Radiology

Cardiac MRI in Patients with Prolonged Cardiorespiratory Symptoms after Mild to Moderate COVID-19 Infection

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See also the editorial by Lima and Bluemke.

Summary:

Previously healthy individuals with prolonged cardiorespiratory symptoms after COVID-19 infection who were not hospitalized at any disease stage had no signs of active cardiac inflammation at cardiac MRI.

Key Results:

- In this prospective study of 41 participants with cardiorespiratory chronic COVID-19 syndrome (CCS) and 42 control participants, cardiac MRI mapping parameters indicating myocardial inflammation were comparable between both groups (T1 relaxation time: 978 ± 23 ms vs 971 ± 25 ms; P = .17, T2 relaxation time: 53 ± 2 ms vs 52 ± 2 ms; P = .47).
- In 3 of 41 (7%) participants with CCS, non-ischemic myocardial late gadolinium enhancement lesions were present while none were observed in the control group.

Abbreviations:

MRI, magnetic resonance imaging (MRI)

COVID-19, coronavirus disease 19

LGE, late gadolinium enhancement

CCS, chronic COVID-19 syndrome

Abstract

Background: Myocardial injury and inflammation on cardiac MRI in patients suffering from coronavirus disease 19 (COVID-19) have been described in recent publications. Concurrently, a chronic COVID-19 syndrome (CCS) after COVID-19 infection has been observed manifesting with symptoms like fatigue and exertional dyspnea.

Purpose: To explore the relationship between CCS and myocardial injury and inflammation as an underlying cause of the persistent complaints in previously healthy individuals.

Materials and Methods: In this prospective study from January 2021 to April 2021, study participants without known cardiac or pulmonary diseases prior to COVID-19 infection with persisting CCS symptoms like fatigue or exertional dyspnea after convalescence and healthy control participants underwent cardiac MRI. Cardiac MRI protocol included T1 and T2 relaxation times, extracellular volume (ECV), T2 signal intensity ratio, and late gadolinium enhancement (LGE). Student *t* test, Mann-Whitney U test, and χ^2 test were used for statistical analysis.

Results: 41 participants with CCS (39±13 years; 18 men) and 42 control participants (39±16 years; 26 men) were evaluated. Median time between initial mild to moderate COVID-19 disease without hospitalization and cardiac MRI was 103 days (interquartile range: 88-158). Troponin T levels were normal. Parameters indicating myocardial inflammation and edema were comparable between participants with CCS and control participants: T1 relaxation time (978±23 ms vs 971±25 ms; P=.17), T2 relaxation time (53±2 ms vs 52±2 ms; P=.47), T2 signal intensity ratio (1.6±0.2 vs 1.6±0.3; P=.10). Visible myocardial edema was present in none of the participants. Three of 41 (7%) participants with CCS demonstrated non-ischemic LGE compared to none in the control group (0 of 42 [0%]; P=.07). None of the participants fulfilled the 2018 Lake Louise criteria for the diagnosis of myocarditis.

Conclusion: Individuals without hospitalization for COVID-19 and with CCS did not demonstrate signs of active myocardial injury or inflammation on cardiac MRI.

Introduction

With the ongoing coronavirus disease 2019 (COVID-19) pandemic, the number of scientific studies as well as our knowledge regarding the novel severe acute respiratory syndrome coronavirus 2 has steadily increased. It is now known that the virus not only affects the lower respiratory airways but can also affect other systems such as for example the central nervous or cardiovascular systems (1–3). Since the start of the COVID-19 pandemic at the end of 2019, reports have been emerging of patients suffering from persistent COVID-19 symptoms such as fatigue or exertional dyspnea after having been tested negative via polymerase chain reaction (PCR) tests. This has led to a new pathology termed chronic COVID-19 syndrome (CCS) or long COVID (4, 5). Unfortunately, the exact etiology of CCS remains unknown.

Recent studies have reported on structural myocardial damage in patients who have suffered a COVID-19 infection in the form of acute myocarditis or myocardial scar formation (2, 6–11). Puntmann et al demonstrated that about 78% of recently recovered COVID-19 patients had abnormal cardiac magnetic resonance (MRI) findings including increased native T1 and T2 myocardial relaxation times, decreased ejection fractions, and increased left ventricular volumes (8). A study from China showed that 7 to 15% of hospitalized COVID-19 patients had elevated troponin T levels as an indirect sign of myocardial infarction (12). On the other hand, a more recent study of 149 health care workers demonstrated no detectable difference on MRI regarding cardiovascular abnormalities between a seropositive cohort with mild COVID-19 symptoms 6-months after initial diagnosis and a healthy seronegative control group (13). While cardiac injury on cardiac MRI was found to be also a component of the systemic immune response or direct myocardial damage of SARS-CoV-2 usually observed in severely ill patients (14), the possible long-term effects of COVID-19 on recovered, but still symptomatic CCS patients has not been sufficiently determined.

In this prospective study, previously healthy COVID-19 patients who continue to suffer from CCS with symptoms such as chest pain, exertional dyspnea, or fatigue underwent

multiparametric cardiac MRI. The purpose of our explorative study was to evaluate to which extent inflammatory or structural changes in the myocardium are present in patients with convalescent COVID-19 infection who continue to suffer from cardiorespiratory symptoms.

Materials and Methods

This prospective study was performed in concordance with the Declaration of Helsinki and International Conference on Harmonization of Good Clinical Practice. Study design, information processing, and study implementation was approved by the institutional review board (Lfd. Nr. 039/21). Written informed consent was obtained from each patient after being provided information regarding the study and potential risks of participation.

Study Participants

Recruitment occurred consecutively between January 2021 and April 2021. Participants over the age of 18 without known cardiac or pulmonary diseases, as outlined in **Figure 1**, who also reported persisting fatigue, exertional dyspnea, or cardiac symptoms after COVID-19 convalescence were included in this single center, case-control study. As viral load clearance in mild to moderate infections typically requires 10 to 13 days, leading to a negative PCR test, we defined CCS as failure of symptom resolution within 30 days of initial diagnosis (15, 16). Cardiac symptoms were defined as persisting, occasional, or provoked chest pain, tachycardia, or shortness of breath. Participants with CCS must have had a negative PCR test and resolution of acute COVID-19 symptoms for at least two weeks before cardiac MRI was performed. Acute COVID-19 symptoms were defined as fever, dry or wet cough, change in taste and smell with or without dyspnea, and a positive PCR test. Participants were referred by local medical offices and university centers. Clinical manifestations of initial COVID-19 disease were classified as previously described (17). All participants with CCS had unremarkable results in previous examinations (including echocardiography, electrocardiogram, and normal troponin T levels) ruling out other causes for their complaints after COVID-19 infection. The stringent recruitment process with inclusion and exclusion criteria is summarized in **Figure 1**. The control group consisted of an age-matched healthy participants without prior COVID-19 infection. All control participants had an unremarkable past medical history of cardiovascular disease.

Electrocardiographic results were unremarkable and no cardiac risk factors were present. Initial date of COVID-19 diagnosis was defined as the day of the first positive PCR test.

Cardiac MRI protocol

Each participant underwent a multiparametric cardiac MRI examination, which was performed using the same clinical whole-body MRI system (Ingenia 1.5T; Philips Healthcare, Best, The Netherlands). A 32-channel torso coil with a digital interface was used for signal reception. A signal intensity correction algorithm (constant level appearance; Philips Medical Systems) was used to correct for torso-coil related signal inhomogeneities. Electrocardiogram-gated steady state free-precession cine images were obtained in short-axis, two-chamber, and four-chamber views for functional analysis. T2-weighted short-tau inversion-recovery sequences in short axis and transversal views were performed for visualization of myocardial edema and calculation of T2 signal intensity ratio. Segmented inversion-recovery gradient-echo sequences were used for LGE imaging and were obtained in short axis, two-chamber, four-chamber, and transversal views. The Look-Locker method was utilized to determine the optimal inversion time for LGE image acquisition (18). Myocardial T1 and T2 mapping was performed in end-diastolic short axis views with acquisition of apical, midventricular and basal sections. For myocardial T1 mapping, a standard 3(3)3(3)5 modified Look-Locker inversion recovery (MOLLI) acquisition scheme was applied (19). Post-contrast T1 maps using the same acquisition scheme were obtained 10 minutes after contrast administration. For myocardial T2 mapping, a six-echo gradient spin-echo sequence (GraSE) was applied (20). For contrast enhancement, a 0.2 mmol/kg of body weight bolus of gadoterate meglumine (Clariscan; GE Healthcare, Chicago, IL) was administered. Directly prior to every cardiac MRI scan, blood samples were drawn for blood count and hematocrit assessment. Additionally, a transversal respiratory-gated T2-weighted fast spin echo sequence (Philips MultiVane XD, Philips Healthcare, Best, The Netherlands) for the assessment of lung pathologies was performed. A detailed description of the sequence parameters is provided in Appendix E1 (**Table E1**).

Image Analysis

Image analysis was performed by a board-certified radiologist (J.A.L. with 8 years of experience in cardiac MRI) and a radiology resident (D.K. with 2 years of experience in cardiac MRI) using dedicated software (IntelliSpace Portal, version 10.6.32.82.; Philips Medical Systems). Readers were blinded to the clinical information. Papillary muscles were included in the volumetric quantification of the left ventricle. The presence of focal areas of regional high signal intensities in a non-ischemic distribution pattern on T2 short-tau inversion-recovery and on LGE images was visually assessed by consensus agreement of the two readers. Semi-quantitative markers of myocardial edema (T2 signal intensity ratio) and myocardial injury and fibrosis (enhanced volume percentage on short-axis LGE images using full width half maximum technique) were calculated as previously reported (14). Myocardial T1 and T2 relaxation maps were motion corrected using a software-implemented algorithm (fast elastic image registration, IntelliSpace Portal, version 10.1) and global T1 and T2 relaxation times as well as hematocrit-corrected global ECV values were calculated, as previously described (14, 21). For the assessment of the 2018 Lake Louise criteria, institution specific cutoffs were employed as previously described. The cutoffs for the diagnosis of myocardial inflammation were ≥ 1000 ms for myocardial T1 relaxation times and ≥ 55.9 ms for myocardial T2 relaxation times. The imaging protocol in this study was the same as used in our previous studies of patients with suspected acute myocarditis (21, 22).

Symptom Questionnaire

Participants completed a questionnaire pertaining to novel symptoms they experienced during and after the acute COVID-19 infection immediately before undergoing the cardiac MRI examination. Each symptom was then rated on a 0 to 10 numeric rating scale for subjective symptom burden during acute infection and current symptom status. No symptoms were prescribed, so that each participant was free to fill out their own symptom constellation. A copy of the questionnaire is provided in Appendix E1 (**Figure E1**).

Statistical Analysis

Prism (version 8.4.1; GraphPad Software, San Diego, Calif) was used for statistical analysis. Participant characteristics are given as means ± standard deviation or as percent to absolute frequency. Data were checked for normal distribution using Shapiro-Wilk test. Dichotomous variables were compared by using the χ^2 test. For comparison of continuous variables, between inter-individual variables Student *t* test was used. Mann-Whitney-U test was used for non-normal distributed data. For intra-individual comparisons, the Wilcoxon rank test was used. The level of statistical significance was set to $P < 0.05$.

Results

Participant characteristics

A total of 83 participants were included in this prospective study: 41 participants with CCS (mean age ± standard deviation, 39 ± 13 years; 18 men) and 42 control participants (mean age, 39 ± 16 years; 26 men). There were no significant differences between the groups regarding age (P = .88), sex (P = .10), weight (P = .78), height (P = .28), or body mass index (P = .20). Initial COVID-19 disease in participants with CCS was mild (37 of 41, 90%) or moderate (4 of 41, 10%) . Participant characteristics are summarized in **Table 1**. Excluded patients are summarized in **Figure 1**: Two referred participants had to be excluded due to having a date of symptom onset before COVID-19 infection, one participant did not show up to their appointment, and one participant had to be excluded due to demonstrating persistent pulmonary infection most likely due to COVID-19. No participant with CCS required hospitalization during acute COVID-19 infection. Two participants with CCS received symptomatic treatment with dexamethasone and fenoterol.

Median time between initial COVID-19 diagnosis and cardiac MRI was 103 days (inter quartile range: 88-158 days). Participants with CCS reported dyspnea (32 of 41, 78%), fatigue (28 of 41, 70%) as well as improving anosmia (26 of 41, 63%), headaches (26 of 41, 63%), cough (12 of 41, 32%), and fever (21 of 41, 51%). The only preexisting medical conditions in participants with CCS were allergic asthma (1 of 41, 2%), past medical history of pituitary adenoma (1 of 41, 2%), and arterial hypertension (2 of 41, 5%). Results of the symptom burden questionnaire are summarized in **Table 2.**

Cardiac MRI results

All control participants had normal cardiac MRI results without structural abnormalities or signs of previous myocarditis. No differences in left ventricular ejection fraction (62 ± 5% vs 61 ± 3%; P = .38) or left ventricular end-diastolic volume index (77 ± 14 ml/m^2 vs 74 ± 13 ml/m^2; P = .23) were observed between the groups. No regional wall motion abnormalities were

observed in any group. T2 signal intensity ratio was within normal range for both groups (see **Table 1**). No focal myocardial edema was visually observed.

No differences were found in native T1 relaxation times (978 ± 23 ms vs 971 ± 25 ms; P = .17) and T2 relaxation times (53 ± 2 ms vs 52 ± 2 ms; P=.47) between participants with CCS and control participants (see **Figure 2**).

Focal non-ischemic LGE lesions were present in 3 of 41 (7%) participants with CCS. Two of 3 (67%) LGE lesions were found in the subepicardium of the basal inferolateral wall and 1 of 3 (33%) LGE lesions was midventricular at the right ventricular attachment (see **Figure 3**). ECV values did not differ between participants with CCS and control participants (24.1 ± 2.3% vs 25.1 ± 2.6%; P = .15). None of the participants fulfilled the 2018 Lake Louise criteria for the diagnosis of inflammatory cardiomyopathies.

Six of 41 (15%) participants with CCS had incidental findings on cardiac MRI with potential impact on the prolonged cardiorespiratory symptoms while the control group did not demonstrate any incidental findings. These findings were: a small aberrant accessory lung (1 of 41, 2%), pericardial effusion without signs of pericarditis (1 of 41, 2%), visual signs of right ventricular high-pressure overload (1 of 41, 2%), persisting slight pulmonary opacities in the lower left lobe (1 of 41, 2%), and discrete pleural effusions (2 of 41, 5%) with a maximum anterior-posterior distance of 5 and 7 mm respectively.

Discussion:

COVID-19 has now been established to be a multi-system disease, affecting many parts of the human body. Fatigue and dyspnea have been described to be some of the most common COVID-19 symptoms (4, 23, 24). Unfortunately, some of these symptoms persist in negatively tested patients leading to CCS. The long-term risks and costs of CCS remain unknown, and the exact etiology of CCS is poorly understood. We hypothesized that CCS may be caused by ongoing myocardial injury and inflammation. However, none of our patients fulfilled the diagnostic criteria of ongoing myocardial inflammation and markers of myocardial edema were not elevated. Myocardial T1 and T2 relaxation times were not different amongst participants with CCS and healthy controls (myocardial T1 relaxation, 978 ± 23 ms vs 971 ± 25 ms, P = .17; myocardial T2 relaxation: 53 ± 2 ms vs 52 ± 2 ms; P = .47). Three of 41 (7%) analyzed participants with CCS showed myocardial changes on LGE, e.g. consistent with myocardial scarring, although none of these participants fulfilled the 2018 Lake Louise criteria for an active inflammatory cardiomyopathy. Furthermore, one lesions was an unspecific lesion at the right ventricular insertion point, which is an uncommon finding in myocarditis. As the burden of LGE lesions was very low and the participants showed no signs of ongoing myocardial inflammation (i.e. signs of myocardial edema on cardiac MRI), these findings are likely not causative for the described CCS symptoms. Our percentage of positive cardiac findings is considerably lower than previously reported by Puntmann et al. (78%), Huang et al. (58%), or Wang et al. (30%) (8, 10, 25).

We did not find any evidence to support the hypothesis that CCS in young, previously healthy post COVID-19 patients is caused by structural myocardial damage. Puntmann et al. analyzed 100 recovered COVID-19 patients irrespective of preexisting conditions, showing that up to 78% of patients had myocardial involvement (8). This is an over ten-fold difference in incidence compared to our observed 7 % of positive LGE findings. The patient population from Puntmann et al. differed from ours regarding selection in two major ways. Firstly, they did not screen for

CSS but recruited with broad selection criteria. Secondly, 33 (33%) of their patients had a severe course of the disease requiring hospitalization. Only one of our participants required hospitalization but was excluded from final analysis due to continuous signs of active pneumonia most likely due to COVID-19. Additionally, we excluded patients with preexisting cardiac or respiratory conditions whereas other research groups, for example Huang et al. and Wang et al. recruited recovered previously hospitalized patients and included these patients for analysis (10, 22). This naturally begs the question if these reported cardiac findings were present before COVID-19 infection or not. The discrepancy in findings between ours and the above-mentioned studies is most likely due to patient selection, more specifically disease severity as reflected by hospitalization rate. Most participants in the CCS group had a mild initial course of COVID-19 disease. In another cardiac MRI study by Joy et al. in healthcare workers after asymptomatic to mild COVID-19 disease, cardiovascular abnormalities were also no more common compared to a control group, supporting our findings (13). Interestingly, the only significant difference we found between the two groups was septal thickness at end-diastole (7.8 ± 1.7 mm CSS vs 9.3 ± 1.6 mm control, P = <.001) but both groups were within normal limits (26). Six participants demonstrated incidental findings on MRI which could theoretically also impact cardiopulmonary symptoms. However, no distinct pattern in incidental findings were present, which might be specific for the CCS symptoms described in our study.

The subjective symptom burden did not differ between active infection and current symptomatic burden for dyspnea (4.1 ± 3.6 vs. 5.6 ± 2.6; P = .11) or fatigue (5.5 ± 3.6 vs 4.4 ± 3.0; P = .26) with even worsening of symptom burden for dyspnea (mean difference 1.5 points) albeit an improvement in fatigue like symptoms over the course of time (mean difference: 2.0 points). This suggests that overall, most participants did not perceive a significant difference in symptom burden between acute infection and CCS for fatigue and exertional dyspnea. However, other symptoms such as anosmia, headache, cough, myalgia, and fever improved markedly.

Our study has a few limitations. For one, due to the single cardiac MRI examination after symptom onset, we cannot be sure that the reported cardiac MRI findings were also present before COVID-19 infection. In this regard it is important to mention that non-ischemic LGE lesions might be unspecific and can be caused by previous unperceived myocarditis before COVID-19 infection (14). Also, no histopathological analysis was performed regarding the presence of active myocarditis. However, the applied quantitative MRI techniques have been reported to very sensitively detect even subclinical myocardial edema and inflammation in various medical conditions (27). The questionnaire was administered only once at the time of cardiac MRI examination thus possibly leading to a recall bias for acute symptoms. Finally, our findings are not applicable to patients during acute COVID-19 infection.

In conclusion we found no evidence to support that CSS in non-hospitalized participants is caused by active myocardial inflammation. Our observed incidence of cardiac specific positive findings on cardiac MRI was lower than previously reported. CCS symptoms might not be caused by myocardial inflammation induced by COVID-19 infection.

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Tables

Table 1. Clinical and Cardiac MRI Characteristics of Participants with CCS and Control Participants

Variable	CCS (n = 41)	Controls (n = 42)	P value
Clinical parameters			
Age (years)	39±13	40±16	0.88
Men*	18 (44)	26 (62)	0.10
Weight (kg)	77±15	76±17	0.78
Height (cm)	173±9	175±9	0.28
Body mass index (kg/m^2)	25.6±3.9	24.7±3.8	0.20
Body surface area (m^2)	1.9±0.2	1.9±0.2	0.97
Heart rate (beats/min)	70±13	66±14	0.07
Cardiac MRI parameters			
LVEDV (ml)	148±33	142±36	0.50
LVEDVi (ml/m^2)	77±14	74±13	0.23
Left ventricular ejection fraction (%)	62±5	61±3	0.38
Interventricular septal thickness (mm)	7.8±1.7	9.3±1.6	<0.001
White blood cell count, (n/cells)	6.5±1.8	6.7±1.9	0.60
Hematocrit (%)	42±3	41±4	0.18
T2 signal intensity ratio	1.6±0.2	1.6±0.3	0.10
Visible myocardial edema*	0 (0)	0 (0)	0.99
Visible late gadolinium enhancement*	3 (7)	0 (0)	0.07
T1 relaxation time, native (ms)	978±23	971±25	0.17
Extracellular volume fraction (%)	24.1±2.3	25.1±2.6	0.08
T2 relaxation time (ms)	53±2	52±2	0.47

Numbers are given as mean ± standard deviation.
CCS, chronic COVID-19 Syndrome; LVEDV, left ventricular end diastolic volume; LVEDVi, left ventricular end-diastolic volume index.

*Data are absolute frequencies with percentages in parentheses.

Table 2. Subjective Symptom Burden of CSS Patients during Acute COVID-19 Infection and CCS

Symptoms	Number of participants (n = 41)	Symptom burden scores acute COVID-19	Symptom burden scores CCS	Mean difference	P value
Exertional dyspnea	32 (78)*	4.1 (3.6)	5.6 (2.6)	+1.5	0.11
Fatigue	29 (71)*	5.5 (3.6)	4.4 (3.0)	-2.0	0.26
Anosmia	26 (63)*	7.6 (2.7)	2.7 (3.4)	-6.0	< .001
Cardiac arrhythmia	5 (12)*	6.6 (3.7)	6.4 (1.3)	-1.1	0.86
Headache	26 (63)*	5.4 (3.2)	2.0 (3.2)	-5.0	0.02
Cough	13 (32)*	5.9 (2.5)	0.8 (1.9)	-5.5	0.002
Lymph node swelling	2 (5)*	4.0 (4.2)	1.5 (2.1)	-2.5	0.50
Chest pain	11 (27)*	5.4 (4.0)	4.2 (4.0)	-1.0	0.41
Fever	21 (51)*	5.9 (2.6)	0.1 (0.2)	-6.0	< .001
Muscle aches	13 (32)*	8.1 (1.6)	1.3 (2.8)	-7.0	0.002
Concentration problems	9 (22)*	4.6 (4.6)	5.2 (4.0)	+0.7	0.93

Data is represented as mean (standard deviation). P values indicate group differences in the severity score during acute COVID-19 and CCS. Wilcoxon rank sum test was used for group comparisons. The symptom burden score consists of a numeric rating scale ranging from 0 to 10 (0 no symptom burden, 10 most severe symptom burden) to gauge subjective symptom burden during acute infection and persisting symptoms after testing negative for COVID-19. COVID-19, coronavirus disease 19; CCS, chronic COVID-19 syndrome.

*Data are absolute frequencies with percentages in parentheses.

Figures

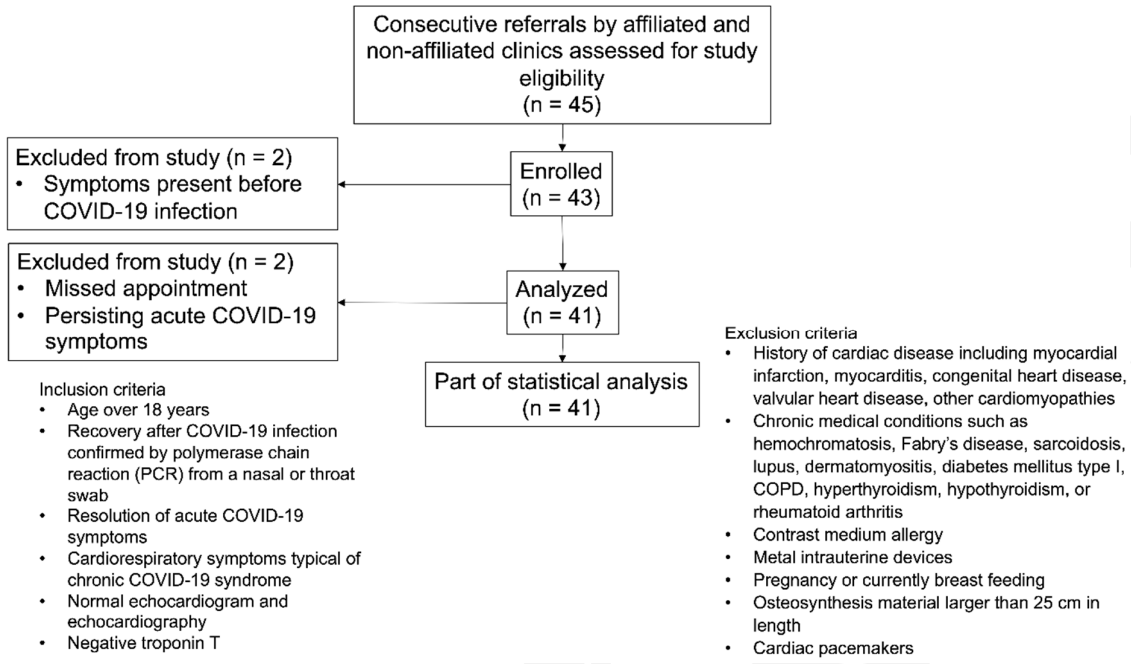

Figure 1. Flowchart depicting the recruitment process, inclusion, and exclusion criteria, and included participants with chronic COVID-19 syndrome.

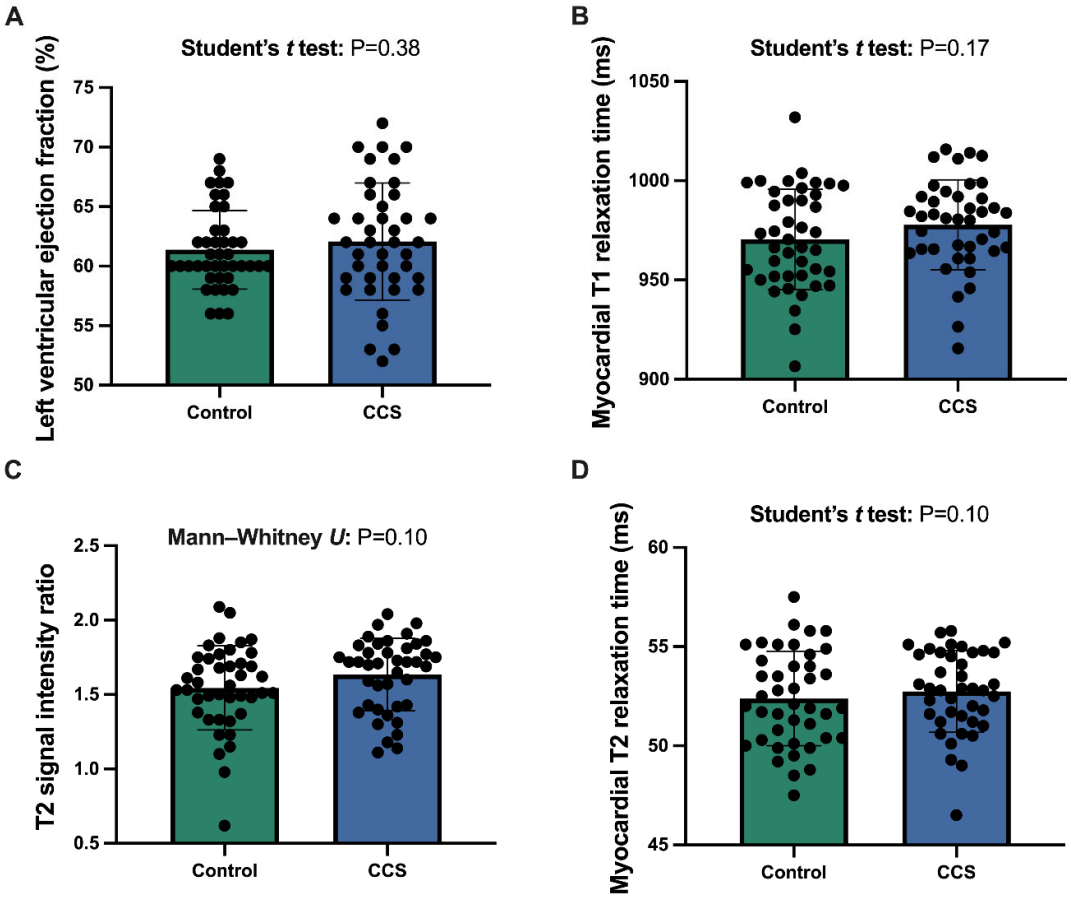

Figure 2. Column graphs with individual plotted values show distribution of MRI parameters in the control group and the chronic COIVD-19 (CCS) group. Mean of data is represented by bar. Whiskers represent standard deviation. Distribution is shown for **(A)** left ventricular ejection fraction, **(B)** myocardial T1 relaxation time, **(C)** T2 signal intensity ratio, and **(D)** myocardial T2 relaxation time.

Figure 3. Positive late gadolinium enhancement (LGE) in 3 of 41 patients (7%). Subepicardial LGE along the basal inferolateral wall (arrows) in a 63-year-old male **(A)** and a 54-year-old male **(B)**. **(C)** LGE at the right ventricular attachment (arrow) of a 19-year-old male.

Supplemental Table

Table E1. MRI Sequence Parameters

Parameter	**Short axis SSFP Cine**	**Short axis black-blood T2 STIR**	**Short axis LGE**	**T1 Mapping**	**T2 Mapping**	**T2 MultiVane XD**
Field of view (mm)	350 x 350	350 x 350	360 x 311	300 x 300	300 x 347	400 x 400
Time of repetition (ms) Time to echo (ms)	2.8 1.38	2 RR intervals 70	3.5 1.71	2.2 1.02	1 RR interval 23.6/ ΔTE = 11.8 (6Ec)	1114 60
Flip angle (°)	60	90	15	35	90	90
Voxel size (mm^3) acquired reconstructed	1.79 x 2 x 8 0.99 x 0.99 x 8	1.51 x 2.43 x 8 0.91 x 0.91 x 8	1.65 x 1.88 x 10 0.9 x 0.9 x 5	1.97 x 2 x 10 1.17 x 1.17 x 10	1.97 x 2.03 x 10 1.03 x 1.03 x 10	1.49 × 1.49 × 5 0.83 × 0.83 × 5
Parallel imaging factor	3	2.5	2	2	2	1.5
Scan duration	1 min 24 sec	01 min 36 sec	27 sec	45 sec	42 sec	3 min 54 sec
Scan time/ breath-hold (s)	00:13	00:08	00:12	00:15	00:14	-
Cardiac phases per RR interval Shot duration (ms)	40 -	- 134	- 151	- 167	83	- -

SSFP, steady-state free precession; STIR, short-tau inversion recovery; LGE, late gadolinium enhancement; Ec, Echo.

Supplemental Figure

Questionnaire: Multiparametric cardial MRI for the detection and quantification of myocardial changes after COVID-19 infection (chronic COVID-19 syndrome).

Dear study participants,

we kindly ask you to completely fill out this questionnaire in order to allow us to carry out a systematic analysis. We thank you for your cooperation.

Surname, name: ______________________________

Date of birth: ______________________________

Date of COVID-19 diagnosis: ________________

Weight: _______kg

Height: _______ cm

Are there any known preexisting cardiovascular or respiratory conditions that you are aware of that you have had before COVID-19 infection (e.g. hypertension, heart attacks, asthma, COPD, etc..)? If yes, please list them.

____

____

Did you at any time receive COVID-19 specific treatment? (e.g. dexamethasone)?

☐ no ☐ yes: ______________________________

Were you hospitalized due to your COVID-19 infection?

☐ no ☐ yes,

If you answered yes, for how many days?

____

Which new symptoms were present during your **acute COVID-19 infection**? Please list each symptom and give it a rating on a scale of 0 (not present or resolved) to 10 (most burdening) describing your perceived symptom burden.

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Which symptoms were present after your acute infection **in the chronic phase**? Please list each symptom and give it a rating on a scale of 0 (not present or resolved) to 10 (most burdening) describing your perceived symptom burden.

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Symptom: ________________

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

Not present Worst burden imaginable

Thank you for your participation!

Figure E1. Utilized questionnaire consisting of a 0 to 10 numeric rating scale for the symptom burden score based on subjective well-being (0 no symptoms, 10 most severe symptom burden). Blank spaces were left for participants to fill out the appropriate symptom during the acute and chronic phase of COVID-19 allowing for a direct comparison of symptom burden.