferoseptal walls.

CHARACTERISTICS OF AMBULATORY AND HOSPITALIZED PATIENTS. Clinical and CMR characteristics of ambulatory (n = 663) and hospitalized (n = 377) patients are shown in **Table 3**. Hospitalized patients were older (53.1 ± 16.2 years vs 44.1 ± 15.7 years, *P* < 0.0001) and had a higher burden of comorbidities (Supplemental Table 5).

Biventricular function, as measured by CMR, was lower in the hospitalized cohort (mean LVEF: 53.7% ± 13.0% vs 58.3% ± 9.5%, *P* < 0.0001; mean RVEF: 52.5% ± 11.0% vs 54.9% ± 8.3%, *P* = 0.0003), but indexed biventricular end-diastolic volumes were similar in both cohorts. LGE was more common in the hospitalized group (46.0% vs 34.5%, *P* = 0.0003), with predominantly midmyocardial LGE in both groups but a higher percentage of subendocardial LGE in the hospitalized group.

Nonischemic patterns of injury were more frequent than ischemic patterns in both cohorts. There was no difference in the frequency of acute myocarditis patterns between the hospitalized and ambulatory patients. However, ischemic patterns were more frequent in the hospitalized cohort than in the ambulatory cohort (**Table 3, Figure 4A**).

Clinical and CMR characteristics of hospitalized patients by intubation status (n = 55) are shown in Supplemental Table 6. Intubated patients had a lower LVEF (50.7% ± 12.4% vs 54.6% ± 12.8%,

FIGURE 1 Representative Images on CMR of Patients With Acute Myocarditis and Nonacute/Nonischemic Patterns
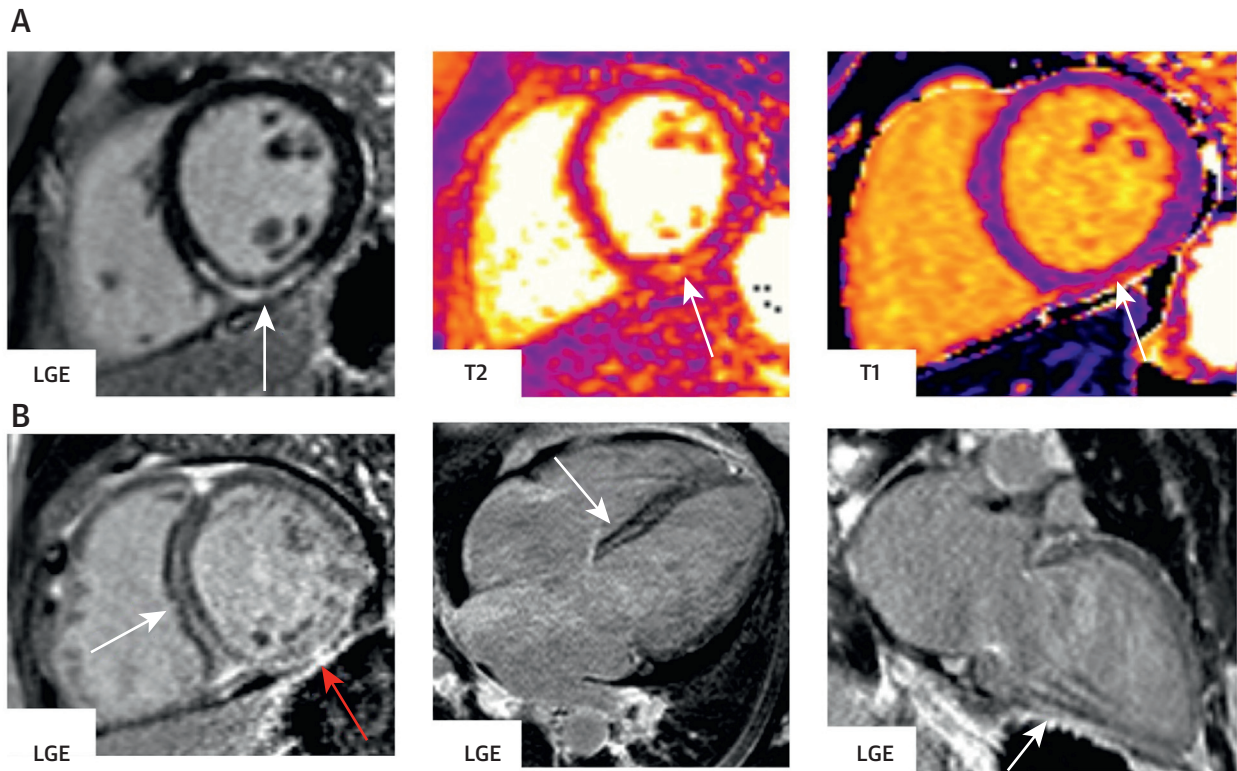
(A) Representative cardiac magnetic resonance (CMR) images of a patient with acute myocarditis pattern in the setting of a recent COVID-19 infection, demonstrating subepicardial late gadolinium enhancement (LGE) in the mid inferior and inferoseptal walls **(left, white arrow)**, with corresponding elevation in native T2 times **(middle, white arrow)** and native T1 times **(right, white arrow)** in the mid inferior wall. **(B)** Representative CMR images of a patient presenting after a prolonged, complicated hospitalization with COVID-19, found to have CMR evidence of nonacute/nonischemic injury, with extensive midmyocardial LGE in the septum **(left, white arrow)** and subepicardial LGE in the inferior and inferolateral walls on the short axis view **(left, red arrow)**. Midmyocardial LGE in the septum is again noted on the 4-chamber view **(middle, white arrow)**, and subepicardial LGE in the inferior wall is noted on the 2-chamber view **(right, white arrow)**.

$P = 0.04$), similar RV function and biventricular volumes, and a similar prevalence and pattern of LGE. Nonischemic patterns and ischemic patterns were not significantly different between the 2 groups (**Figure 4B**).

CHARACTERISTICS OF PATIENTS STRATIFIED BY KNOWN CAD. In this study cohort, coronary anatomy was known in 364 patients. Of these patients, 270 (74.2%) did not have apparent CAD, 45 (12.4%) had obstructive CAD, and 49 (13.5%) had nonobstructive CAD. Clinical and CMR characteristics of this study population, stratified by coronary anatomy, are shown in Supplemental Table 7.

Nonacute nonischemic patterns of injury were more common in patients with no apparent CAD than in patients with either obstructive or nonobstructive CAD. Acute ischemic patterns were more common in

patients with obstructive CAD than in patients with either nonobstructive CAD or no apparent CAD. Nonacute ischemic patterns were significantly more common in patients with obstructive CAD than in patients with nonobstructive CAD or no apparent CAD, and were also more common in patients with nonobstructive CAD than in patients with no apparent CAD (**Figure 4C**).

CHARACTERISTICS OF PATIENTS WITH AND WITHOUT TROPONIN ELEVATION AT THE TIME OF COVID-19 INFECTION OR CMR. Clinical and CMR characteristics of patients with (n = 191) and without (n = 518) troponin elevation at the time of COVID-19 presentation or CMR are shown in **Table 4**.

Biventricular function on CMR was lower in troponin-positive patients compared with troponin-negative patients (LVEF: 50.3% ± 14.1% vs 58.0% ±

FIGURE 2   Representative Images on CMR of Patients With Ischemic Patterns in the Setting of Acute and Prior COVID-19 Infections
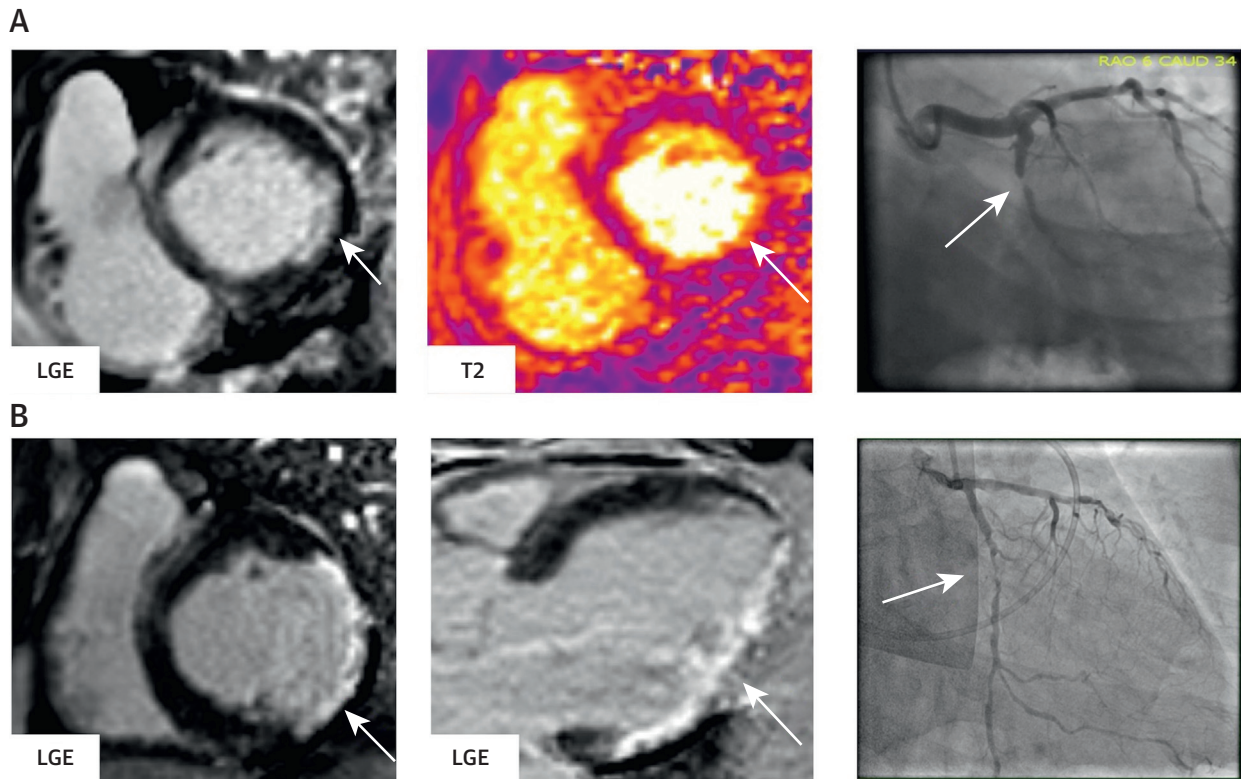
(A) Representative CMR images of a patient presenting with an acute myocardial infarction (MI) in the setting of an active COVID-19 infection, demonstrating sub-endocardial LGE in the basal inferolateral wall on the short axis view **(left, arrow)**, with corresponding elevation in native T2 times **(middle, arrow)**. Coronary angiography **(right)** revealed a 99% proximal left circumflex occlusion **(arrow)**. **(B)** Representative CMR images of a patient presenting 7 months after a COVID-19 infection that was complicated by a medically managed ST-segment elevation MI, with dyspnea and a reduced left ventricular ejection fraction. CMR showed evidence of a large prior infarct in the circumflex territory. There is transmural delayed enhancement in nearly the entire lateral wall, seen on the short axis view **(left, arrow)** and 3-chamber view **(middle, arrow)**. Coronary angiography revealed an 80% stenosis in the mid circumflex **(right, arrow)**, with diffuse distal disease. Abbreviations as in **Figure 1**.

9.4%, $P < 0.0001$; RVEF: 50.8% ± 12.0% vs 53.9% ± 8.7%, $P = 0.002$), and indexed biventricular volumes were larger (LV end-diastolic volume index: 90.7 ± 29.9 mL/m^2 vs 81.7 ± 20.2 mL/m^2, $P = 0.0002$; RV end-diastolic volume index: 85.6 ± 24.9 mL/m^2 vs 81.3 ± 19.0 mL/m^2, $P = 0.03$). LGE was significantly more prevalent in the troponin-positive cohort (61.9% vs 33.4%, $P < 0.0001$).

Compared with the troponin-negative cohort, the troponin-positive cohort was more likely to have evidence of acute myocarditis patterns (18.3% vs 5.8%, $P < 0.0001$), acute ischemic patterns (8.9% vs 0.4%, $P < 0.0001$), and nonacute ischemic patterns (13.6% vs 2.5%, $P < 0.0001$) **(Figure 4D)**.

ASSOCIATION OF VARIOUS FACTORS WITH PATTERNS OF INJURY. In a univariate analysis, variables associated with acute myocarditis patterns included chest discomfort (OR: 2.00; 95% CI: 1.17-3.40, $P = 0.01$), abnormal ECG (OR: 1.90; 95% CI: 1.12-3.23; $P = 0.02$), natriuretic peptide elevation (OR: 2.99; 95% CI: 1.60-5.58; $P = 0.0006$), and troponin elevation (OR: 4.21; 95% CI: 2.41-7.36; $P < 0.0001$). In a multivariate analysis, only troponin elevation was significantly associated with acute myocarditis patterns (OR: 4.98; 95% CI: 1.76-14.05; $P = 0.003$) (Supplemental Table 8).

Factors associated with acute ischemic patterns in a univariate analysis included chest discomfort (OR: 3.14; 95% CI: 1.04-9.49; $P = 0.04$), abnormal ECG (OR:

FIGURE 3 Representative Images of LGE in Patients With Nonischemic Injury Patterns
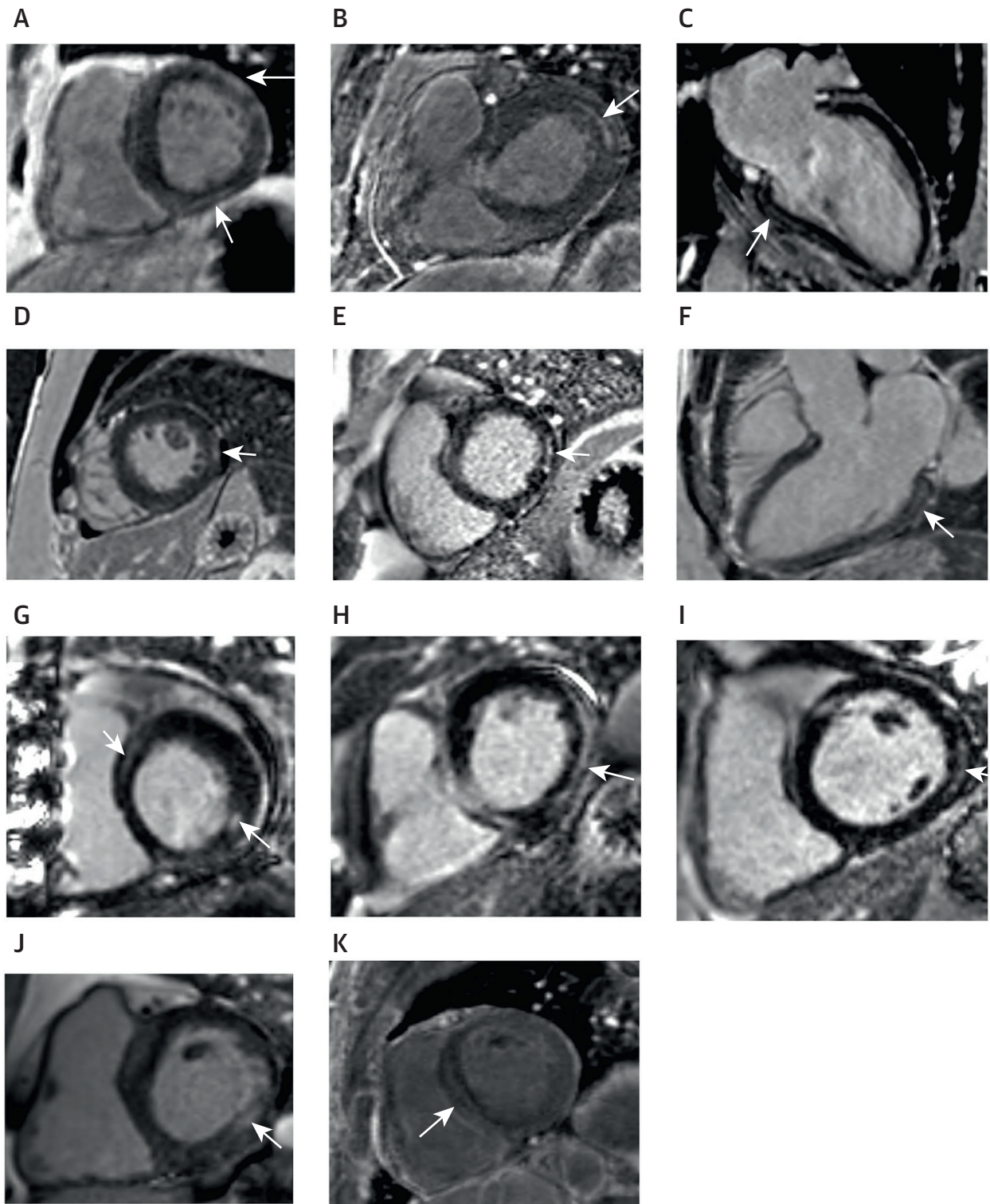
4.06; 95% CI: 1.10-14.92; $P = 0.04$), known coronary disease (OR: 33.30; 95% CI: 4.04-274.53; $P = 0.001$), hospitalization (OR: 4.98; 95% CI: 1.55-16.05; $P = 0.007$), natriuretic peptide elevation (OR: 4.19; 95% CI: 1.30-13.51; $P = 0.02$), and troponin elevation (OR: 25.27; 95% CI: 5.55-115.03; $P < 0.0001$) (Supplemental Table 8). Multivariate analysis was limited by the small number of patients, because of the exclusion of patients with missing data.

DISCUSSION

This is a large, international, multicenter retrospective study of patients with PCR-confirmed COVID-19 and suspected cardiac involvement who underwent CMR. In this study, we characterized myocardial injury by CMR and identified differences in 3 comparison groups: 1) hospitalized vs ambulatory patients; 2) patients with and without known CAD; and 3) patients with and without troponin elevation. In the overall cohort, we found that patterns of myocardial injury were frequent, and were most commonly nonischemic. In addition, we found that nonischemic patterns of injury were detected at similar rates in hospitalized and ambulatory patients, but ischemic patterns were more common in the hospitalized cohort. Our findings also suggest that patients with known obstructive CAD were more likely to have ischemic patterns than patients with either nonobstructive disease or without apparent CAD. Furthermore, we found that both nonischemic and ischemic patterns were more frequently detected in patients with troponin elevation at the time of COVID-19 presentation or CMR. Finally, we identified several clinical factors associated with acute myocarditis and acute ischemic patterns on CMR. These findings further our understanding of the

characteristics and patterns of myocardial injury in patients with COVID-19.

The overall cohort represents a large patient population from across the United States, Poland, the United Kingdom, and Germany, with heterogeneous comorbidities and COVID-19 manifestations. This cohort consists of a patient population with a high likelihood of cardiac involvement by COVID-19, as most patients (1,000 of 1,047; 95.5%) underwent CMR for further evaluation of cardiac symptoms, abnormalities on echocardiography or ECG, further investigation of an elevated troponin, or because of high clinical suspicion of myocardial involvement or myocarditis. This study cannot determine the overall prevalence of specific types of myocardial injury in all patients with COVID-19. It remains unclear whether the abnormalities observed can be attributed to COVID-19, because we do not have CMR data for these patients before their diagnosis with COVID-19. In addition, questions remain regarding the prognostic significance of these findings, for which long-term follow-up data will be required.

In our analysis of patients hospitalized with COVID-19, the rates of nonischemic patterns of injury, and specifically acute myocarditis patterns, were similar when compared with patients who were treated in the ambulatory setting, which is concordant with a prior study.[24] However, hospitalized patients were significantly more likely to have CMR evidence of ischemic injury, including acute ischemic injury patterns. The differences in these patterns of injury may be related to the burden of comorbidities in the hospitalized and ambulatory cohorts. Similar to prior studies,[14,29] the hospitalized patients in our analysis had a high burden of comorbidities and cardiovascular risk factors, which likely increased their risk for experiencing an acute or prior MI.

FIGURE 3 Continued

(A) Patient with patchy subepicardial late gadolinium enhancement (LGE) in the basal anterolateral wall and midmyocardial LGE in the basal inferior wall **(arrows)**, with corresponding elevated T1 and T2 mapping values in those regions, consistent with acute inflammation. **(B)** Patient with subepicardial LGE in the basal anterolateral wall **(arrow)**, with corresponding elevated T1 and T2 mapping values in that region, consistent with acute inflammation. **(C)** Patient with subepicardial LGE involving the basal to mid inferior wall **(arrow)**, with normal T2 mapping values in that region, consistent with nonacute nonischemic injury. **(D)** Patient with a small focus of subepicardial LGE in the mid inferolateral wall **(arrow)**, with normal T2 mapping values in that region, consistent with nonacute nonischemic injury. **(E)** Patient with a small focus of midmyocardial LGE in the basal inferolateral wall **(arrow)**, with normal T2 mapping values in that region, consistent with nonacute nonischemic injury. **(F)** Patient with midmyocardial LGE in the basal inferolateral wall **(arrow)**, with elevated T1 and T2 mapping values in that region, consistent with acute inflammation. **(G)** Patient with midmyocardial LGE in the basal anteroseptum and basal inferolateral wall **(arrows)**, with elevated T1 and T2 mapping values in those regions, consistent with acute inflammation. **(H)** Patient with subepicardial LGE involving the basal inferolateral wall and inferior wall **(arrow)**, with normal T2 mapping values in that region, consistent with nonacute nonischemic injury. **(I)** Patient with subepicardial LGE in the basal inferolateral wall **(arrow)**, with elevated T1 and T2 mapping values in those regions, consistent with acute inflammation. **(J)** Patient with midmyocardial LGE involving the basal inferolateral wall **(arrow)**, with normal T2 mapping values in that region, consistent with nonacute nonischemic injury. **(K)** Patient with midmyocardial LGE involving the basal to mid septum **(arrow)**, with normal T2 mapping values in that region, consistent with nonacute nonischemic injury.

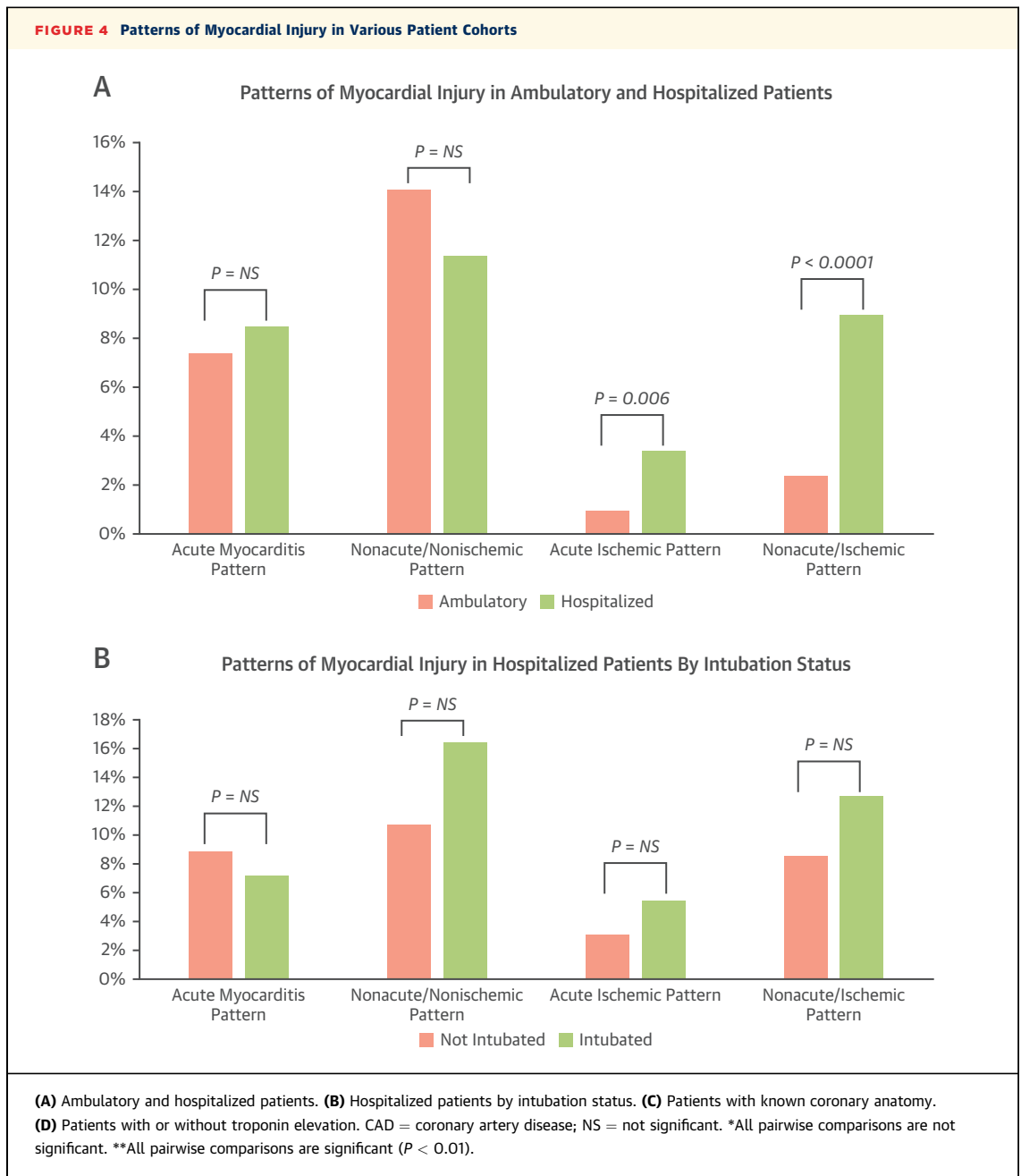**TABLE 3 Clinical and CMR Characteristics of the Ambulatory and Hospitalized Cohorts**

	Ambulatory (n = 663)	Hospitalized (n = 377)	*P* Value
Age, y	44.1 ± 15.7	53.1 ± 16.2	<0.0001
Female	351 (52.9)	144 (38.2)	<0.0001
Race			<0.0001
White	469 (82.3)	218 (64.5)	
Black	65 (11.4)	71 (21.0)	
Asian	14 (2.5)	27 (8.0)	
Multiracial	3 (0.5)	2 (0.6)	
Other	19 (3.3)	20 (5.9)	
Hispanic	28 (5.3)	23 (8.3)	0.13
CMR findings			
Days to CMR	133.6 ± 90.1	128.1 ± 102.0	0.39
LV ejection fraction, %	58.3 ± 9.5	53.7 ± 13.0	<0.0001
RV ejection fraction, %	54.9 ± 8.3	52.5 ± 11.0	0.0003
LV end-diastolic volume, mL	162.7 ± 51.9	170.3 ± 59.5	0.039
LV end-diastolic volume index, mL/m^2	83.6 ± 21.9	85.0 ± 27.1	0.40
LV end-systolic volume, mL	70.3 ± 38.3	83.7 ± 55.3	<0.0001
LV end-systolic volume index, mL/m^2	36.0 ± 17.6	41.6 ± 26.5	0.0003
RV end-diastolic volume, mL	161.0 ± 48.0	164.2 ± 52.1	0.33
RV end-diastolic volume index, mL/m^2	82.7 ± 20.9	81.7 ± 22.2	0.49
RV end-systolic volume, mL	73.6 ± 29.2	80.6 ± 42.3	0.005
RV end-systolic volume index, mL/m^2	37.7 ± 13.4	39.9 ± 18.9	0.045
LV mass, g	106.8 ± 35.6	117.2 ± 41.8	0.0002
LV mass index, g/m^2	54.8 ± 14.2	59.1 ± 22.7	0.002
LGE presence	227 (34.5)	172 (46.0)	0.0003
LGE type			<0.0001
None	431 (65.5)	202 (54.0)	
Subepicardial	68 (10.3)	35 (9.4)	
Midmyocardial	138 (21.0)	93 (24.9)	
Subendocardial	21 (3.2)	44 (11.8)	
Extracellular volume, %	26.8 ± 5.5	28.8 ± 6.9	<0.0001
CMR patterns of myocardial injury			
Nonischemic patterns			0.29
None	475 (71.6)	266 (70.6)	
Acute myocarditis pattern	49 (7.4)	32 (8.5)	
Nonacute nonischemic pattern	93 (14.0)	43 (11.4)	
Possible nonischemic pattern	46 (6.9)	36 (9.5)	
Ischemic patterns			<0.0001
None	638 (96.2)	326 (86.5)	
Acute ischemic pattern	6 (0.9)	13 (3.4)	
Nonacute ischemic pattern	16 (2.4)	34 (9.0)	
Possible ischemic pattern	3 (0.5)	4 (1.1)	

Values are mean ± SD or n (%).
LV = left ventricle; RV = right ventricle; other abbreviations as in Table 2.

Furthermore, MI is a serious event often requiring hospitalization, which may also explain the higher rate of ischemic injury in the hospitalized cohort. Interestingly, rates of acute myocarditis patterns were similar in both groups, suggesting that baseline comorbidities are not significant risk factors for developing myocardial inflammation. It is also possible that the patients who were hospitalized had reduced cardiac reserve to tolerate nonischemic injury because of their higher burden of comorbidities. In addition, the similar rates of acute myocarditis patterns or nonacute nonischemic patterns in hospitalized patients who were intubated and those who were not intubated suggests that severity of pulmonary involvement of COVID-19 is unlikely to be a risk factor for myocardial inflammation. Indeed, hospitalization status and intubation status were not factors that were significantly associated with acute
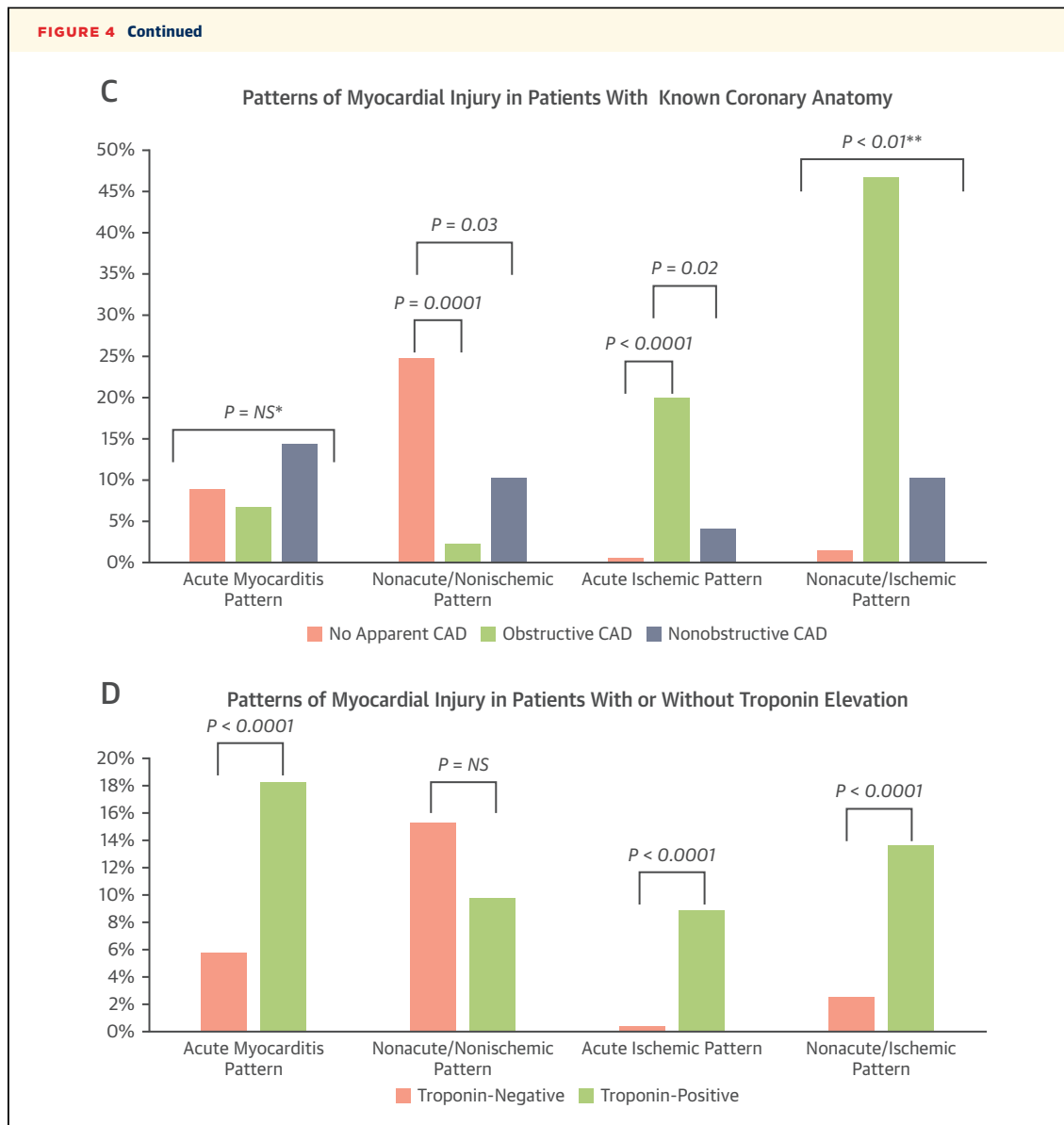
FIGURE 4   Patterns of Myocardial Injury in Various Patient Cohorts

(A) Ambulatory and hospitalized patients. (B) Hospitalized patients by intubation status. (C) Patients with known coronary anatomy. (D) Patients with or without troponin elevation. CAD = coronary artery disease; NS = not significant. *All pairwise comparisons are not significant. **All pairwise comparisons are significant (P < 0.01).

myocarditis patterns in our regression analyses. It is important to note that compared with a prior study by Puntmann et al,[24] our study found lower incidence of nonischemic injury, possibly because of the significantly larger sample size in this study, referral bias for CMR, reference standards of mapping, and differences in evaluation of nonischemic injury.

When stratified by known coronary disease, ischemic injury patterns were significantly more common in patients with known obstructive disease, but these ischemic patterns also occurred in patients with nonobstructive disease and patients without apparent CAD. Although patients with obstructive CAD are known to be at higher risk for type I and type II MIs, patients with nonobstructive CAD or without apparent CAD may experience acute coronary syndromes through a variety of previously proposed mechanisms, such as development of a

FIGURE 4 Continued

C Patterns of Myocardial Injury in Patients With Known Coronary Anatomy

No Apparent CAD   Obstructive CAD   Nonobstructive CAD

D Patterns of Myocardial Injury in Patients With or Without Troponin Elevation

Troponin-Negative   Troponin-Positive

proinflammatory state resulting in plaque rupture and thrombus formation, direct viral injury of the endothelium, thromboembolism, or coronary spasm.[30] Nonischemic patterns of injury were more common in patients without apparent CAD, further suggesting that known cardiovascular disease or risk factors may not elevate the risk of developing myocardial inflammation in the setting of COVID-19.

We also stratified patients by troponin elevation and found that both nonischemic and ischemic patterns of injury were frequent in this cohort. Non-ischemic injury was present in 37.7% of patients with elevated troponin levels, and ischemic injury was present in 25.1%. These rates are slightly higher than those reported in a prior smaller study of 148

troponin-positive patients, which found myocarditis-like injury in 26% of patients and MI in 19%.[31] In addition, a proportion of patients without troponin elevation were diagnosed with acute myocarditis patterns (5.8%), suggesting that biomarker elevation may not always be present or identified in patients with CMR evidence of acute nonischemic myocardial inflammation. Understanding the prognosis of these patients will be critical to guide further therapy and monitoring.

Finally, we identified several clinical variables associated with findings of acute myocarditis patterns and acute ischemic patterns on CMR, which may help guide clinicians in deciding which patients may benefit from further investigation with CMR. Based

TABLE 4 Clinical and CMR Characteristics of Troponin-Negative and Troponin-Positive Patients

	Troponin-Negative (n = 518)	Troponin-Positive (n = 191)	P Value
Age, y	46.6 ± 16.2	51.3 ± 18.5	0.002
Female	259 (50.0)	62 (32.5)	<0.0001
Race			<0.0001
White	372 (78.5)	88 (54.0)	
Black	63 (13.3)	47 (28.8)	
Asian	22 (4.6)	11 (6.7)	
Multiracial	1 (0.2)	3 (1.8)	
Other	16 (3.4)	14 (8.6)	
Hispanic	23 (5.4)	14 (9.8)	0.08
CMR findings			
Days to CMR	130.7 ± 86.6	109.8 ± 109.2	0.02
LV ejection fraction, %	58.0 ± 9.4	50.3 ± 14.1	<0.0001
RV ejection fraction, %	53.9 ± 8.7	50.8 ± 12.0	0.002
LV end-diastolic volume, mL	160.6 ± 48.4	182.0 ± 67.5	<0.0001
LV end-diastolic volume index, mL/m^2	81.7 ± 20.2	90.7 ± 29.9	0.0002
LV end-systolic volume, mL	69.9 ± 37.6	95.8 ± 61.4	<0.0001
LV end-systolic volume index, mL/m^2	35.4 ± 16.9	47.5 ± 29.4	<0.0001
RV end-diastolic volume, mL	159.9 ± 45.0	172.4 ± 58.6	0.009
RV end-diastolic volume index, mL/m^2	81.3 ± 19.0	85.6 ± 24.9	0.03
RV end-systolic volume, mL	74.8 ± 29.6	87.8 ± 48.1	0.0007
RV end-systolic volume index, mL/m^2	37.9 ± 13.0	43.5 ± 21.6	0.001
LV mass, g	106.8 ± 33.8	124.6 ± 46.0	<0.0001
LV mass index, g/m^2	54.2 ± 13.4	63.9 ± 27.6	<0.0001
LGE present	172 (33.4)	117 (61.9)	<0.0001
LGE type			<0.0001
None	343 (66.6)	73 (38.1)	
Subepicardial	57 (11.1)	23 (12.2)	
Midmyocardial	102 (19.8)	53 (28.0)	
Subendocardial	13 (2.5)	41 (21.7)	
Extracellular volume, %	27.3 ± 5.5	29.9 ± 7.4	0.0005
CMR patterns of myocardial injury			
Nonischemic patterns			<0.0001
None	371 (71.6)	119 (62.3)	
Acute myocarditis pattern	30 (5.8)	35 (18.3)	
Nonacute nonischemic pattern	79 (15.3)	19 (9.9)	
Possible nonischemic pattern	38 (7.3)	18 (9.4)	
Ischemic patterns			<0.0001
None	503 (97.1)	143 (74.9)	
Acute ischemic pattern	2 (0.4)	17 (8.9)	
Nonacute ischemic pattern	13 (2.5)	26 (13.6)	
Possible ischemic pattern	0 (0)	5 (2.6)	

Values are mean ± SD or n (%).
Abbreviations as in **Tables 2 and 3**.

on this analysis, CMR may identify acute myocarditis or acute ischemic patterns in patients with certain cardiac symptoms, specifically chest discomfort or abnormal ECG findings, and in patients with troponin elevation or natriuretic peptide elevation. On the other hand, CMR may not be as helpful if there is no or low concern for cardiac involvement, as seen by the very low yield of injury patterns in the research cohort and in the group of patients without definite clinical suspicion for cardiac involvement.

Our study should be considered in the context of its strengths and limitations. The strengths of this study include the large sample size and the inclusion of patients who underwent CMR for high suspicion of myocardial involvement by COVID-19. There are also limitations. First, in this retrospective study of a selected cohort of patients, we are unable to define the prevalence of myocardial injury in patients with COVID-19 because of the referral bias of the included population. However, we provide characterization of

myocardial injury in patients with high likelihood of cardiac involvement, which can help inform clinical practice. Second, a proportion of these CMR findings may have been preexisting or unrelated to COVID-19 infection, and a causal relationship to COVID-19 cannot be established. Third, study center differences were not evaluated. Fourth, for this retrospective analysis, we did not standardize CMR imaging protocols for the detection of myocardial injury (such as uniform performance of tissue mapping sequences vs T2STIR sequences), and we relied on each site's own expertise to determine the patterns of myocardial injury and diagnose myocarditis based on the Modified Lake Louise criteria. Although the CMR findings and diagnoses were not adjudicated, this is a real-world situation with expert CMR physicians making clinical diagnoses based on their assessment of the CMR images that were obtained locally. Furthermore, in this real-world study, there was significant variation in the time from COVID diagnosis to CMR, likely due to a variety of factors including acuity of illness, scanner availability, and ability to undergo CMR, thereby potentially limiting the ability to detect acute edema. In addition, CMR scans were not systematically reviewed for pericardial effusion, therefore limiting this study's contributions to the understanding of pericardial abnormalities in COVID-19. Finally, sparse outcomes were reported and therefore the prognostic value of the CMR findings could not be reported. Future studies should focus on the prognostic value of myocardial injury in patients with COVID-19.

CONCLUSIONS

In this large, international, multicenter CMR study, we characterized myocardial injury in patients with PCR-confirmed COVID-19 and suspicion for cardiac involvement. We found that nonischemic and ischemic injury patterns are frequent in this patient cohort across various patient subgroups, and identified clinical variables associated with acute myocarditis and acute ischemic patterns. These findings further our understanding of the characteristics and patterns of myocardial injury in patients diagnosed with COVID-19, and future studies are required to understand the prognostic significance of these findings.

ADDRESS FOR CORRESPONDENCE: Dr Yuchi Han, The Ohio State University, Biomedical Research Tower, Room 216, 460 West 12th Avenue, Columbus, Ohio 43210, USA. E-mail: yuchi.han@osumc.edu.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Nonischemic and ischemic patterns of injury are frequently identified on CMR in patients with COVID-19 and suspected cardiac involvement, especially in patients with cardiac symptoms, ECG abnormalities, and biomarker elevations.

TRANSLATIONAL OUTLOOK: Patients with COVID-19 with clinical findings including cardiac symptoms, ECG abnormalities, and biomarker elevations are at higher risk of having CMR findings consistent with acute myocarditis or acute infarction. Further studies with longer-term follow-up are required to identify the prognostic significance of the nonischemic and ischemic patterns of injury identified in this cohort of patients with COVID-19.

REFERENCES

1. COVID-19 Map. Johns Hopkins Coronavirus Resource Center. Accessed January 10, 2022. https://coronavirus.jhu.edu/map.html

2. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol.* 2020;5(7):811. https://doi.org/10.1001/jamacardio.2020.1017

3. 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;5(7):802. https://doi.org/10.1001/jamacardio.2020.0950

4. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: a review. *JAMA Cardiol.* 2020;5(7):831. https://doi.org/10.1001/jamacardio.2020.1286

5. Kang Y, Chen T, Mui D, et al. Cardiovascular manifestations and treatment considerations in COVID-19. *Heart.* 2020;106(15):1132–1141. https://doi.org/10.1136/heartjnl-2020-317056

6. Inciardi RM, Lupi L, Zaccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol.* 2020;5(7):819. https://doi.org/10.1001/jamacardio.2020.1096

7. Fried JA, Ramasubbu K, Bhatt R, et al. The variety of cardiovascular presentations of COVID-19. *Circulation.* 2020;141(23):1930–1936. https://doi.org/10.1161/CIRCULATIONAHA.120.047164

8. Hu H, Ma F, Wei X, Fang Y. Coronavirus fulminant myocarditis treated with glucocorticoid and human immunoglobulin. *Eur Heart J.* 2021;42(2):206–206. https://doi.org/10.1093/eurheartj/ehaa190

9. Basso C, Leone O, Rizzo S, et al. Pathological features of COVID-19-associated myocardial injury: a multicentre cardiovascular pathology study. *Eur Heart J.* 2020;41(39):3827–3835. https://doi.org/10.1093/eurheartj/ehaa664

10. Halushka MK, Vander Heide RS. Myocarditis is rare in COVID-19 autopsies: cardiovascular findings across 277 postmortem examinations. *Cardiovasc Pathol.* 2021;50:107300. https://doi.org/10.1016/j.carpath.2020.107300

11. Garcia S, Dehghani P, Grines C, et al. Initial findings from the North American COVID-19 Myocardial Infarction Registry. *J Am Coll Cardiol*. 2021;77(16):1994–2003. https://doi.org/10.1016/j.jacc.2021.02.055

12. Rothstein ES, Welch TD, Andrus BW, Jayne JE. Management of a patient presenting with anterior STEMI with concomitant COVID-19 infection early in the course of the U.S. pandemic. *Catheter Cardiovasc Interv*. 2021;97(3):E333-E338. https://doi.org/10.1002/ccd.28967

13. Salido-Tahoces L, Sánchez-Recalde A, Pardo-Sanz A, Zamorano Gómez JL. Unusual presentation of acute coronary syndrome in a patient with SARS-CoV-2 infection. *Eur Heart J Cardiovasc Imaging*. 2020;21(9):1053-1053. https://doi.org/10.1093/ehjci/jeaa147

14. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061. https://doi.org/10.1001/jama.2020.1585

15. Du Y, Tu L, Zhu P, et al. Clinical features of 85 fatal cases of COVID-19 from Wuhan. A retrospective observational study. *Am J Respir Crit Care Med*. 2020;201(11):1372-1379. https://doi.org/10.1164/rccm.202003-0543OC

16. Sala S, Peretto G, Gramegna M, et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. *Eur Heart J*. 2020;41(19):1861-1862. https://doi.org/10.1093/eurheartj/ehaa286

17. Meyer P, Degrauwe S, Van Delden C, Ghadri JR, Templin C. Typical Takotsubo syndrome triggered by SARS-CoV-2 infection. *Eur Heart J*. 2020;41(19):1860-1860. https://doi.org/10.1093/eurheartj/ehaa306

18. Tavazzi G, Pellegrini C, Maurelli M, et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. *Eur J Heart Fail*. 2020;22(5):911-915. https://doi.org/10.1002/ejhf.1828

19. Bhatt AS, Adler ED, Albert NM, et al. Coronavirus disease-2019 and heart failure: a scientific statement from the Heart Failure Society of America. *J Card Fail*. 2022;28(1):93-112. https://doi.org/10.1016/j.cardfail.2021.08.013

20. Lala A, Johnson KW, Januzzi JL, et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. *J Am Coll Cardiol*. 2020;76(5):533-546. https://doi.org/10.1016/j.jacc.2020.06.007

21. Smilowitz NR, Jethani N, Chen J, et al. Myocardial injury in adults hospitalized with COVID-19. *Circulation*. 2020;142(24):2393-2395. https://doi.org/10.1161/CIRCULATIONAHA.120.050434

22. Agewall S, Beltrame JF, Reynolds HR, et al. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. *Eur Heart J*. 2017;38(3):143-153. https://doi.org/10.1093/eurheartj/ehw149

23. Cosyns B, Lochy S, Luchian ML, et al. The role of cardiovascular imaging for myocardial injury in hospitalized COVID-19 patients. *Eur Heart J Cardiovasc Imaging*. 2020;21(7):709-714. https://doi.org/10.1093/ehjci/jeaa136

24. 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(11):1265. https://doi.org/10.1001/jamacardio.2020.3557

25. Huang L, Zhao P, Tang D, et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. *J Am Coll Cardiol Img*. 2020;13(11):2330-2339. https://doi.org/10.1016/j.jcmg.2020.05.004

26. Salerno M, Kwong RY. CMR in the era of COVID-19. *J Am Coll Cardiol Img*. 2020;13(11): 2340-2342. https://doi.org/10.1016/j.jcmg.2020.06.013

27. Petersen SE, Friedrich MG, Leiner T, et al. Cardiovascular magnetic resonance for patients with COVID-19. *J Am Coll Cardiol Img*. 2022;15(4):685-699. https://doi.org/10.1016/j.jcmg.2021.08.021

28. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular magnetic resonance in non-ischemic myocardial inflammation. *J Am Coll Cardiol*. 2018;72(24):3158-3176. https://doi.org/10.1016/j.jacc.2018.09.072

29. Inciardi RM, Adamo M, Lupi L, et al. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. *Eur Heart J*. 2020;41(19):1821-1829. https://doi.org/10.1093/eurheartj/ehaa388

30. Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nat Rev Cardiol*. 2020;17(9):543-558. https://doi.org/10.1038/s41569-020-0413-9

31. 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:(ehab075). https://doi.org/10.1093/eurheartj/ehab075