Cardiac T1 and T2 Mapping Showed Myocardial Involvement in Recovered COVID-19 Patients Initially Considered Devoid of Cardiac Damage

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Background: Myocardial injury has been found using magnetic resonance imaging in recovered coronavirus disease 2019 (COVID-19) patients unselected or with ongoing cardiac symptoms.
Purpose: To evaluate for the presence of myocardial involvement in recovered COVID-19 patients without cardiovascular symptoms and abnormal serologic markers during hospitalization.
Study Type: Prospective.
Population: Twenty-one recovered COVID-19 patients and 20 healthy controls (HC).
Field Strength/Sequence: 3.0 T, cine, T2-weighted imaging, T1 mapping, and T2 mapping.
Assessment: Cardiac ventricular function includes end-diastolic volume, end-systolic volume, stroke volume, cardiac output, left ventricle (LV) mass, and ejection fraction (EF) of LV and right ventricle (RV), and segmental myocardial T1 and T2 values were measured.
Statistical Tests: Student's *t*-test, univariate general linear model test, and chi-square test were used for analyses between two groups. Ordinary one-way analyses of variance or Kruskal–Wallis *H* test were used for analyses between three groups, followed by post-hoc analyses.
Results: Fifteen (71.43%) COVID-19 patients had abnormal magnetic resonance findings, including raised myocardial native T1 (5, 23.81%) and T2 values (10, 47.62%), decreased LVEF (1, 4.76%), and RVEF (2, 9.52%). The segmental myocardial T2 value of COVID-19 patients (49.20 [46.1, 54.6] msec) was significantly higher than HC (48.3 [45.2, 51.7] msec) ($P < 0.001$), while the myocardial native T1 value showed no significant difference between COVID-19 patients and HC. The myocardial T2 value of serious COVID-19 patients (52.5 [48.1, 57.1] msec) was significantly higher than unserious COVID-19 patients (48.8 [45.9, 53.8] msec) and HC (48.3 [45.2, 51.7]) ($P < 0.001$). COVID-19 patients with abnormally elevated D-dimer, C-reactive protein, or lymphopenia showed higher myocardial T2 values than without (all $P < 0.05$).
Data Conclusion: Cardiac involvement was observed in recovered COVID-19 patients with no preexisting cardiovascular disease, no cardiovascular symptoms, and elevated serologic markers of myocardial injury during the whole course of COVID-19.
Level of Evidence: 1
Technical Efficacy: Stage 5

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Since December 2019, COVID-19 has been rapidly spreading throughout the world.[1, 2] COVID-19 has had a devastating impact on the world's health system, economy, and human well-being.

Now, it has been demonstrated that severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) may affect multiple human organs by binding of the viral spike protein to angiotensin-converting enzyme 2 (ACE2) on the surface of the host cell receptors, including cardiac receptors.[3] As one of the core systems of the body, cardiac damage plays an important role in the prognosis of COVID-19.[4–6]

In the acute phase of COVID-19, the detection of myocardial injury mainly depends on clinical symptoms, electrocardiogram, and serological markers without direct imaging evidence due to its severe infectivity and the shortage of global health resources.[7–9] However, some researchers have observed persistent myocardial injury induced by COVID-19 through cardiac magnetic resonance imaging (MRI) in convalescent patients.[10, 11] Huang et al reported that a myocardial edema or scar was found on late gadolinium enhancement (LGE) magnetic resonance (MR) images in 58% of recovered patients with ongoing cardiac symptoms.[10] Puntmann et al revealed cardiac involvement in 78 (78%) and ongoing myocardial inflammation in 60 (60%) of 100 patients recently recovered from COVID-19 infection.[11]

However, whether there was myocardial involvement in recovered COVID-19 patients who were considered to have no myocardial injury based on clinical symptoms and serologic markers of myocardial injury is not clear, and the aim of this study was to evaluate whether there was myocardial involvement in recovered COVID-19 patients who were considered to have no myocardial injury based on clinical symptoms and serologic markers of myocardial injury.

Materials and Methods

Study Design and Participants

This study was approved by our Institutional Review Board, and informed consent was obtained before MRI examinations.

A single-center, prospective observational cohort study was conducted. Thirty-three COVID-19 patients who presented to our hospital between March 2020 and April 2020 and whose virus detection was negative were selected consecutively, and clinical observation was performed. The inclusion and exclusion criteria are as follows Inclusion criteria were: 1) Patients were previously confirmed to have SARS-CoV-2 infection by reverse-transcription polymerase chain reaction (RT-PCR) swab test; 2) patients were considered recovered by the discharge criteria (a—normal temperature lasting for more than 3 days; b—resolved respiratory symptoms; c—substantially improved acute exudative lesions on chest computed tomography images; d—two consecutive negative RT-PCR test results separated by at least 24 hours and was isolated for 14 days); and 3) the recovery of respiratory function and being able to tolerate the special respiration requirements of cardiac MR. Exclusion criteria were: 1) a history of coronary artery disease, hypertension, diabetes, or myocarditis and 2) cardiovascular symptoms, high-sensitivity cardiac troponin I (hs-cTnI), creatine kinase (CK), creatine kinase-MB (CK-MB), or brain natriuretic peptide (BNP) positive, symptoms that have been present since the onset of COVID-19. Age- and gender-matched healthy controls (HC) without cardiovascular disease or systemic inflammation were selected and underwent cardiac MR of same protocol at the same time. COVID-19 patients were further divided into subgroups based on clinical type as unserious (mild and moderate) and serious (severe and critical) or normal and abnormal result of several laboratory indices during hospitalization (D-dimer, high-sensitivity C-reactive protein [Hs-CRP], and lymphocyte count).

Cardiac MR Data Acquisition and Postprocessing

MRI was performed on clinical 3-T scanners (GE Signa Pioneer, USA). The MRI scanning protocol included: 1) conventional sequences: short-axis and long-axis cine and T2-weighted imaging (T2WI), and 2) quantitative mapping sequences: native T1/T2 mapping. The stack of short-axis slices covered the left ventricle (LV) from apex to mitral annulus. The imaging plane of T2WI and native T1/T2 mapping were set as the short-axis cine.

Parameters are as follows: 1) Fast imaging employing steady-state acquisition was used for cine imaging with echo time (TE) = 1.4 msec, repetition time (TR) = 3.4 msec, field of view (FOV) = 360 × 360 mm, matrix = 192 × 224, flip angle (FA) = 50°, slice thickness = 8 mm, slice gap = 0 mm. 2) T2WI, short tau inversion recovery (IR) and black blood triple IR sequence was performed using TR = 3 RR intervals, TE = 15 msec, slice thickness = 8 mm, FOV = 360 mm × 360 mm. 3) Native T1 mapping was performed using electrocardiograph-gated, diastole-triggered, single-shot modified Look-Locker IR sequence with protocol 3 (3 sec) 3 (3 sec) 5, acquiring seven images in 17 heartbeats, with TE = 1.2 msec, TR = 2.8 msec, FOV = 360 × 360 mm, matrix = 128 × 128, FA = 35°, bandwidth = 100 kHz, slice thickness = 8 mm, slice gap = 0 mm. 4) T2 mapping was generated using double IR fast spine echo sequence with four different TE (11 msec, 33 msec, 55.1 msec, and 77.1 msec) for a total echo train length = 16, TR = 1RR, FA = 90°, matrix = 160 × 160, bandwidth = 83.33 kH, slice thickness = 8 mm., slice gap = 3 mm.

MRI Images Analysis

Three radiologists (Cunxue Pan with 10-year MRI diagnosis experience, Zuoquan Zhang with 15-year MRI diagnosis, and Shaolin Li with 20-year MRI diagnosis experience) evaluated all MRI images. All the sequences were evaluated in 16 American Heart Association segments.[12] Myocardial edema was evaluated on T2WI images as follows[13]: myocardial edema ratio (ER) was defined as the ratio between myocardial signal intensity (SI) to skeletal muscle SI,[14] and an ER greater than 2.0 represented edema (Cunxue Pan, Zuoquan Zhang, and Shaolin Li drew the Region of Interest). Sixteen segmental myocardial T1/T2 values were measured manually twice on a T1/T2 map by two radiologists (Cunxue Pan and Zuoquan Zhang), and the two measurements were averaged and recorded as the final myocardial T1/T2 values if the interclass correlation coefficient of two measurements ≥0.5. Cutoff values for abnormal native T1 and T2 were defined as a standard deviation (SD) two times above the mean of the sequence-specific normal ranges (which was calculated

TABLE 1. Patient Characteristics, Cardiac MR Imaging Findings, and Blood Test Results During Hospitalization

Characteristic	Median (IQR)/M ± SD		*P*-Value
	COVID-19 (*N* = 21)	Health Controls (*N* = 20)	
Patient characteristics			
Male, *N* (%)	10 (47.62%)	8 (40%)	0.623
Age (Years)	36 (31–47)	50 (32–61)	0.095
Body mass index	23 ± 4	23 ± 4	0.812
Heart rate, beats per minute	72 (63–81)	71 (60–78)	0.763
Duration between confirming of COVID-19 to CMR examination (day)	46 (43–50)		
Clinical types, mild/moderate/severe/critical	4/14/3/0		
Laboratory findings			
D-dimer abnormal elevated	8 (38.10%)		
Hs-CRP abnormal elevated	9 (42.85%)		
Lymphopenia	8 (38.10%)		
Treatment before discharge			
Antiviral therapy	17 (80.96%)		
Antibiotic therapy	14 (66.67%)		
Use of corticosteroid	4 (19.05%)		
Intensive immunotherapy	19 (90.48%)		
Nasal cannula oxygen	11 (52.38%)		
Noninvasive ventilation or high-flow nasal cannula oxygen	1 (4.76%)		
CMR findings			
LV function			
EDMass/BSA (g/m^2)	49.7 ± 7.4	47.8 ± 11.0	0.511
EDV/BSA (mL/m^2)	71.8 ± 11.0	69.6 ± 15.1	0.580
ESV/BSA (mL/m^2)	27.8 ± 6.9	24.2 ± 8.1	0.137
SV/BSA (mL/m^2)	44.1 ± 7.2	45.3 ± 12.7	0.706
CI (L/min/m^2)	2.9 (2.6, 3.9)	3.3 (2.7, 3.5)	0.754
LVEF, %	61.6 ± 6.5	64.8 ± 9.5	0.211
RV function			
EDV/BSA (mL/m^2)	69.6 ± 15.0	69.6 ± 15.0	0.266
ESV/BSA (mL/m^2)	27.1 ± 9.9	27.3 ± 9.9	0.543
SV/BSA (mL/m^2)	35.6 ± 9.3	42.6 ± 8.3	<0.05
RVEF	54.7 ± 7.1	60.3 ± 6.9	<0.05
CI (L/min/m^2)	2.5 ± 0.7	2.9 ± 0.6	<0.05
Myocardial native, T1 (msec)	1208.4 ± 64.2	1213.6 ± 61.7	0.231

TABLE 1. Continued

Characteristic	Median (IQR)/M ± SD		*P*-Value
	COVID-19 (*N* = 21)	Health Controls (*N* = 20)	
Myocardial native, T2 (msec)	49.2 (46.1,54.6)	48.3 (45.2,51.7)	<0.001

Data are reported as counts and percentages for categorical data and medians and interquartile ranges (IQRs) (for nonnormal distribution) or mean ± standard deviation (M ± SD) (for normal distribution) for continuous data.
Hs-CRP = high-sensitivity C-reactive protein; LV = left ventricle; RV = right ventricle; BSA = body surface area; EDV = end-diastolic volume; ESV = end-systolic volume; SV = stroke volume; CI = cardiac index; LVEF = left ventricle ejection fraction; RVEF = right ventricle ejection fraction.

by the data of HC in this study) according to the methods that have been previously published.[11, 15] LV and right ventricle (RV) function parameters were automatically calculated from endocardial and epicardial contours. Ventricular functional parameters included LV/RV end-diastolic volume, end-systolic volume, stroke volume (SV), cardiac index (CI), LV mass, and ejection fraction (EF). All volumes and masses were automatically normalized by body surface area (BSA) through commercial software cvi 42.

Statistical Analyses

Data were shown in counts and percentages for categorical data and medians and interquartile ranges (IQRs) (for nonnormal distribution) or mean ± SD (for normal distribution) for continuous data. The Shapiro–Wilks test was used to indicate the appropriateness of parametric testing. Comparison between two groups was performed by independent sample *t*-test (for normal distribution), Mann–Whitney *U* test (for nonnormal distribution), or chi-square test with categorical variables, and comparison between the T1/T2 values of HC and COVID-19 patients was performed using a univariate general linear model with group and segment as fixed factor. Comparison between three groups was performed by ordinary one-way analyses of variance (for normal distribution) or Kruskal–Wallis *H* test (for no-normal distribution) for continuous variables with Bonferroni-corrected post-hoc comparisons (for normal distribution)

TABLE 2. Myocardial T1 and T2 Grouped by Different Indices

	Native T1		Native T2	
	Native T1 (msec)	*P*-Value	Native T2 (msec)	*P*-Value
Clinical type				
Serious	1195.0 ± 45.1	0.163	52.5* (48.1,57.1)	<0.001
Unserious	1210.9 ± 66.9		48.8 (45.9,53.8)	
Health control	1213.6 ± 61.7		48.3 (45.2,51.7)	
D-dimer				
Normal	1205.3 (1172.31241.7)	0.088	48.3 (45.9,51.9)	<0.001
Abnormal	1220.4 (1173.0,1259.5)		51.6 (47.2,57.1)	
Hs-CRP				
Normal	1198.1 ± 64.8	0.01	48.0 (45.2,51.3)	<0.001
Abnormal	1222.7 ± 60.8		52.50 (47.5,56.9)	
Lymphopenia				
Yes	1207.6 (1170.21241.1)	0.840	50.7 (47.4,55.8)	<0.05
No	1210.5 (1175.31247.9)		48.4 (45.8,52.8)	

Data are reported as counts and percentages for categorical data and medians and interquartile ranges (IQRs) (for non-normal distribution) or mean ± standard deviation (SD) (for normal distribution) for continuous data.
Hs-CRP = high-sensitivity C-reactive protein.
*Post-hoc comparisons found a statically significant difference between this group and other groups.

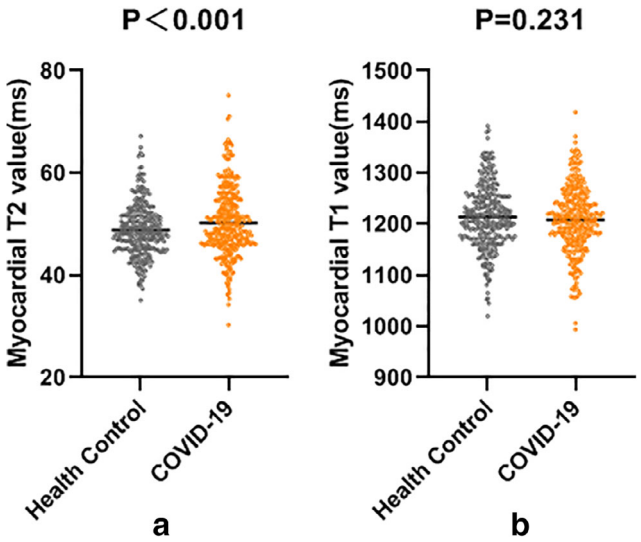

FIGURE 1: Scatterplots of native T1 and native T2 of COVID-19 patients and healthy controls.

or Mann–Whitney *U* tests with post-hoc pairwise comparisons (for nonnormal distribution), as appropriate. $P < 0.05$ was considered statistically significant for all the comparisons except Kruskal–Wallis tests with post-hoc pairwise comparisons, for which $P < 0.05$/post-hoc pairwise times was considered statistically significant.

Results

Patients Characteristics

Thirty-three COVID-19 patients were selected consecutively; 21 patients were finally enrolled in this study based on the inclusion and exclusion criteria, of which 10 (47.62%) were male, and the median (IQR) age was 36 (31–47) years. Twenty age- and gender-matched HCs without cardiovascular disease history who underwent the same MRI examinations in our hospital were included. Baseline characteristics were provided in Table 1. Of 21 COVID-19 patients, 14 (66.67%) were diagnosed as moderate type, 4 (19.05%) as mild type, and 3 (14.29%) as severe type according to the Diagnosis and Treatment Protocol of Novel Coronavirus issued by the National Health Commission of the People's Republic of China.[16] During COVID-19-caused hospitalization, 80.95% (17/21) patients were administered antiviral therapy, 66.67% (14/21) patients were administered antibiotic therapy, 19.05% (4/21) patients were administered corticosteroid therapy, 90.48% (19/21) patients were administered intensive immunotherapy, and 52.38% (11/21) patients received oxygen support. Antiviral drugs included oseltamivir and lopinaviritonavir. Antibiotic drugs included moxifloxacin hydrochloride, ceftriaxone sodium, and cefoperazone sulbactam. Intensive immunotherapy drugs included thymalfasin, recombinant human interferon-α2b, and human immunoglobulin.

Results of Conventional T2WI and Cine Sequences

Edema was not found on T2WI of COVID-19 patients. Compared to HCs, patients who recovered from COVID-19 had lower RVEF (COVID-19 54.7% ± 7.1%, HCs 60.3% ± 6.9%, $P < 0.05$), SV/BSA of RV (COVID-19 35.6 mL/m^2 ± 9.3 mL/m^2, HCs 42.6 mL/m^2 ± 8.3 mL/m^2, $P < 0.05$), and CI of RV (COVID-19 2.5 L/min/m^2 ± 0.7 L/min/m^2, HCs 2.9 L/min/m^2 ± 0.6 L/min/m^2, $P < 0.05$). Two patients (2/21, 9.52%) showed decreased RVEF (RVEF: 42.2%, 39.3%), and one patient (1/21, 4.76%) showed decreased LVEF (LVEF: 46.6%). The detailed values were shown in Table 1.

Results of native T1 and T2 Mapping

The results of the myocardial native T1 and T2 are shown in Tables 1 and 2 and Figure 1. A total of 336 myocardial segments of 21 patients were analyzed. A total of 304 and 325 segments were available for T1 and T2 measurements,

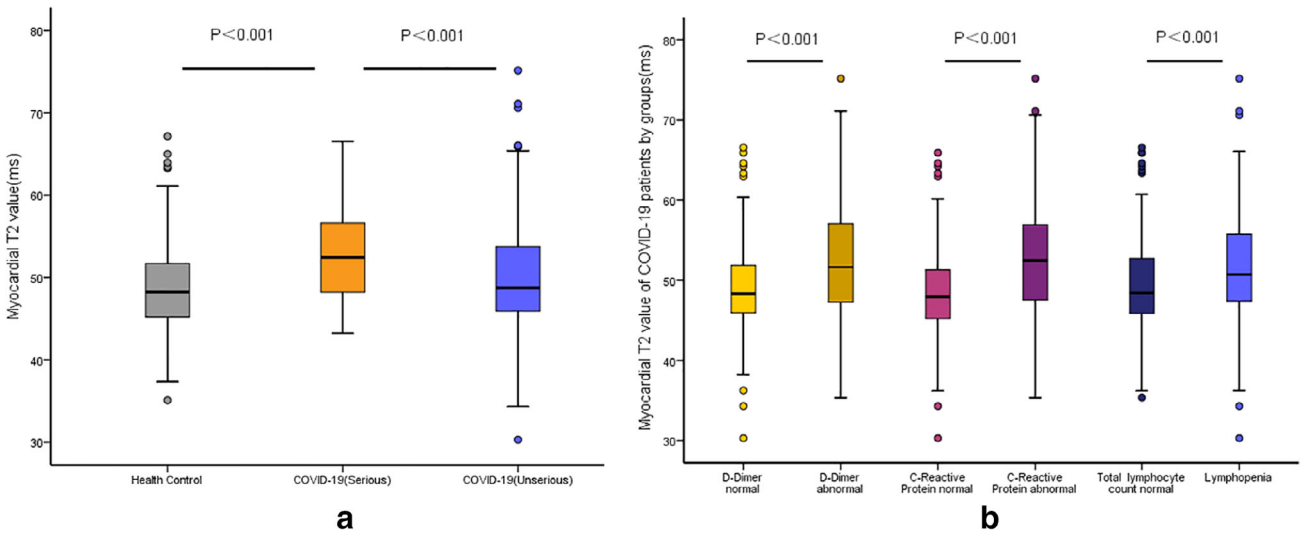

FIGURE 2: Box plots of myocardial T2 value of COVID-19 patient measured by group.

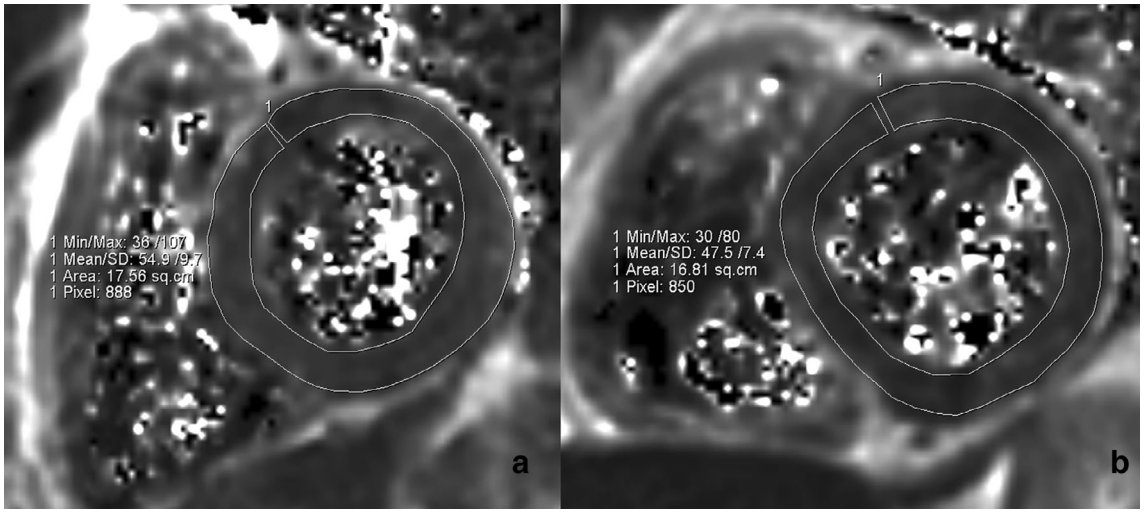

FIGURE 3: Myocardial T2 measurement of a COVID-19 patient and a healthy control. A 36-year-old male infected with SARS-CoV-2 and positive virus nucleic acid test presented with a fever for 5 days before moving to the infection department. He had no preexisting cardiovascular disease; no cardiovascular symptoms; and no elevated myocardial enzyme, troponin, or brain natriuretic peptide during the whole course of COVID-19. High-sensitivity C-reactive protein and D-dimer were abnormally elevated at 46.57 mg/L (normal value 0.068–8.2 mg/L) and 423 ng/mL (normal value 0–243 ng/mL), respectively, and lymphocyte count was abnormally decreased at 0.68 × 109/L (normal value 1.1–3.2 × 109/L) during hospitalization. T2 map on day 51 after admission showed a significantly increased myocardial T2 value (54.9 msec) (a) compared to another 40-year-old male healthy control (47.5 msec) (b).

respectively. Taking an SD two times above the mean of HCs as cutoff values for abnormal myocardial T1 (1337.1 msec) or T2 value (59.8 msec), 13 (61.90%) patients who recovered from COVID-19 had abnormal MR myocardial performance, including raised myocardial native T1 value (5/21 [23.81%], involving 2.30% [7/304] of LV segments) and raised myocardial native T2 value (10/21 [47.62%], involving 7.69% [25/325] of LV segments) (Table 1).

The means of myocardial segmental native T2 value were significantly elevated in COVID-19 patients (49.2 [46.1, 54.6]) compared to HCs (48.3 [45.2, 51.7]) ($P < 0.05$). Myocardial native T2 values of serious COVID-19 patients (52.5 [48.1, 57.1] msec) was significantly higher than unserious COVID-19 patients (48.8 [45.9, 53.8]) and HCs (48.3 [45.2, 51.7]) ($P < 0.001$). The myocardial native T2 value was significantly higher in COVID-19 patients with abnormally elevated D–dimer (51.6 [47.2, 57.1]) than without (48.3 [45.9, 51.9]) ($P < 0001$), in COVID-19 patients with abnormally elevated Hs-CRP (52.5 [47.5, 56.9]) than without (48.0 [45.2, 51.3]) ($P < 0.001$), and in COVID-19 patients with lymphopenia (50.7 [47.4, 55.8]) than without (48.4 [45.8, 52.8]) ($P < 0.05$), while myocardial native T1 values were only significantly higher in patients with abnormally elevated Hs-CRP (1222.7 ± 60.8 msec) than without (1198.1 ± 64.8 msec) ($P < 0.05$) (Table 2, Figs. 2 and 3).

Discussion

Fifteen (71.43%) patients had abnormal Cardiac MR findings in our cohort, and these results showed a higher myocardial injury rate than that of recovered COVID-19 patients with ongoing cardiac symptoms who were more prone to myocardial injury in the study by Huang et al;[10] different methods for detecting myocardial injury may be the reason as conventional MR sequences, including LGE and T2WI, were used in Huang's study, while native T1 and T2 measurements were used in our study.[10] Previous studies have suggested that T1 and T2 measurement are more sensitive to myocardial injury than conventional MR.[13, 17–19]

On the other hand, a higher myocardial injury rate was found in Puntmann's study (78%) than in our study (71.43%).[11] First, the cohort of COVID-19 patients was different. COVID-19 patients who were positive with a history of coronary artery disease; hypertension; diabetes; myocarditis; cardiovascular symptoms; or hs-cTnI, CK, CK-MB, and BNP since the onset of COVID-19 until the day of cardiac MR examination were excluded from our study, while 15% of COVID-19 patients were positive with TroponinT for TnT, Coronary Artery Disease for CAD during hospitalization, 22% with known hypertension, 18% with known diabetes, 13% with known CAD, and 17% with atypical chest pain on the day of CMR examination in Puntmann's study.[11] Second, the methods for detecting myocardial injury are different: native T1 and T2 measurements and LGE were combined in Puntmann's study, while native T1 and T2 measurements and LVEF and RVEF were combined in our study.[11] It was noted that myocardial injury detected by LGE (32%) was also lower than the T1 or T2 measurement (73%, 60%, respectively) in Puntmann's study.[11] Our findings suggest that myocardial involvement is common in patients with

COVID-19 regardless of whether they had a history of cardiovascular disease, cardiovascular symptoms, or elevated serologic markers of myocardial injury during the course of COVID-19.

Our results show that the myocardial T2 value was higher in COVID-19 patients than in HCs; however, no difference in myocardial T1 values between patients and HCs was found. Although the T1 value was elevated abnormally in 23.81% patients, it is lower than the T2 value elevated in our study (47.62%) and the T1 value elevated in Puntmann's study (60%).[11] Increased native T1 values represent diffuse myocardial fibrosis and/or edema, whereas prolonged native T2 symbolizes edema,[15, 20] which may indicate that edema was the main pathological change of myocardial involvement in convalescent COVID-19 patients with no preexisting cardiovascular disease, no cardiovascular symptoms, and no elevated serologic markers of myocardial injury during the whole course. However, the ranges of myocardial T2 values of COVID-19 patients and HCs broadly overlap; this indicates that myocardial involvement (maybe edema) was minimal.

The proposed pathophysiological mechanisms of cardiac injury include infection via the ACE2 receptors causing systemic endotheliitis, immune-mediated cardiac injury, inflammatory plaque rupture, and cardiac stress due to high cardiac output.[21–23] Our results showed that the myocardial T2 value was higher in serious COVID-19 patients than unserious COVID-19 patients and HCs. Patients with abnormally elevated Hs-CRP had higher myocardial native T1 and T2 values than those without. Patients with abnormally elevated D-dimer had a higher myocardial T2 value than those without, and patients with lymphopenia had a higher myocardial T2 value than those without. The variation of the T2 value coincided with the hypothesis of myocardial injury, indicating that inflammatory reaction, hypercoagulability, and decreased leukomonocyte rate might cause myocardial edema. This suggests that myocardial fibrosis or serious edema was rare in COVID-19 patients with no preexisting cardiovascular disease, no cardiovascular symptoms, and elevated serologic markers of myocardial injury during the course of COVID-19. In addition, inflammatory reaction might be high for myocardial injury than for hypercoagulability and lymphopenia.

Limitations

First, the sample size was small, limited by the current capacity of medical resources and unwillingness to undergo cardiac MR examination by COVID-19 patients who were initially considered to have no myocardial injury. Second, our study population included recovered COVID-19 patients who were considered to have no cardiac injury before; therefore, our report cannot reflect cardiac involvement during the acute COVID-19 infection or the full spectrum of recovered COVID-19 patients and cannot be extrapolated to a larger population. Third, enhanced MRI was not performed on this cohort of patients, which restricted the detection of myocardial fibrosis.

Conclusion

Cardiac involvement was present in recovered COVID-19 patients with no preexisting cardiovascular disease, no cardiovascular symptoms, and elevated serologic markers of myocardial injury during the whole course of COVID-19.

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References

1. Zhu N, Zhang D, Wang W, et al. China novel coronavirus investigating and research team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382(8):727-733.
2. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020;579(7798): 270-273.
3. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020;181(2):271-280.
4. 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):802-810.
5. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 2020;395(10229):1054-1062.
6. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Prog Cardiovasc Dis 2020;63(3):390-391.
7. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223): 497-506.
8. 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):1061-1069.
9. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet 2020;395(10223):507-513.
10. Huang L, Zhao P, Tang D, et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. JACC Cardiovasc Imaging 2020;13(11):2330-2339.
11. 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):1265-1273.
12. Cerqueira MD, Weissman NJ, Dilsizian V, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002;105(4):539-542.
13. Luetkens JA, Doerner J, Thomas DK, et al. Acute myocarditis: Multiparametric cardiac MR imaging. Radiology 2014;273(2):383-392.

14. Friedrich MG, Sechtem U, Schulz-Menger J, et al. Cardiovascular magnetic resonance in myocarditis: A JACC White paper. J Am Coll Cardiol 2009;53(17):1475-1487.

15. Puntmann VO, Valbuena S, Hinojar R, et al. Society for Cardiovascular Magnetic Resonance (SCMR) expert consensus for CMR imaging endpoints in clinical research: Part I—Analytical validation and clinical qualification. J Cardiovasc Magn Reson 2018;20(1):67.

16. National Health Commission of the People's Republic of China. Diagnosis and Treatment Protocol of Novel Coronavirus (Trial Version 7th). Available from: http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml

17. Ugander M, Bagi PS, Oki AJ, et al. Myocardial edema as detected by pre-contrast T1 and T2 CMR delineates area at risk associated with acute myocardial infarction. JACC Cardiovasc Imaging 2012;5(6):596-603.

18. Radunski UK, Lund GK, Saring D, et al. T1 and T2 mapping cardiovascular magnetic resonance imaging techniques reveal unapparent myocardial injury in patients with myocarditis. Clin Res Cardiol 2017;106(1):10-17.

19. Messroghli DR, Moon JC, Ferreira VM, et al. Clinical recommendationsfor cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI). J Cardiovasc Magn Reson 2017;19(1):75.

20. Puntmann VO, Peker E, Chandrashekhar Y, et al. T1 mapping in characterizing myocardial disease: A comprehensive review. Circ Res 2016;119(2):277-299.

21. Chen L, Li X, Chen M, Feng Y, Xiong C. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. Cardiovasc Res 2020;116(6):1097-1100.

22. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet 2020;395(10234):1417-1418. https://doi.org/10.1016/S0140-6736(20)3097-5.

23. Liu PP, Blet A, Smyth D, Li H. The science underlying COVID-19: implications for the cardiovascular system. Circulation 2020;142(1):68-78.