Utility of cardiovascular magnetic resonance imaging in COVID-19 recovered patients: a short-term follow-up study

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Abstract

Objective: To evaluate for cardiac involvement in recovered COVID-19 patients using cardiac magnetic resonance imaging (MRI). **Methods:** A total of 30 subjects recently recovered from COVID-19 and abnormal left ventricular global longitudinal strain were enrolled. Routine investigations, inflammatory markers and cardiac MRI were done at baseline with follow-up scan at 6 months in individuals with abnormal baseline scan. Additionally, 20 age-and sex-matched individuals were enrolled as healthy controls (HCs). **Results:** All 30 enrolled subjects were symptomatic during active COVID-19 disease and were categorized as mild: 11 (36.7%), moderate: 6 (20%) and severe: 13 (43.3%). Of the 30 patients, 16 (53.3%) had abnormal CMR findings. Myocardial edema was reported in 12 (40%) patients while 10 (33.3%) had LGE. No difference was observed in terms of conventional LV parameters however, COVID-19 recovered patients had significantly lower right ventricular (RV) ejection fraction, RV stroke volume and RV cardiac index compared to HCs. Follow-up scan was abnormal in 4/16 (25%) with LGE persisting in 3 patients. Myocardial T1 (1284 + 43.8 ms vs 1147.6 + 68.4 ms; P<0.0001) and T2 values (50.8+16.7 ms vs 42.6+3.6 ms; P=0.04) were significantly higher in post COVID-19 subjects compared to HCs. Similarly, T1 and T2 values of severe COVID-19 patients were significantly higher compared to mild and moderate cases. **Conclusions:** An abnormal CMR was seen in half of recovered patients with persistent abnormality in one-fourth at six months. Our study suggests a need for closer follow-up among recovered subjects in order to evaluate for long term cardiovascular sequalae.

Introduction:

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome (SARS) Cov-2 has affected a majority of the global population in multiple waves of infection.[1] Multisystem involvement in COVID-19 is common with pulmonary and cardiovascular system being most commonly affected.[2] A majority of subjects often completely recover from COVID-19 infection however, a proportion of patients might have persistent symptoms despite recovery from COVID-19. This emerging clinical entity is termed as chronic COVID-19 syndrome (CCS) or long haul COVID.[3] Most of these patients present with fatigue, chest pain and palpitations with a marked negative impact on the quality of life. Though the exact etiology of CCS is still unclear, limited studies have attributed myocardial injury, ongoing inflammation and sub-clinical myocardial dysfunction to be the potential causes of CCS.[4]

Myocardial injury in COVID-19 is not uncommon and has been reported in up to one-third of patients with COVID-19 infection.[5]A majority of these patients with acute myocardial injury have severe COVID-19 infection with raised inflammatory markers and multiple co-morbidities. Multiple mechanisms have been postulated for myocardial injury in COVID-19 including the direct viral injury leading to myocarditis, sys-

temic inflammation and cytokine storm, microvascular damage and thrombosis.[6] Cardiovascular magnetic resonance (CMR) imaging is the gold standard proven diagnostic modality to evaluate cardiac structure, function, myocardial scar (late gadolinium enhancement) and oedema. CMR being a non-invasive imaging modality can detect the presence and extent of myocardial injury as well detection of sub-clinical LV dysfunction even before overt regional wall motion abnormalities become apparent.[7] There is limited data utilising CMR in detection of myocardial injury/inflammation in COVID-19 recovered subjects.[8-12] In the present study, we assessed CMR findings in symptomatic COVID-19 recovered patients both at baseline and at six months of follow-up.

Materials and methods:

This was a prospective single center study in the Department of Cardiology at a tertiary care center in India. A total of 400 consecutive subjects recently recovered (within 30-45 days) from COVID-19 infection were screened. All these subjects were COVID-19 positive in the past using reverse transcription-polymerase chain reaction (RT-PCR) swab test. Patients were considered recovered by the discharge criteria (normal temperature lasting longer than 3 days, resolved respiratory symptoms and two consecutive negative RT-PCR test results separated by at least 24 hours) and were isolated for a minimum of 14 days. Of the 400 subjects, 140 underwent two-dimensional (2D) speckle tracking echocardiography (STE) for detection of sub-clinical left ventricular dysfunction. Impaired global longitudinal strain (GLS) was reported in 39/140 (27.8%) of them. All COVID-19 recovered subjects with abnormal GLS were further screened for suitability for CMR. Subjects with: (1) a history of coronary artery disease, myocarditis, moderate to severe valvular dysfunction, atrial fibrillation or prior cardiomyopathy; (2) contradictions to gadolinium contrast; (3) severe renal insufficiency (creatinine clearance rate < 30 mL/min/1.73 m^2; (4) pregnancy ; (5) unable to breath-hold and cooperate during CMR examination, (6) MRI image quality was not sufficient for analysis and (7) unwillingness to participate or provide informed consent were excluded. Post exclusion, 30 subjects were finally enrolled who underwent CMR at baseline and a follow-up scan six months later in those with abnormal findings in the initial scan. Additionally, 20 age and sex-matched healthy controls were enrolled who underwent CMR. All the control subjects had a normal electrocardiogram (ECG), echocardiography and had no antecedent history or serological evidence of prior COVID-19 infection. Baseline clinical and biochemical parameters including hemogram, liver and kidney function tests as well as inflammatory markers such as C-reactive protein (CRP), serum ferritin, interleukin (IL)-6, lactate dehydrogenase (LDH) and D-dimer were obtained at the time of admission during COVID-19 infection for all subjects. A written informed consent was obtained from all the subjects prior to a CMR scan. The study protocol was approved by the institutional ethics committee.

Cardiac MRI protocol:

All the enrolled patients underwent CMR on a 3T MR scanner (Magnetom Skyra, Siemens, Healthineers, Germany). The MRI scanning protocol has been included in the supplementary appendix. CMR was done at baseline for all enrolled subjects and a follow-up scan after six months was planned in individuals who had abnormal imaging findings on the initial scan.

CMR image analysis:

The acquired CMR images were independently analyzed by two cardiac radiologists with 12 and 10 years of MRI diagnosis experience. Discrepancies in the analysis of the two radiologists were adjudicated by a senior radiologist having 20 years of experience in MRI diagnosis. The CMR images were post processed and cardiac chamber volumes, mass and function were measured using software based automated cardiac contour detection along with manual correction if required. All the image sequences were analyzed as per the 16-segment model proposed by the American Heart Association.[13] The location as well as the pattern (epicardial, mid-wall, or transmural) of LGE were assessed independently by two observers. The global T1/T2 values were computed by manually delineating the entire LV myocardium on the T1/T2 map. Myocarditis was diagnosed based on the 2018 revised Lake Louis criteria (LLC)[14] in the presence of both of the main criteria: (1) myocardial edema (T2 mapping or T2 darkblood TIRM-Sequences) and (2) non-ischemic myocardial

injury (abnormal T1, ECV or LGE).

Statistical analysis:

Continuous data was expressed as mean ± standard deviation (SD) while categorical data was represented as proportions. The normality of distribution was assessed using the using Shapiro-Wilk test. Comparison of means of continuous variables was done using Student's t-test or Mann-Whitney U test as appropriate while Fisher exact test or $\chi 2$ test was used for categorical variables. In addition, ANOVA or Kruskal Wallis was used to compare mean values of continuous variables between the three groups based on severity of COVID-19. A two-sided P value of < 0.05 was considered to be statistically significant. SPSS version 24.0 (IBM Corp, Armonk, NY) and GraphPad Prism version 8.0.0 (GraphPad Software, San Diego, CA) software were used for statistical analysis.

Results:

A total of 30 COVID-19 recovered patients were included in the final analysis (Figure 1: Central figure). The mean age of the enrolled patients was 40.6+ 12.4 years and the cohort mostly comprised of males (18; 60%). Among the healthy controls, the mean age was 39.2+ 5.3 years. The mean duration from discharge to cardiac MRI examination was 62.3+ 21.8 days. All the patients were symptomatic at the time of cardiac MRI examination with chest pain in 18 (60%), shortness of breath in 8 (13.3%), palpitations in 5 (16.7%) and dizziness in 2 (6.7%) being the predominant symptoms. None of the patients had typical anginal symptoms or syncope. Co-morbidities such as diabetes mellitus, hypertension and bronchial asthma were reported in 6 (20%), 2 (6.7%) and 1 (3.3%) patient respectively. During the index COVID-19 hospitalization, fever, cough and dyspnea were the predominant symptoms observed in 24 (80%), 18 (60%) and 17 (56.7%) patients respectively. The mean duration of hospital stay was 12.5+ 7.9 days. Of the 30 patients, 11 (36.7%) were diagnosed as mild, 6 (20%) as moderate and 13 (43.3%) as severe COVID-19 infection based on the NIH severity classification.[15] In this group of patients, 2 (6.7%) underwent mechanical ventilation and one (3.3%) required noninvasive ventilation with positive airway pressure. Oxygen supplementation was required in 19 (63.3%) patients with high flow nasal cannula (HFNC) in 3 (10%). Therapy for COVID-19 included broad spectrum antibiotics in all patients, corticosteroids and anticoagulation in 21 (70%) patients each, antivirals such as Remdesivir in 19 (63.3%), antiplatelets in 10 (30%) and immunomodulators such as Tocilizumab in one patient (3.3%). The laboratory parameters and demographic profile have been reported in Table 1.

CMR findings:

A total of 480 myocardial segments of the thirty patients were evaluated. Sixteen patients of the 30 (53.3%) had abnormal CMR findings in terms of increased T2 signal and/or LGE (Figure 2 and Figure 3). Myocardial edema was reported in 12 (40%) patients while 10 (33.3%) patients had LGE. Majority of the patients had a focal linear sub-epicardial LGE (6/10; 60%) while patchy mid-wall LGE was reported in 4 (40%) [Figure 3]. Most of the LGE lesions were localized in the inferior, infero-septal segments at base and mid-LV cavity level. None of the subjects in the healthy controls had any LGE on CMR. A diagnosis of active myocarditis based on the revised LLC[14] was made in 7/30 (23.3%) individuals. In terms of conventional left ventricular CMR parameters such as LVEF, LV end diastolic volume (EDV), LV end systolic volume (ESV) and stroke volume (SV), there was no significant difference between patients who recovered from COVID-19 and healthy controls (Table 2). However, COVID-19 recovered patients had significantly lower RVEF, RV SV and RV cardiac index (CI) as compared to healthy controls. Follow-up CMR was performed six months later in sixteen subjects who had an abnormal CMR findings. All these sixteen patients had been on medical therapy comprising beta-blockers and ACE inhibitors/ARBs. Of the sixteen subjects, follow-up scan was abnormal in four of them (25%) with LGE persisting in three individuals (Figure 4) while one had raised myocardial T2 value. Of the four patients with abnormal CMR on follow-up, moderate COVID-19 was present in one and severe COVID-19 in three individuals.

Results of native T1 and T2 Mapping:

Using the 2SD above the mean T1 (1284.4 ms) and T2 (49.8 ms) values of the healthy controls as a cut-off,

raised T1 was reported in 16 (53.3%) patients and raised T2 in 12 (40%) patients. Myocardial T1 (1284+ 43.8 ms vs 1147.6 + 68.4 ms; P<0.0001) and T2 values (50.8+ 16.7 ms vs 42.6+ 3.6 ms; P=0.04) were significantly higher among post COVID-19 recovered subjects as compared to healthy controls (Table 2). Additionally, subjects with abnormal CMR findings had significantly higher myocardial T1 (1301.04+ 42.19 vs 1264.62+ 38.41; P=0.022) and T2 values (55.62+ 21.85 ms vs 45.25+ 3.02 ms; P=0.004) as compared to those with normal CMR findings (Table 3).

CMR parameters based on severity of COVID-19 illness:

A significant proportion of severe COVID-19 patients had abnormalities on CMR as compared to mild and moderate cases. In terms of the conventional CMR parameters, there was a significant difference in only LVEF, LVEDV among the three groups based on severity of COVID-19 illness (Supplementary table 1). Myocardial native T1 values of severe COVID-19 patients were significantly higher as compared to mild and moderate COVID-19 patients (mild: 1253.9+ 35.6 ms vs moderate: 1283.2+ 37.6 ms vs severe: 1309.9+ 38.1 ms; P=0.007). Similarly, myocardial native T2 values of severe COVID-19 patients were also significantly higher as compared to mild and moderate COVID-19 patients (mild: 44.1+ 1.5 ms vs moderate: 48.5+ 6.1 ms vs severe: 57.4+ 23.8 ms; P=0.002).

Discussion:

The present prospective study evaluated the presence of myocardial injury and subclinical myocardial dysfunction using CMR in COVID-19 recovered subjects. The major findings of our study were the presence of abnormal CMR in 16 (53.3%) patients who had recently recovered from COVID-19. A significant proportion of patients had either raised T2 (40%) and/or LGE (33.3%). These findings persisted even on follow-up (13.3% of patients had abnormal CMR scan at six months). These findings are important as myocardial injury and subclinical cardiac involvement is not well elucidated and is often overlooked in patients who have recovered from COVID-19 infection. The authors have earlier reported sub-clinical left ventricular dysfunction in one-third of COVID-19 recovered subjects using speckle tracking echocardiography.

There is a limited data regarding the role of CMR in COVID-19 recovered patients. Previous studies have reported the prevalence of abnormal CMR findings in COVID-19 recovered subjects to be ranging between 1.4% and 78%.[8-12] This marked degree of heterogeneity can be explained based on the differences in population studied (asymptomatic to severe COVID) and varying methods for detection of myocardial injury (conventional CMR sequences such as LGE and T2WI versus native T1 and T2 measurements). In a study from China, among 26 COVID-19 recovered subjects, myocardial edema was reported in 14 (54%) while 8 (31%) patients had LGE.[9] However, the authors had included patients recovering from moderate or severe COVID-19 illness and utilized only conventional MR sequences such as LGE and T2WI for detection of myocardial damage. Previous small studies have reported variable myocardial inflammation in heterogenous group of patients[10,11]. Major limitation was either the absence of a control group or inclusion of large number of patients with various comorbidities such as diabetes mellitus, hypertension, coronary artery disease that may have otherwise contributed to the ongoing inflammation.[10,11]Our study addresses all the previous limitations including incorporation of both the conventional parameters such as LGE and T2WI as well as T1 and T2 mapping.

Findings on CMR in our study included the presence of myocardial edema and or LGE in more than 50% of the patients recovering from COVID-19 infection. Additionally, our results showed that the myocardial T1 and T2 values were higher in COVID-19 patients as compared to healthy controls. In our study, elevated T1 was reported in 53.3% while raised T2 was reported in 40% subjects. These findings are concurrent to those in previous studies [9-12]. Prior studies have documented that elevated T2 values corresponds to areas of myocardial edema while elevated T1 values reflect development of myocardial interstitial fibrosis.[16,17] These findings often reflect the inflammatory damage to the myocardium during active COVID-19 infection or an ongoing low-grade localized inflammation during the convalescent phase. Additionally, myocardial edema could be due to increased vascular permeability which is mediated by the endothelial angiotensin converting enzyme (ACE-2).[18] In subjects with viral myocarditis, edema and LGE commonly occurs in the inferior and

inferior-lateral wall with most of the lesions being patchy sub-epicardial in nature.[19] Similar findings were observed in our study too where the predominant distribution of LGE was sub-epicardial involving inferior and infero-septal segments at base and mid-LV cavity level. Severity of the initial COVID-19 infection has an important bearing on findings on CMR. Severe COVID-19 patients with higher levels of inflammatory markers and greater immune mediated myocardial damage often have significantly higher T1 and T2 values as compared to those with mild and moderate COVID-19 infection.[11]

In our study, COVID-19 recovered patients had evidence of right ventricular (RV) dysfunction on CMR as compared to healthy controls. Previous studies using CMR and echocardiogram have reported RV dysfunction among COVID-19 survivors.[4,9,20] Most of this has been attributed to development of pulmonary fibrosis following lung injury and ARDS in COVID-19 recovered subjects. This often results in increased pulmonary vascular

resistance, raised systolic pulmonary arterial pressure with an increased RV afterload along with hypoxia and oxidative stress.[21,22]

Though use of CMR as a routine investigation in COVID-19 recovered patients is not possible, but it did provide some important insights and serves as an important tool in detection of viral myocarditis and subclinical left ventricular dysfunction. Since, inflammation, LGE and fibrosis plays an important role in the development of dilated cardiomyopathy, it becomes all the more prudent to follow-up these patients with an abnormal baseline CMR. There is limited data regarding follow-up CMR imaging in recovered COVID-19 patients. The present study reported abnormal follow-up CMR in 4/16 (25%) with LGE persisting in 3 while one had a raised myocardial T2 value. Earlier reports showed complete resolution of both T2 abnormalities and LGE in 11/27 athletes (40.7%) while 16 athletes (59.3%) still had persistent LGE.[23]

Study limitations:

One of the important limitations of the study is the modest sample size and the heterogeneity of population group studied. Since a significant proportion of severe COVID-19 patients succumb to the illness, patients surviving COVID-19 infection might not reflect the true severity of the disease leading to a survival bias. Lastly, a longer duration of follow-up is needed to determine the sequence of evolution of CMR changes in COVID-19 recovered subjects and long-term prognostic implications.

Conclusion:

The findings from our study reveal that there is an unmet need for close monitoring of cardiovascular status in COVID recovered subjects. CMR serves as an important and sensitive imaging modality in detection of cardiac involvement in patients with COVID-19. Findings such as myocardial edema or LGE points towards systemic inflammation mediated myocardial damage. All the more presence of fibrosis and/or edema calls for follow-up cardiac imaging in form to CMR to detect long term outcomes in COVID-19.

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Figure legends:

Figure 1: Central illustration of CMR in 30 COVID-19 recovered subjects

Figure 2: Cardiac MRI (CMR) images of a 52-year-old male post recovery from severe Covid-19 showing mid myocardial scar at the basal septum (Figure 2A, 2B, black arrows) and elevated T1 and T2 values (Figure 2C and 2D) LA: left atrium; RA: right atrium; LV: left ventricle; RV: right ventricle

Figure 3: CMR scan of a 26-year-old healthcare worker following moderate Covid-19 infection showing sub epicardial to mid myocardial scar in the mid anterior LV (Figure 3A, white arrow) along with mild pericardial effusion (Figure 3B) LV: left ventricle; RV: right ventricle

Figure 4: CMR scan of a 47-year-old recovered from severe Covid-19 with hyper intensity indicating enhancement on LGE sequence in the sub epicardial at the basal septal and mid myocardial in the inferoseptal wall on short axis views with raised T1 and T2 values were

suggestive of post covid myocarditis (Figure 4A, white arrows). Follow-up scan done six months later reporting patchy sub-epicardial LGE (Figure 4B, white arrows). LV: left ventricle; RV: right ventricle

Characteristic	
Age (years)	
Male sex	
Comorbidities Hypertension Diabetes mellitus Bronchial Asthma	
Durations of symptoms (days)	
Duration of hospitalization (days)	
Heart Rate (per minute)	
Symptoms on admission Fever Cough Dyspnoea Sore throat Chest pain Fatigue Loss of smell Loss of taste Headache	
Post COVID-19 symptoms Chest Pain Palpitations Dyspnoea Fatigue Dizziness	
Severity of COVID-19 illness Mild Moderate Severe	
Laboratory parameters	
Haemoglobin (gm%)	
TLC (per mm^3)	
Serum creatinine (mg/dl)	
D-dimer (µg/L)	
CRP (mg/L)	
IL-6 (pg/ml)	
Ferritin (µg/L)	
LDH (U/L)	

Table 1: Baseline demographic and laboratory parameters of COVID recovered subjects and healthy controls

Abbreviations: CRP - C reactive protein; IL - interleukin; LDH - lactate dehydrogenase; TLC - total leukocyte count.

Table 2: Comparative evaluation of CMR parameters between COVID-19 recovered subjects and healthy controls

Cardiac MRI Parameter	**COVID-19 (n=30)**	**Healthy Controls (n=20)**	**P-value**
Left Ventricle			
EF (%)	59.6+6.4	64.5+14.7	0.17
EDV (ml)	99.78+30.39	103+13.20	0.658
ESV (ml)	38.83+15.85	41.86+9.58	0.447
SV (ml)	58.3+16.5	61.1+8.4	0.49
SI (ml/m^2)	33.59+9.52	38.14+7.15	0.075
CO (l/min)	4.45+1.21	5.33+0.72	**0.005**
CI ($l/min/m^2$)	2.57+0.69	3.33+0.66	**0.0001**
Myocardial native T1 (ms)	1284.04+43.86	1147.6+68.4	**0.0001**
Myocardial native T2 (ms)	50.8+16.7	42.6+3.6	0.04
Right ventricle			

Cardiac MRI Parameter	COVID-19 (n=30)	Healthy Controls (n=20)	P-value
EF (%)	48.03+11.85	56.51+8.54	**0.008**
EDV (ml)	76.92+39.78	107.88+13.40	**0.002**
ESV (ml)	40.37+33.13	47.24+12.65	0.382
SV (ml)	35.17+17.95	60.64+10.85	**0.0001**
SI (ml/m^2)	20.36+10.36	37.74+7.49	**0.0001**
CO (l/min)	2.73+0.97	5.27+0.79	**0.0001**
CI (l/min/m^2)	1.57+0.54	3.29+0.62	**0.0001**

Abbreviation: EDV: end-diastolic volume; ESV: end-systolic volume; EF: ejection fraction; CO: cardiac output; CI: cardiac index; SI: stroke index; SV: stroke volume; ml:millilitres; l: litres; min: minute; ms: milli-second

Table 3: Comparative evaluation between COVID-19 recovered subjects with abnormal and normal CMR

	Abnormal CMR (n=16)	Normal CMR (n=20)	P-value
Age (years)	41.9+14.1	39+10.2	0.749
Male sex	10 (62.5%)	8 (40%)	0.73
Heart Rate (per minute)	84+14.3	89.3+13.1	0.804
Severity of COVID-19 illness Mild Moderate Severe	4 (25%) 3 (18.7%) 9 (56.2%)	7 (35%) 3 (15%) 4 (20%)	0.27
Laboratory parameters			
Haemoglobin (gm%)	12.21+1.75	12.90+2.32	0.129
TLC (per mm^3)	10245.63+3091.05	6527.14+2396.89	**0.003**
CRP (mg/L)	43.20+40.13	36.54+54.08	0.28
IL-6 (pg/ml)	11.37+12.71	7.80+9.92	0.205
Ferritin (µg/L)	596.53+384.43	463.65+336.12	0.506
LDH (U/L)	467.69+143.08	417.86+238.80	0.253
D-dimer (µg/L)	394.57+192.72	716.88+545.93	**0.044**
Cardiac MRI Parameter			
Left Ventricle			
EF (%)	60.8+14.5	68.6+14.2	0.195
EDV (ml)	105.98+31.93	92.69+27.96	0.237
ESV (ml)	42.05+14.38	35.14+17.15	0.653
SV (ml)	59.78+17.62	56.70+15.73	0.683
SI (ml/m^2)	34.42+10.18	32.63+8.97	0.120
CO (l/min)	4.36+1.35	4.55+1.05	**0.009**
CI (l/min/m^2)	2.51+0.78	2.62+0.60	**0.001**
Myocardial native T1 (ms)	1301.04+42.19	1264.62+38.41	**0.022**
Myocardial native T2 (ms)	55.62+21.85	45.25+3.02	**0.004**
Right ventricle			
EF (%)	47.75+10.98	48.35+13.20	**0.018**

	Abnormal CMR (n=16)	**Normal CMR (n=20)**	**P-value**
EDV (ml)	72.71+28.53	81.72+50.43	**0.0001**
ESV (ml)	37.08+16.03	44.12+46.09	**0.007**
SV (ml)	35.03+19.55	35.33+16.67	0.965
SI (ml/m^2)	20.28+11.31	20.44+9.58	0.966
CO (l/min)	2.56+0.75	2.92+1.17	0.321
CI (l/min/m2)	1.46+0.40	1.70+0.67	0.237

Abbreviation: CRP - C reactive protein; IL - interleukin; LDH - lactate dehydrogenase; TLC - total leukocyte count; EDV: end-diastolic volume; ESV: end-systolic volume; EF: ejection fraction; CO: cardiac output; CI: cardiac index; SI: stroke index; SV: stroke volume; ml:millilitres; l: litres; min: minute; ms: milli-second

Supplementary table 1: Comparison between the three groups based on severity of illness

	Mild (n=11)	**Moderate (n=6)**	**Severe (n=13)**	**P-value**
Age	45.18+15.67	34.33+7.55	39.54+10.08	0.341
Male sex	6 ()	4 ()	8 ()	0.878
Laboratory parameters				
Haemoglobin (gm%)	12.37+2.30	12.93+1.96	12.50+1.95	0.72
TLC (per mm^3)	7540.91+2698.54	7015.00+2689.92	10020.77+3638.17	**0.012**
Serum creatinine (mg/dl)	0.65+0.11	0.71+0.12	0.64+0.14	0.433
D-dimer (µg/L)	476.64+519.95	535.77+346.48	797.67+482.36	**0.003**
CRP (mg/L)	20.82+37.09	45.10+54.80	54.09+47.39	**0.028**
IL-6 (pg/ml)	7.45+9.22	8.08+13.39	12.12+10.97	**0.021**
Ferritin (µg/L)	418.03+427.08	537.72+435.76	585.57+272.50	**0.008**
LDH (U/L)	342.55+185.27	459.50+71.65	523.69+204.30	**0.05**
Cardiac MRI Parameter				
Left Ventricle				
EF (%)	76.36+8.74	69.33+14.97	52.23+8.04	**0.0001**
EDV (ml)	85.24+28.11	95.61+16.99	114.0+32.12	**0.031**
ESV (ml)	34.11+15.65	38.26+17.60	43.07+15.28	0.314
SV (ml)	50.06+10.91	57.18+14.31	65.88+18.78	0.06
Myocardial native T1 (ms)	1253.96+35.64	1283.22+37.62	1309.87+38.06	**0.007**
Myocardial native T2 (ms)	44.15+1.54	48.55+6.09	57.43+23.78	**0.002**
Right ventricle				
EF (%)	50.90+6.93	56.83+10.72	41.53+12.63	0.738
EDV (ml)	67.21+32.96	86.76+33.45	80.58+47.99	0.263
ESV (ml)	31.24+15.68	35.75+16.92	50.23+46.23	0.251
SV (ml)	34.80+19.0	50.85+24.31	28.25+7.56	0.763

Abbreviation: CRP - C reactive protein; IL - interleukin; LDH - lactate dehydrogenase; TLC - total leukocyte count; EDV: end-diastolic volume; ESV: end-systolic volume; EF: ejection fraction; CO: cardiac output; CI: cardiac index; SI: stroke index; SV: stroke volume; ml:millilitres; l: litres; min: minute; ms: milli-second