Received: 16 October 2022 | Revised: 24 November 2022 | Accepted: 28 November 2022

DOI: 10.1002/jcu.23416

RESEARCH ARTICLE

WILEY

Cardiac magnetic resonance findings in acute and post-acute COVID-19 patients with suspected myocarditis

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Abstract

Introduction: Cardiac injury is commonly reported in COVID-19 patients, resulting associated to pre-existing cardiovascular disease, disease severity, and unfavorable outcome. Aim is to report cardiac magnetic resonance (CMR) findings in patients with myocarditis-like syndrome during the acute phase of SARS-CoV-2 infection (AMCovS) and post-acute phase (cPACS).

Methods: Between September 2020 and January 2022, 39 consecutive patients (24 males, 58%) were referred to our department to perform a CMR for the suspicion of myocarditis related to AMCovS ($n = 17$) and cPACS ($n = 22$) at multimodality evaluation (clinical, laboratory, ECG, and echocardiography).

CMR was performed for the assessment of volume, function, edema and fibrosis with standard sequences and mapping techniques. CMR diagnosis and the extension and amount of CMR alterations were recorded.

Results: Patients with suspected myocarditis in acute and post-COVID settings were mainly men (10 (59%) and 12 (54.5%), respectively) with older age in AMCovS (58 [48–64]) compared to cPACS (38 [26–53]). Myocarditis was confirmed by CMR in most of cases: 53% of AMCovS and 50% of cPACS with negligible LGE burden (3 [IQR, 1–5] % and 2 [IQR, 1–4] %, respectively).

Myocardial infarction was identified in 4/17 (24%) patients with AMCovS. Cardiomyopathies were identified in 12% (3/17) and 27% (6/22) of patients with AMCovS and cPACS, including DCM, HCM and mitral valve prolapse.

Conclusions: In patients with acute and post-acute COVID-19 related suspected myocarditis, CMR improves diagnostic accuracy characterizing ischemic and non-ischemic injury and unraveling subclinical cardiomyopathies.

Abbreviations: cACS, cardiac acute COVID-19 syndrome; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CMR, cardiac magnetic resonance; cPACS, cardiac post-acute COVID-19 syndrome; HCM, hypertrophic cardiomyopathy; hs-cTn, high-sensitivity cardiac troponins; DCM, idiopathic dilated cardiomyopathy.

KEYWORDS
arrhythmia, cardiac magnetic resonance, COVID-19, infarction, myocarditis

1 | INTRODUCTION

Cardiovascular injury is a common event in patients affected by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection.[1] This is due by the coexistence of direct and indirect organ damage. Indeed, the angiotensin-converting enzyme 2 (ACE-2) receptor in expressed not only in the pulmonary tissue[2] but in many other organs, including the heart and the vascular system[3,4] being responsible of direct cytotoxic damage. Additionally, a wide pool of indirect mechanisms including the cytokine storm, the mismatch in oxygen demand and supply, and the vascular damage due to endotheliitis and thrombosis[5,6] can cause a wide range of cardiac injury including myocardial inflammation, ischemia and dysfunction.

In hospitalized COVID-19 patients, several acute cardiovascular complications and test alteration (electrocardiographic, ECG, and cardiac biomarkers) have been reported,[7,8] resulting associated to severity of diseases and higher rate of unfavorable events.[6]

On the other hand, some patients infected with SARS-CoV-2 complain the persistence of chest pain, dyspnea, fatigue, and palpitations weeks and months after the initial illness (cardiac post-acute COVID-19 Syndrome, cPACS).[9]

Although high-sensitivity cardiac troponins (hs-cTn) is highly sensitive for myocardial damage, cardiac magnetic resonance (CMR) allows to non-invasively characterizing the myocardial involvement also with the capability to detect occult cardiac involvement.[10]

Aim of the present study is to report CMR findings in patients with suspected myocarditis during the acute phase of SARS-CoV-2 infection (AMCovS) and with persistence of cardiovascular symptoms in post-acute COVID-19 phase (cPACS).

2 | MATERIALS AND METHODS

2.1 | Study population

In this single center retrospective study, we collected data of consecutive patients with RT-PCR confirmed COVID-19 infection[11] who underwent 1.5 T cardiac Magnetic Resonance Imaging from September 2020 to January 2022 for the clinical suspicion of COVID-19 related myocarditis during the acute phase (AMCovS) and post-acute phase (more than four weeks after recovery) (cPACS). Clinical suspicion of cardiac injury was based on the evidence of (1) symptoms (chest pain, shortness of breath, dyspnea, palpitation, and arrhythmias), (2) high-sensitivity cardiac troponin T (hs-cTnT) rise not reaching the diagnostic criteria for myocardial infarction, and (3) abnormal ECG and/or echocardiography not suggestive for myocardial infarction.[9]

We collected detailed medical history for each patient from electronic patient records including anthropometric parameters, cardiovascular comorbidities, and laboratory data during COVID-19 disease for AMCovS and at time of CMR study for cPACS.

The study was approved by the Ethic Committee (protocol no. 34/int/2020) and written informed consent was obtained.

2.2 | Cardiac MRI protocol

Cardiac MRI was performed on a 1.5 T system (Achieva dStream; Philips Medical Systems, Eindhoven, the Netherlands) equipped with a 32-channel phased-array coil. T2 short-tau inversion-recovery (STIR) images were acquired using body coil. Detailed CMR protocol has been previously reported.[12]

Briefly, the protocol included cine steady-state free precession (cine-SSFP) images for the assessment of wall motion alteration and cardiac chambers volumes and function, STIR images and T2 mapping for the assessment of focal and diffuse edema, LGE imaging for the identification of myocardial scars, and native and post-contrast T1 for the assessment of extracellular volume fraction.

2.3 | Cardiac MRI analysis

All CMR studies were analyzed by two experienced observers in consensus (5 and 10 years of experience in cardiac imaging, respectively) using a dedicated cardiac analysis software (CVI42 v.5.6.6, Circle Cardiovascular Imaging, Calgary, Canada).

Focal myocardial edema was assessed on STIR images qualitatively as focal myocardial hyperintensity and semi-quantitatively (T2-ratio, positive >1.9).

Native T1 and T2 maps were analyzed drawing endocardial and epicardial contours on the 3 short-axis (base, mid-ventricle, apex) slices with a 10% automatic offset from borders aimed to minimizing partial volume effect.

LV end-diastolic volume (LVEDV), LV ejection fraction (LVEF) and LV mass were calculated after manual correction of automatic segmentation of the endocardial and epicardial contours in the end-diastolic and end-systolic short-axis cine-SSFP images.

Myocardial segments involved by LGE and its transmural pattern was reported. The percentage of myocardial mass involved by LGE quantified according to FWHM method.

ECV was calculated according to the following formula: $ECV = (1 - \text{hematocrit}) \times [\Delta R1\text{myocardium}]/[\Delta R1\text{blood-pool}]$, where $\Delta R1$ is the difference in pre- and post-contrast relaxation rates (1/T1).

Categorical and data continuous variables are reported as frequencies or percentages and as median and interquartile range [IQR], respectively.

3 | RESULTS

Between September 2020 and January 39, 2022 consecutive patients (24 males, 61.5%) were referred to our department to perform a CMR for the suspicion of myocarditis related to AMCovS ($n = 17$) or cPACS ($n = 22$) at multimodality evaluation (clinical, laboratory, ECG, and echocardiography).

Patient clinical features are listed in Table 1.

TABLE 1 Clinical and laboratory characteristics

	AMCovS patients ($n = 17$)	cPACS patients ($n = 22$)
Age, median (IQR), years	58 (48–64)	38 (26–53)
Body surface area, kg/m^2	1.82 (1.7–1.96)	1.95 (1.72–2.16)
Gender, male	10 (59%)	12 (54.5%)
Time between positive swab and CMR, days	6.5 (5–21)	68.0 (40.0–212.0)
Cardiovascular symptoms, *N* (%)		
Dyspnea	2 (12%)	10 (45%)
Chest pain	12 (71%)	12 (54.5%)
Arrhythmia	1 (6%)	13 (59%)
Cardiogenic shock	3 (18%)	0 (0%)
EKG alteration		
ST elevation	5 (29%)	-
Non-specific ST-T changes	9 (53%)	4 (18%)
Atrial fibrillation	1 (6%)	2 (9%)
Ventricular ectopic beat	-	10 (45%)
TT echocardiography		
Biventricular dysfunction (FE < 40%)	3 (18%)	2 (9%)
Wall motion alteration	7 (41%)	4 (18%)
Isolated left ventricle dysfunction (FE < 50%)	4 (23.5%)	1 (4.5%)
COVID-19 pneumonia severity, *N* (%)		
Mild	10 (59%)	21(95%)
Moderate	3 (18.5%)	1 (5%)
Severe	4 (23.5%)	0 (0%)
ICU admission	6 (35%)	0 (0%)
Laboratory		
Peak troponin T, (ng/L) during COVID-19	122 (66–250)	238 (183–664)
Troponin T, (ng/L) before CMR	48 (40–120)	23 (18–50)
Peak NT-proBNP, (pg/mL)	365 (176–1665)	82 (67–131)
Peak White blood cells (WBC), 10^9/L	6.75 (5.5–11.9)	6.5 (5.7–7.1)
Peak AST, (U/L)	32 (23–54)	26.5 (15.0–49.5)
Peak ALT, (U/L)	27.5 (18–73)	47 (17.5–71)
Peak CRP, (mg/dL)	19 (6–49)	6.1 (1.1–28.6)
Comorbidities		
Hypertension	6 (35%)	2 (9%)
Dyslipidemia	2 (12%)	3 (14%)
Asthma/COPD	1 (6%)	1 (4.5%)
Smoker (previous or current)	2 (12%)	2 (9%)
Diabetes mellitus	2 (12%)	1 (4.5%)
Autoimmune disease	2 (12%)	7 (32%)
Neoplasia	3 (18%)	3 (14%)
Known cardiomyopathy	1(6%)	-
More than one comorbidity	6 (35%)	6 (27%)

3.1 | Acute myocarditis-like COVID-19 syndrome (AMCovS)

Patients with AMCovS were mostly man (10/17, 59%), with a median age of 57 [IQR, 47–60] years, with hs-cTnT elevation (median peak hs-cTnT 122 [IQR, 66–250] ng/L, normal value <14 ng/L) during hospitalization mostly associated to acute chest pain (12/17, 71%) with non-specific ST-T changes (9, 53%). Most patients had at least one comorbidity (13/17, 76%).

Six out of 17 (35%) patients were admitted to ICU, four of them for acute respiratory distress syndrome (ARDS) associated with cardiogenic shock requiring mechanical ventilation and cardiopulmonary support, the remaining two for cardiogenic shock but with mild COVID-19 pneumonia extent.

CMR was performed during the hospitalization with a median interval between first positive nasopharyngeal swab performed at hospital admission and CMR of 6.5 [IQR, 5.0–21.2] days.

Detailed CMR findings are summarized in Table 2.

At CMR, left ventricular systolic function was preserved (>50%) in 15/17 (88%) patients (LV-EF: 65 [IQR, 54–67] %) and median left ventricular volume index was normal (LV-EDVi: 57 [IQR, 44–71] ml/m).[2]

Left ventricular systolic function was depressed in two cases, one associated with right ventricle dysfunction. Right ventricular systolic function was preserved in the remaining 16/17 (94%) cases (RV-EF: 63 [IQR, 57–69]%), with normal median right ventricular volume index (RV-EDVi: 56 [IQR, 52–64] ml/m),[2]) with the exception of a single patient admitted to ICU showing mild right ventricular dilation (RV-EDVi: 97 ml/m)[2] with moderate systolic dysfunction (RV-EF: 40%) associated with diffuse edema and LGE of right ventricle free wall, suggestive for myocarditis (Figure 1) confirmed at biopsy which showed necrotizing myocarditis.

Nine out of 17 (53%) patients had positive diagnostic criteria for myocarditis, with focal edema on STIR images in 7/9 (78%) patients, mainly involving the septum and the inferior mid-basal wall (5/9, 67%), and T2 mapping elevation in all cases (55 [IQR, 52–56] ms, normal value <50 ms). All patients except one had LGE with non-ischemic pattern that involved mainly the septum and the inferior wall (5/8 cases, 63%), with negligible scar burden (1% [IQR, 1–3]% of myocardial mass) (Figure 2). One patient was diagnosed with pericarditis with negative criteria for coexisting myocarditis.

In 4/17 (24%) patients, CMR showed focal edema and LGE with ischemic pattern ($n = 2$ subendocardial, $n = 2$ transmural), involving a median of 4 [2–7] myocardial segments, suggesting acute myocardial infarction. These patients underwent coronary computed tomography angiography (CCTA) or invasive coronary angiography (ICA) with evidence of obstructive coronary artery disease (CAD) in two cases (Figure 3). Infarct size (LGE%) was larger in patients with obstructive CAD (35% and 11% in patients with obstructive CAD vs 5% and 1% in patients with non-obstructive CAD, respectively).

Mapping alteration showed larger segmental extension compared to STIR and LGE images (Table 1) independently by the ischemic or non-ischemic etiology of cardiac injury.

The remaining patients had evidence of hypertrophic cardiomyopathy (HCM) in two cases, and idiopathic hypokinetic dilated cardiomyopathy (DCM) in the last case.

TABLE 2 Cardiac magnetic resonance findings

	AMCovS patients ($n = 17$)	cPACS patients ($n = 22$)
LVEF, median (IQR), %	64.5 (54–67)	58.0 (54.0–61.5)
LVEDV, ml	107 (89–140)	165 (123.0–187.0)
LVEDVI, ml/m^2	57 (44–71)	81 (66–101)
EDWM, g	92 (72–112)	146 (124–186)
EDWM, g/m^2	47 (45–62)	73.0 (64–98)
RVEF, %	62.5 (56.5–69)	54.5 (51.0–58.7)
RVEDV, ml	107 (94–129)	100 (82.8–113)
RVEDVI, ml/m^2	56 (51.6–64.3)	52 (42–59)
T2-STIR		
Any, *N* (%)	12 (70.5%)	4 (64%)
Overall Positive Segments	59/272 (21.6%)	57/352 (16%)
Median Positive Segments, *N*	2.5 (2–3)	2 (1.8–2.2)
Median maximum T2-ratio	2.5 (2–2.9)	2.0 (1.0–3.0)
LGE		
Any, *N* (%)	16 (94%)	14 (63%)
Overall Positive Segments	45/272 (16.5%)	39/352 (11%)
Median Positive Segments	2 (1–4)	3 0.0 (2.0–5.0)
Ischemic pattern	3 (19%)	1 (7%)
Non-ischemic pattern	13 (81%)	13 (93%)
LGE burden (%)	3 (1.25–5)	2 (1–4)
Myocardial Mapping		
Global median native T1 (ms)	1095 (1046–1127)	1047 (1013–1090)
Median maximum native T1 (ms)	1158 (1113–1199)	1096 (1074–1115)
Segments >1045 ms per patient	9 (5–15)	8 (1–13)
Global median T2 (ms)	55 (49–56)	50.0 (48.2–53)
Median maximum T2 (ms)	62 (53–64)	54.0 (50–55)
Segments >50 ms per patient	10 (7–13)	8 (3–12)
Global median ECV (%)	28 (25–29)	27 (25–29)
Median maximum ECV (%)	30.4 (28–32)	30 (27–33)
Segments >27% per patient	5 (2–10)	10 (2–15)

3.2 | Cardiac post-acute COVID-19 syndrome (cPACS)

Twenty-two patients (male 64%; median age 38 [IQR, 26–53] years) recovered from COVID-19 infection, performed CMR examination after a median of 68 [IQR, 40–212] days after healing for persistence

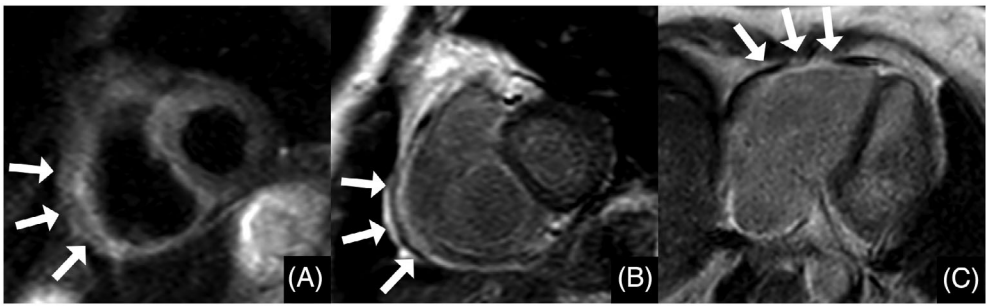

FIGURE 1 CMR of a 58-years-old woman presenting for acute chest pain 10 days after COVID-19 diagnosis. ECG showed ST elevation in the anterior leads. Echocardiography showed diffuse hypokinesia with depressed ejection fraction (35%). High-sensitivity cardiac troponin T (hs-cTnT) was severely elevated (13′722 ng/L, normal value <14 ng/L). The patient underwent ICA in the suspicion of ST-elevation acute myocardial infarction, which however showed normal coronary arteries. After 16 days, the patient underwent CMR to identify the etiology of myocardial damage, which showed transmural edema of the right ventricle free wall in STIR images (arrows in A) corresponding to transmural LGE (arrows in B and C), suggesting acute myocarditis. The diagnosis was confirmed with endomyocardial biopsy documenting necrotizing myocarditis.

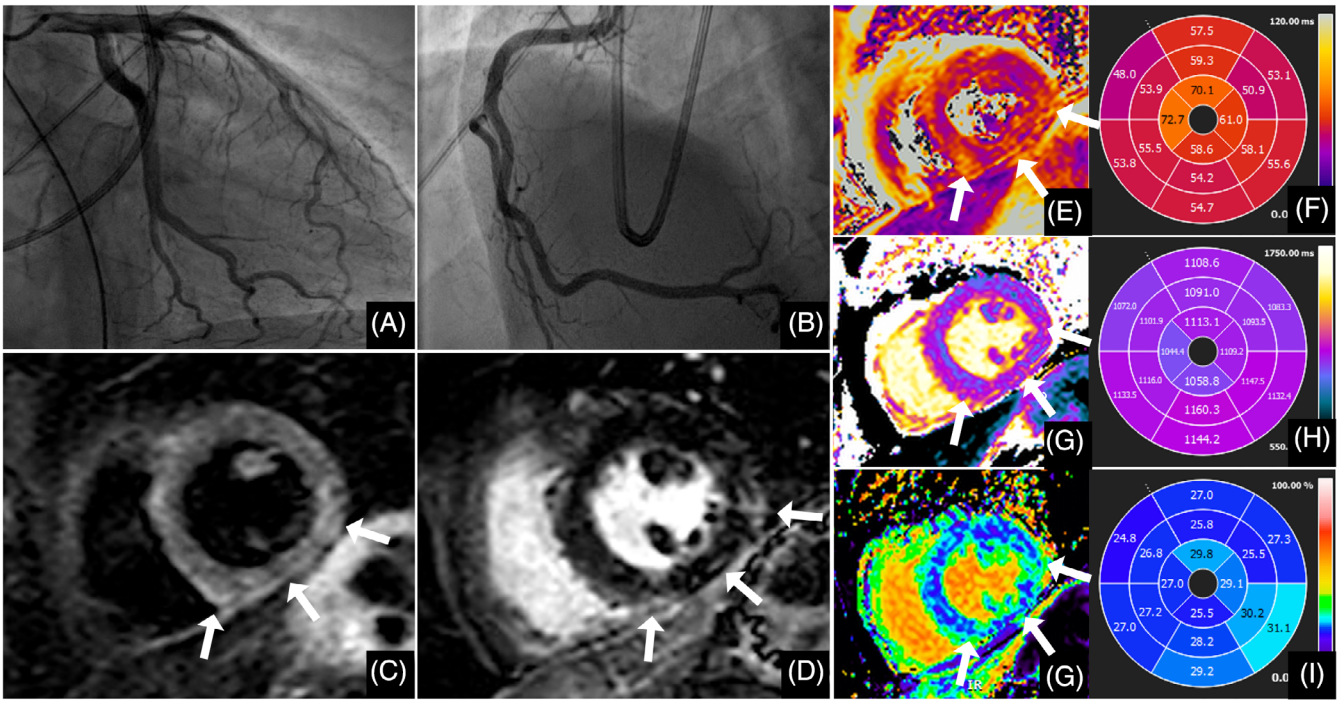

FIGURE 2 Esemplyfing case of COVID-19 related acute myocarditis. A 46-years-old male patient presented to the ED for fever, cough, and diarrhea. ECG showed mild ST elevation in the anterior leads. Echocardiography showed diffuse biventricular hypokinesia with depressed ejection fraction (30%). High-sensitivity cardiac troponin T (hs-cTnT) was severely elevated (730 ng/L, normal value <14 ng/L). A nasopharyngeal swab resulted positive for SARS-CoV-2 infection. The patient underwent ICA in the suspicion of ST-elevation acute myocardial infarction, which however showed normal coronary arteries (A and B). After 11 days, the patient underwent CMR to identify the etiology of myocardial damage, which showed focal patchy areas of edema in STIR images and T2 map (arrows in C and E) involving the infero-lateral and inferior mid-ventricle walls associated with diffuse alteration of T2 values, as for subtle diffuse edema associated (F). In site of hyperintensity on STIR images, were also evident patchy subepicardial areas of LGE (arrows in D) associated to increased native-T1 values (G and H) and corresponding areas of increased ECV (arrow in G and values in I). CMR was suggestive for myocarditis which was confirmed with endomyocardial biopsy.

of cardiovascular symptoms, mainly recurrent chest pain (12/22, 54.5%) and dyspnea (10/22, 45%) occurred during illness.

Ten patients (45%) had history of hospitalization for COVID-19 with elevated hs-cTnT level in seven cases (median peak hs-cTnT 238 ng/L [IQR, 183–664] ng/L) in absence of obstructive coronary artery disease at CCTA or ICA. Hs-cTnT level in acute phase was not assessed in all the remaining cases. All patients performed echocardiography and ECG showing wall motion alteration and ventricles dysfunction in a few cases (Table 1), while ventricular arrhythmias were found in most of patients (59%).

CMR documented active myocarditis in 8/22 (36%) patients, healed myocarditis in 3/22 (14%) patients, pericarditis in 2/22 (9%)

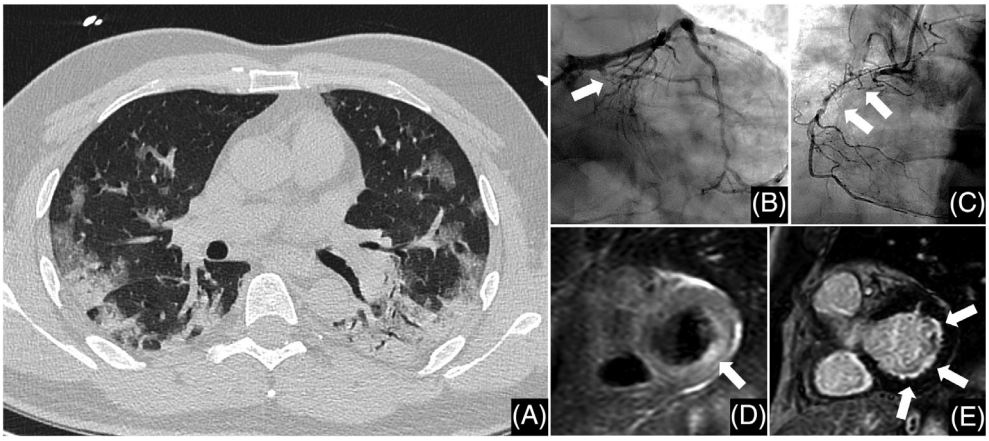

FIGURE 3 Exemplifying case of COVID-19 associated acute coronary syndrome. A 58-years-old male patient presented to the ED for resting chest pain, mild dyspnea, and convulsive syncope. Electrocardiogram showed inverted T waves in the lateral leads. Echocardiography showed normal contractility with preserved ejection fraction. Initial high-sensitivity cardiac troponin T (hs-cTnT) was mildly elevated (16 ng/L, normal value <14 ng/L), with no significant change at 1 h. A nasopharyngeal swab resulted positive for SARS-CoV-2 infection, thus establishing the diagnosis of COVID-19 associated to non-ST elevation acute coronary syndrome (NSTE-ACS). The patient then underwent chest CT for lung parenchyma evaluation, showing a moderate interstitial pneumonia with typical pattern for COVID-19 (figure A), and invasive coronary angiography (ICA), showing total occlusion of left circumflex artery (arrow in B), promptly treated with stenting, and proximal occlusion of right coronary artery (arrowheads in C). After six days, the patient underwent CMR showing focal edema in STIR images in the infero-lateral basal wall (arrow in D) associated to subendocardial LGE (arrows in E), confirming the diagnosis of acute myocardial infarction in the territory of left circumflex artery.

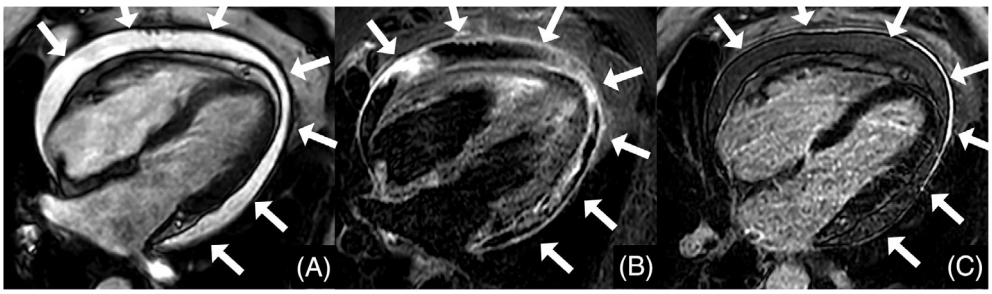

FIGURE 4 CMR images of an 80-years-old male patient presenting to the ED for persisting chest pain two months after COVID-19 pneumonia. Electrocardiogram showed no signs of ischemia. Echocardiography showed normal contractility with preserved ejection fraction and circumferential pericardial effusion. High-sensitivity cardiac troponin T (hs-cTnT) was mildly elevated (45 ng/L, normal value <14 ng/L) with no significant increase at 1 h. The patient then underwent CMR, which showed a significant circumpherential pericardial effusion (thickness 1.5 cm) (arrows in A) associated with significant thickening of the pericardial layers (4 mm) characterized by marked increased intensity on both STIR (arrows in B) and LGE images (arrows in C), suggesting active essudative pericarditis.

patients (Figure 4). Six (27%) patients had miscellaneous cardiomyopathies (three had DCM, two had mitral valve prolapse with arrhythmogenic features, one had myocardial non-compaction). Three (14%) patients had normal CMR findings.

Patients with active myocarditis had focal edema on STIR images in six cases, involving a median of 2 [IQR, 1–4] segments, with increased T2 values in all patients (55 ms [IQR, 54–60] ms). LGE with non-ischemic pattern involved mainly the lateral mid-basal wall (5/8, 63%) with a median of 2 [IQR, 1.5–5] myocardial segments and a scar burden of 2 [IQR, 1–8]%. The three patients with healed myocarditis had absent edema on STIR images, normal T2 values (≤50 ms), and LGE involving a median of 4 [IQR, 3–4] segments in the inferior and lateral mid-ventricle walls with a scar burden of 2% (Figure 5).

4 | DISCUSSION

Cardiac troponin elevation suggestive for myocardial injury is commonly associated to SARS-CoV2 infection, with higher prevalence in case of pre-existing cardiovascular disease and more severe infection, resulting also associated to clinical worsening.[13–16]

CMR is a highly sensitive method for the detection of myocardial abnormalities associated with COVID-19, since it can characterize both non-ischemic and ischemic injury non-invasively thus improving diagnostic accuracy and guiding clinical decision making.[13,17]

In the present study we reported CMR findings in patients with clinical suspicion of myocarditis during the acute infective phase

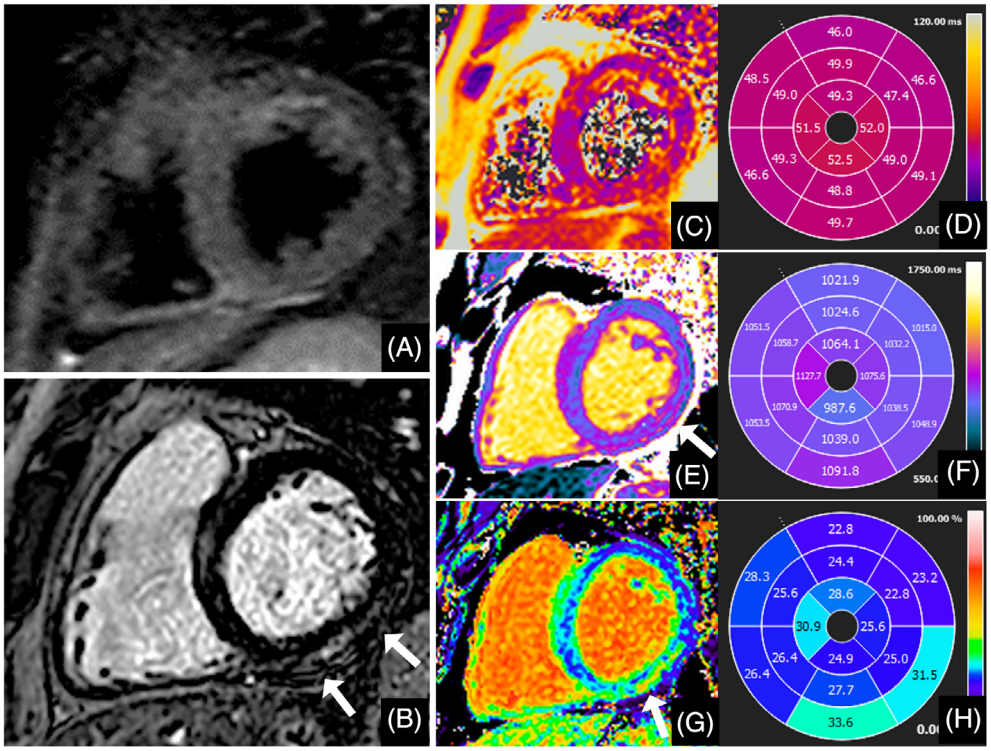

FIGURE 5 CMR images of a 38-years-old male patient presenting for chronic exertional dyspnea and palpitation seven months after resolution of mild COVID-19. Echocardiography showed normal contractility with preserved ejection fraction. High-sensitivity cardiac troponin T (hs-cTnT) was slightly elevated (27 ng/L, normal value <14 ng/L) before CMR. CMR showed absent edema in STIR images (A) and at T2 mapping (C and D) and a small subepicardial area of LGE in the infero-lateral basal wall (arrows in B) associated to native T1 and ECV values elevation (arrows in E-F and G-H, respectively), suggesting healed myocarditis.

(AMCovS) and after recovery (cPACS) for persistence of cardiac symptoms.

Myocarditis was the most frequent CMR diagnosis in both acute and post-COVID settings, accounting for 53% of AMCovS and 50% of cPACS, respectively, with complete edema resolution at both STIR and T2 mapping evaluation, as for healing, in 14% of cPACS cases.

In our cohort, the edema on STIR images in patients with myocarditis was mainly located in the interventricular septum and inferior mid-basal walls, differently from most cases of acute viral myocarditis of other etiology.[18] Similarly, Huang et al.[19] found higher prevalence of septal and anterior and inferior wall involvement in AMCovS. LGE had a limited involvement in both AMCovS and cPACS, accounting for 3 [IQR, 1–5] % and 2 [IQR, 1–4] %, respectively. Minimal LGE in COVID-19 related myocarditis like syndrome was also reported in previous case series[6,20,21] and linked to limited necrosis found at pathological specimen.[22,23]

In our setting, the prevalence of myocarditis was similar in both sexes, with a slight prevalence of female in AMCovS (F:M = 5:4 and F:M = 4:4 in AMCovS and cPACS, respectively), while myocardial infarction was mainly found in males (F:M = 1:3), probably due to sex-based differences in cardiovascular risk profile and higher prevalence of CAD in males.[24]

Myocardial infarction was the second most frequent cause of AMCovS in our cohort, accounting for 24% of patients, with larger scars in patients with obstructive CAD than in patients with non-obstructive CAD (35% and 11% vs 5% and 1%, respectively), similarly to what is observed in non-COVID-19 setting.[25]

Acute myocardial injury is reported to be more frequent in ICU patients in comparison to those with mild forms of infection, as they are considered to have a 13-fold higher risk.[26] In our cohort, most patients admitted to ICU had severe pneumonia (4%, 67%), while the remaining two had cardiogenic shock but mild COVID-19 pneumonia. Ejection fraction was preserved in most AMCovS cases at time of CMR, mainly due to the delay between symptoms onset and CMR examination, with the exception of a few cases with persisting ventricular dysfunction. Interestingly, one patient with isolated right ventricle dysfunction was affected by a fulminant myocarditis confirmed at biopsy (Figure 1) associated to mild pneumonia and absent pulmonary thromboembolism. This is a rare occurrence, being right ventricle dysfunction in COVID-19 more commonly related to increased pulmonary resistances, increased RV afterload, and pulmonary thromboembolism.[27–29]

In post COVID syndrome, persistent cardiovascular symptoms were mostly associated to signs of active or healed myocarditis, suggesting delayed resolution of inflammatory process or chronicization of inflammation for virus persistence potentially associated to any long-term damage.[30]

However, in the remaining patients, COVID-19 infection seems to unravel a previously unknown underlying cardiomyopathy. In fact, in our cohort, cardiomyopathies were diagnosed in 12% and 27% of patients with acute and post-COVID sequelae, respectively, including DCM, HCM and mitral valve prolapse, suggesting the capability of SARS-CoV-2 infection to exacerbate clinically latent conditions and to aggravate pre-existing cardiac disease.[31]

Notably, three patients with suspected cPACS (13.6%) resulted completely negative at CMR, with normal volumes, function and absence of structural alterations. All of them were referred to CMR for premature ventricular contraction (PVC). Dysrhythmias (including sinus tachycardia, sinus bradycardia, atrial and ventricular arrhythmias)

are frequent in patients with COVID-19, resulting associated to disease severity and mortality [32] as in patients healed from COVID-19.[33,34] Indeed, Xie et al.[33] compared 153 760 US Veterans with previous COVID-19 to a large population-based control group, finding an increased 1-year risk of dysrhythmias (composite hazard ratio [HR] 1.69; 95% confidence interval [CI] 1.64–1.75). Ingul et al.[34] found a prevalence of arrhythmias of 27% at 24-hour EKGs performed 3–4 months after COVID-19, with PVCs as the most common (18%) followed by non-sustained ventricular tachycardia (5%). Ståhlberg et al found tachycardia or palpitations persisting 12 weeks or longer in approximately 25%–50% of patients after COVID-19.[35] A possible mechanism for post-COVID arrhythmias is myocardial damage from the inflammatory cascade and subsequent fibrosis and negative remodeling. However, differently to other patients with evidence of cardiac alteration at conventional sequences or mapping, these three patients had no structural or functional alteration. However, conduction system damage and drug treatment could explain arrhythmias onset.[34] Otherwise, these patients may have had arrhythmias before COVID-19 infection, even if asymptomatic, but this hypothesis is difficult to demonstrate due to absent baseline evaluation.[36]

Considering the heterogeneity of clinical and CMR scenario, a multidisciplinary approach would improve patient management.[37,38]

Our study has some limitations, firstly the small sample size and the heterogeneous scenario. This is related to the fact that CMR was not performed to all the patients with evidence of cardiac injury at troponin essay but only in those cases in which CMR diagnosis was considered relevant for clinical management, therefore some patients with acute evidence of cardiac injury were scanned weeks and months later from symptoms onset due to the persistence of symptoms. This approach would have the advantage to improve diagnostic specificity in strictly necessary cases, limiting the exposure of healthcare workers. Additionally, CMR was performed according to clinical request, therefore CMR timing was not standardized. Moreover, endomyocardial biopsy was performed only in a few cases with cardiogenic shock. Second, statistical analysis were not performed because of the heterogeneity of data and the case mix allowing only a description of CMR finings. Additionally, data about interobserver reliability lack, but all measurement are performed with a quantitative and semiquantitative approach to overcome subjectivity of visual interpretation. Finally, outcome data are not available, however, the purpose of this case collection was simply to report main CMR findings observed in AMCovS and cPACS patients.

In conclusion, in patients with suspected COVID-19 related myocarditis CMR resulted determinant to solve this challenge diagnosis both in acute and post-COVID-19 setting, identifying structural alteration responsible of clinical condition, distinguishing inflammatory and ischemic damage, and unrevealing underlying cardiomyopathies, probably becoming symptomatic for the respiratory and systemic impairment due to COVID-19. In our population, inflammatory injury was the most frequent damage at CMR, not related to the severity of pneumonia and of ventricular dysfunction. Mapping parameters improved CMR sensitivity for larger extension of segmental alteration compared to conventional sequences and distinguishing active from healed myocarditis in post-COVID-19 setting. Hence, CMR allows a non-invasive characterization of a wide spectrum of clinical condition associated to cardiovascular symptoms in patients with suspected COVID-19 related myocardial injury and should be integrated in a multidisciplinary diagnostic work-flow able to provide an advanced and personalized patient management.

ACKNOWLEDGMENT

Open access funding provided by BIBLIOSAN.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Palmisano A, Vignale D, Bruno E, et al. Cardiac magnetic resonance findings in acute and post-acute COVID-19 patients with suspected myocarditis. *J Clin Ultrasound*. 2022;1-9. doi:10.1002/jcu.23416