Journal of Paediatrics and Child Health

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doi:10.1111/jpc.16363

ORIGINAL ARTICLE

Cardiac effects of multisystem inflammatory syndrome in children: One-year follow-up

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Aim: Cardiovascular involvement is common among children with multisystem inflammatory syndrome (MIS-C) and can cause shock and death. In this study, we evaluated the early and long-term cardiac effects of MIS-C.

Methods: In this observational cohort study, we included all children treated for MIS-C from October 2020 to November 2021 in the Department of Paediatric Infectious Disease at Cukurova University School of Medicine Hospital. The patients underwent serial echocardiographical evaluation during hospitalisation and at 1, 3, 6 and 12 months after discharge. The patients were evaluated using Holter monitorisation between 4 and 6 months and using cardiac magnetic resonance imaging at 6 months and thereafter.

Results: Twenty-six patients diagnosed with MIS-C and with a median age of 84 months were included. Cardiac involvement was found in 19 (73.1%) patients. At initial echocardiographic evaluation, the mean ejection fraction value of the patients was 56.7% (range: 30–75). Coronary artery dilatation was detected in two (7.7%) patients, and mitral regurgitation persisted in only one patient by month 3. Treatment was started in two (7.7%) patients due to ventricular arrhythmia. Cardiac magnetic resonance imaging was performed in 13 (50%) patients at a median of 6 months (range: 5–9). The cardiac magnetic resonance imaging findings were consistent with possible interstitial fibrosis in two (7.7%) patients.

Conclusion: Our results showed that cardiac involvement of patients improved rapidly with treatment, as indicated by previous studies. However, during the 1-year follow-up, frequent extraventricular systole was detected in two patients, one of whom initially did not show cardiac involvement. Moreover, possible interstitial fibrosis was detected in the cardiac magnetic resonance imaging (MRI) evaluation of two patients. In particular, we believe that these findings may be useful to evaluate critically ill paediatric patients and patients with severely low EF with cardiac MRI in their follow-up.

Key words: cardiac involvements; cardiac magnetic resonance imaging; COVID-19; MIS-C.

What is already known on this topic

1 MIS-C entered the medical literature in April of 2020.
2 Multiple organ involvement is seen in MIS-C.
3 The most common involvement is cardiac involvement.
4 The cardiac MRI findings of MIS-C data were limited.

What this paper adds

1 Even though the early cardiac effects are well known, the knowledge on the long term cardiac effects are limited.
2 This study is one first ones to present the long term cardiac MRI findings of MIS-C.

Coronavirus disease (COVID-19) tends to be mild in children. However, in the UK, cases similar to Kawasaki disease or toxic shock syndrome were reported to be associated with COVID-19 in April 2020. Since then, numerous similar cases have been reported world-wide. This condition has been termed as multisystem inflammatory syndrome in children (MIS-C) or paediatric multisystem

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Conflict of interest: None declared.

Author contributions: Dr. Ozlem Ozgur Gundeslioğlu, Dr. Ferhat Pişkin and Dr. Ozden Ozgur Horoz conceptualised and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr. Berivan Subası, Dr. Ummuhan Cay, Dr. Nisanur Tapac, Dr. Fatma Kılınç, Dr.Selime Teleke Kaymaz, Dr. Anıl Atmış and Dr. Ilker Unal designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. Dr. Sevcan Erdem, Dr. Fadli Demir, Dr. Derya Alabaz and Rıza Dinçer Yıldızdaş conceptualised and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Accepted for publication 23 January 2023.

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inflammatory syndrome in children (PIMS).[1] MIS-C is considered a rare complication that is estimated to develop in <1% of children with confirmed SARS-CoV-2 infection, although its true incidence is unclear.[2] In a large-scale study, the incidence of laboratory-confirmed SARS-CoV-2 infection in people aged <21 years was reported to be 322 per 100 000 individuals, whereas the incidence of MIS-C was reported at 2 per 100 000 individuals.[3]

The pathogenesis of MIS-C is currently unknown. Although the clinical laboratory features of MIS-C are similar to those of Kawasaki disease, macrophage activation syndrome, and cytokine storm, MIS-C is considered a separate condition. MIS-C develops because of an abnormal immune response against SARS-CoV-2.[3] Children who have had COVID-19 usually develop MIS-C 2–6 weeks later. Moreover, it has been reported that 67–80% of children with MIS-C exhibit cardiac involvement, such as ventricular dysfunction, coronary artery aneurysm, conduction abnormalities and arrhythmia. In rare cases, patients may develop shock and death due to cardiac involvement.[4–6]

MIS-C appeared as a new disease in 2020, and data on its long-term cardiac effects are limited. Although it has been reported that cardiac involvement rapidly improves with treatment in the early stages, life-threatening arrhythmias have been reported in patients in the later stages. Therefore, the implications of late-stage cardiac complications are not yet fully understood. In this study, we conducted serial cardiological evaluation using cardiac magnetic resonance imaging (MRI) at the beginning of the disease and in the following year, aiming to further understand cardiac involvement associated with MIS-C.

Methods

This single-centre prospective observational cohort study was approved by The Institutional Clinical Research Ethical Committee (15.03.2021/109/8). Informed consent was obtained from the parents of all patients prior to conducting the diagnostic and therapeutic procedures, which were in accordance with the principles of the 1964 Helsinki Declaration.

Table 1 Case definition for multisystem inflammatory syndrome in children (MIS-C)

Individuals aged <21 years presenting with fever†
Laboratory evidence of inflammation‡
Evidence of clinically severe illness requiring hospitalisation, with multisystem (≥2) organ involvement (e.g. cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)
No alternative plausible diagnoses
Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

† Fever ≥ 38.0°C for ≥24 h or report of subjective fever lasting ≥24 h. ‡ Including, but not limited to, one or more of the following: an elevated C-reactive protein, erythrocyte sedimentation rate, fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase or interleukin 6; or elevated neutrophils, reduced lymphocytes and low albumin levels.

Patient population

Twenty-six children with MIS-C who were admitted to the Department of Paediatric Infectious Disease in Cukurova University School of Medicine Hospital between July 2020 and November 2021 were included. The diagnosis of MIS-C was made according to the CDC diagnostic criteria, as shown in Table 1.[7]

Patients with positive results for nasopharyngeal swab testing SARS-CoV-2 nucleic acid using reverse transcriptase quantitative polymerase chain reaction (PCR) assay, positive qualitative detection of SARS-CoV-2 immunoglobulin G antibodies or those who had an epidemiologic link to a person with confirmed SARS-CoV-2 infection were considered as confirmed cases of SARS-CoV-2 infection.[7]

Table 2 Demographic, clinical and treatment characteristics of patients diagnosed with MIS-C

	n (%)
Demographic characteristics	
Age (months)†	84 (18–188)
Female	12 (46.2)
Additional disease	3 (11.5)
Glucose-6-phosphate dehydrogenase deficiency	1 (3.4)
Leukaemia	1 (3.4)
Ventricular septal defect	1 (3.4)
SARS-COV-2 PCR (+)	5 (19.2)
SARS-COV-2 IgG (+)	24 (92.3)
Duration after Covid-19 disease (days)	27 ± 9.5
Patient complaints	
Fever	26 (100)
Cough	2 (7.7)
Rash	6 (23.1)
Stomach ache	12 (46.2)
Nausea and vomiting	7 (26.9)
Physical examination findings	
Fever	26 (100)
Fever value (°C), mean ± SD	38.7 ± 0.6
Tachypnea	12 (46.2)
Tachycardia	11 (42.3)
Rash	9 (34.6)
Lymphadenopathy	2 (7.7)
Konjonktivit	2 (7.7)
Mucositis	2 (7.7)
Treatment characteristics	
IVIG	26 (100)
Oxygen	13 (50)
Steroids	22 (84.6)
Anakinra	8 (30.7)
Clexane and aspirin	26 (100)
Plasmapheresis	2 (7.7)
Inotrope	3 (11.5)
Intensive care hospitalisation	5 (19.2)
Duration of hospitalisation†	12 (2–22)

† Median (min–max). IVIG, intravenous immunoglobulin; PCR, polymerase chain reaction.

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Laboratory tests

All patients underwent routine blood tests, including blood cell counts, biochemical profiles, and evaluation of markers of systemic inflammation. Additionally, cardiac enzymes and markers (troponin I and brain natriuretic peptide) were measured at the time of admission and serially during the hospital stay. Other bacterial and viral infections included in the differential diagnosis were excluded.

Clinical data

Patient demographics, clinical course, laboratory and radiological results, treatment, and outcomes were recorded. The patients were assessed for prior exposure to and documented infections with SARS-CoV-2. All patients were tested using SARS-CoV-2 nasopharyngeal reverse transcription-PCR (RT-PCR) and SARS-CoV-2 G antibodies (colloidal rapid test) on admission.

Cardiac evaluation

Electrocardiography (ECG) and echocardiography were performed at fixed intervals to determine the cardiac effect during hospitalisation. Experienced cardiac sonographers performed two-dimensional standard echocardiography using the GE Vivid T8 Ultrasound System (GE Healthcare, Chicago, IL). Left ventricular (LV) systolic dysfunction was defined as an LV ejection fraction (LVEF) of <55% using the area–length method and was graded as mild (LVEF 45–54%), moderate (LVEF 35–44%) or severe (LVEF <35%), as described previously.[8,9] Right-ventricular (RV) function was assessed using tricuspid annular plane systolic excursion, pulmonary acceleration time and by the estimation of systolic pulmonary artery pressure as assessed by the maximum velocity of tricuspid regurgitation using a continuous-wave Doppler. The classification of coronary artery dilation, aneurysm size and Kawasaki disease was based on the 2017 statement by the American Heart Association. Coronary artery abnormalities were classified using the Boston *z*-score system.[10]

During follow-up, echocardiography controls were examined at 1, 3, 6 and 12 months after hospital discharge. During initial echocardiographic evaluation, patients with abnormal findings underwent weekly review until the results had returned to normal.

Holter monitoring was performed between 4 and 6 months. Patients underwent cardiac MRI at 6 months and thereafter.

Cardiac magnetic resonance imaging

All MRI scans were acquired using a 3.0 T MRI (Ingenia; Philips Healthcare, Best, The Netherlands). Sedative agents were used for sedation in agitated patients.

LV and RV end-diastolic volume, end-systolic volume, and ejection fraction were measured for all patients. Cardiac MRI was analysed to detect myocardial oedema and fibrosis using the standard LV 17-segment model and to specify the pattern (transmural, subendocardial and sub-epicardial). Further, 3D SSFP isovolumetric MR angiography ECG and navigator gating were performed to rule out the possibility of coronary dilatation or aneurysms. Other findings, including pericardial or pleural effusion and the presence of coronary thrombosis, were reported. Extracellular volume (ECV) as a marker of interstitial fibrosis was calculated using the following formula: ECV = (1 − haematocrit) [(1/postcontrastT1 myocardium − 1/nativeT1myocardium)/(1/postcontrastT1 blood pool − 1/nativeT1blood pool)].

Table 3 Laboratory test results

Test	*n* (%)
WBC/μL†	11 450 (2200–26 600)
Leukocytosis (>15 000 μL)	6 (23.1)
Lymphopenia	17 (65.4)
Neutropenia	1 (3.8)
Platelet/μL†	212 500 (64 000–681 000)
Thrombocytosis (>450 000 μL)	3 (11.5)
Thrombocytopenia (<150 000 μL)	7 (26.9)
Haemoglobin (g/dL)†	10.8 (7.7–14.8)
CRP (mg/dL)†	156 (1–475)
Procalcitonin (ng/mL)†	3.5 (0.01–79)
Sedimentation (mL/h)†	28 (2–71)
Ferritin (mg/dL)†	203 (14–2491)
D-dimer (mg/L)†	3.1 (0.2–21)
Fibrinogen (ng/L)†	494 (141–829)
BNP (pg/mL)†	7104 (83–35 000)
Increased BNP (>125 pg/mL)	9 (81.8)
Troponin (ng/L)†	33 (1–722)
Increased troponin (>40 ng/mL)	15 (54.1)
Troponin back to normal level time (days)†	3 (1–21)

† Median (min–max). BNP, brain natriuretic peptide; CRP, C-reactive protein; WBC, white blood cell count.

Table 4 ECG, echocardiography, Holter monitoring and cardiac MRI findings

	n (%)
ECG findings	
Sinus tachycardia	6 (23.1)
Sinus bradycardia	4 (15.4)
Echocardiography findings	
EF†	61.7 ± 11.6
Mild EF impairment	3 (11.7)
Moderate EF impairment	2 (7.7)
Severe EF impairment	1 (3.8)
Mitral regurgitation	15 (57.7)
Tricuspid regurgitation	4 (15.4)
Coronary artery dilatation	2 (7.7)
Pericardial effusion	3 (11.5)
Holter monitoring findings (*n*: 17)	
Ventricular extrasystole	2 (11.7)
Cardiac MRI findings (*n*: 13)	
EF†	56.3 ± 16.5
Myocardial interstitial fibrosis	2 (15.3)

† Mean ± SD. ECG, electrocardiography; EF, ejection fraction; MRI, magnetic resonance imaging.

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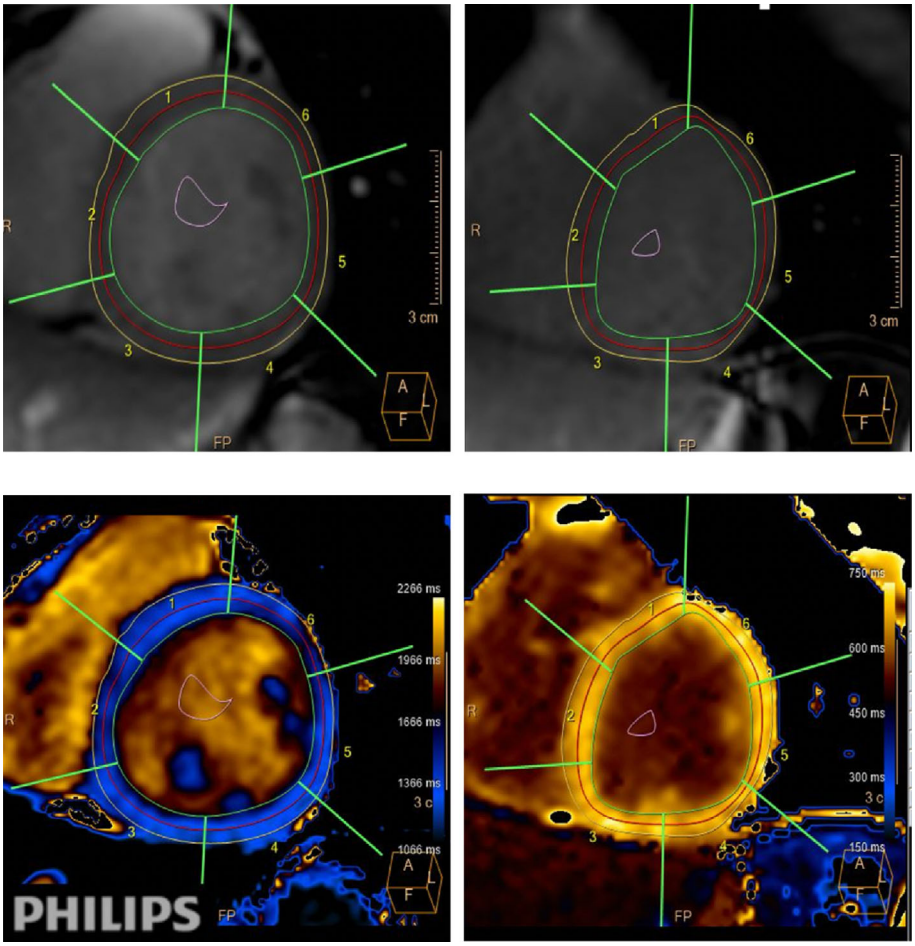


Fig. 1 (a–d) A 13-year-old patient with a diagnosis of MIS-C and shock was admitted to the intensive care unit. Ejection fraction (EF) was measured at 30%. EF improved on the fifth day. The cardiac MRI examination was performed in the ninth month after discharge. The patient's ejection fraction was measured as 55%. Late-phase contrast-enhanced examination revealed no pathological contrast on the left ventricular myocardium. However, in the T1 native imaging, the T1 relaxation value was calculated as 1488 ms in the septum level measurement (increased) (a, c). T1-enhanced 15 min in the calculation performed based on imaging (666 ms) (b, d) and haematocrit values (32.1%); the value of the extracellular matrix increased and was measured as 43%. These findings indicated myocardial interstitial fibrosis. MIS-C, multisystem inflammatory syndrome in children.

Statistical analyses

Categorical variables are expressed as numbers and percentages, and continuous variables are summarised as the mean and standard deviation, and median. Chi-square test was used to compare categorical variables between the groups. The normality of the distribution for continuous variables was confirmed using the Shapiro–Wilk test. The Mann–Whitney *U* test was used for comparison of continuous variables between two groups. All analyses were performed using the IBM SPSS Statistics Version 20.0 statistical software package (IBM Corp. 2011; IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). *P* values <0.05 were considered to show statistically significant differences.

Results

Demographic and clinical features

Overall, 26 patients with MIS-C were included in this study, and their median age was 84 (range: 18–188) months; further, 14 (53.8%) were men and 20 (77%) were followed-up for 1 year. The patients' demographic, clinical and treatment characteristics are presented in Table 2.

Laboratory tests

The patients' median white blood cell count was 11 450/mm^3 (range: 2200–26 600), and lymphopenia was present in 17 (65%) patients. Three (11.5%) patients had thrombocytosis, and seven (27%) had thrombocytopenia. The level of troponin was high (> 40 ng/mL) in 14 (54.1%) patients, and the rate of abnormal findings was high in the echocardiographic evaluation of hospitalised patients with elevated troponin levels ($P = 0.01$). Of the hospitalised patients with low troponin levels, 38.5% had abnormal findings on echocardiography, which was similar to that in patients with high troponin levels at 92.3%. Accordingly, the risk of detecting abnormal echocardiographic findings was 19.2-fold higher (95% confidence interval (CI): 1.9–196.5) in patients with high troponin levels than in those with low troponin levels.

We found that increased troponin levels returned to normal levels within an average of 3 days (range: 1–22 days). The laboratory test results are shown in Table 3.

Initial cardiac involvement

Cardiac involvement was detected in 19 (73.07%) patients at the time of diagnosis and during treatment. Abnormal echocardiographic findings associated with MIS-C were detected in 18 (69.2%) patients. The mean EF value of the patients was 56.7% (range: 30–75). Three

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(11.5%) patients had mild EF and three (11.5%) had significant EF impairment, including severe (<30%) in one (3.8%) and moderate (<50) in two (7.7%) patients. Mitral valve insufficiency was present in 15 (57.7%) patients, and coronary artery dilatation was detected in two (7.7%). During echocardiographic examination of the two patients with coronary dilatation, coronary dilation was normalised at 12 and 30 days. Slight pericardial effusion was observed in three patients, and echocardiographic control of the patients was improved at week 1.

During hospitalisation, sinus tachycardia was detected in six (23.1%) patients, whereas sinus bradycardia was detected in four (15.4%). The cardiac findings observed at the time of diagnosis and during hospitalisation are presented in Table 4. There was no significant difference between the patients with and without cardiac involvement in terms of demographic, clinical and laboratory characteristics and hospital stay ($P < 0.05$).

Cardiac involvement during follow-up

Echocardiographic evaluation was performed in 19 (73%) patients in months 1 and 3. All patient's valve regurgitation has improved by the first month except one patient, which has improved by the third month. Echocardiographic evaluation was performed to 18 patients in month 6, and 13 patients in month 12, which resulted normal in all patients. During follow-up, 17 (65%) patients underwent Holter monitoring, and 2 (7.7%) showed identified monomorphic ventricular extrasystoles. One of the patients with ventricular arrhythmia was symptomatic and initially had no signs of cardiac involvement. The patient had frequent ventricular extrasystole on ECG and received short-term beta-blocker therapy because 90 extrasystoles were detected in 24 h on Holter monitoring. The other patient with ventricular arrhythmia had mild mitral regurgitation on initial echocardiography and had an EF of 55%, which had improved by day 7. There were 18 226 (13%) ventricular extrasystoles in this patient's Holter monitoring at 24 h and beta-blocker was started.

Cardiac MRI findings

Thirteen (50%) patients underwent cardiac MRI at month 6 (range: 5–9 months). The mean EF of the patients was 56.3 ± 16.5% (range: 48.4–71.2) on MRI. Five (19.2%) patients had EF < 60%. No pathological enhancement was detected in any patient with late gadolinium enhancement. However, in two (7.7%) patients, the T1 relaxation times were increased on T1 native mapping. The ECV values of these patients increased by 43% and 41%, respectively on T1 mapping; it was accepted that this finding may be consistent with the findings of interstitial fibrosis. The EF of these two patients was 55% and slightly low. T2 mapping values of all patients were within normal limits. The cardiac MRI findings of the patient who developed possible interstitial fibrosis are presented in Figure 1.

Discussion

MIS-C occurs in individuals aged 1–20 years (median: 8–11 years).[11,12] In this study, the median age of the patients was 7 years (range: 15.5–18 years). The clinical and laboratory characteristics of the patients were consistent with those presented in previous studies and meta-analyses.[11–13]

Cardiovascular system involvement, including ventricular dysfunction, coronary artery dilatation or aneurysms, arrhythmia, valvulitis, pericardial effusion and conduction abnormalities, is common in patients with MIS-C, with an estimated incidence of between 67–80%. In the present study, 73.07% of the patients initially presented with cardiac involvement.[4,14]

An increase in cardiac enzymes, such as troponin and B-type natriuretic peptide (BNP), has been reported as a marker of myocardial damage in MIS-C. In a study by Sirico *et al.*, of the 23 patients with MIS-C who were evaluated, 65% reported an increase in troponin, and 86.9% reported an increase in BNP. A multicentre study involving 55 centres from 17 European Countries found an increase in troponin in children diagnosed with MIS-C in 93% of patients and an increase in BNP in 94% of patients.[15–17] MIS-C may cause severe cardiac damage due to hyperinflation, severe myocarditis, and shock; thus, it is recommended that patients be followed up serially with cardiac enzymes. It has also been reported that increased troponin and BNP levels may be markers for the development of shock and may also be a criterion of hospitalisation in the ICU.[16,18] In the current study, we detected an increase in troponin in 54.1% of patients and an increase in BNP in 81.8% of patients, which was similar to the findings of previous studies. However, the actual rate may be higher as BNP could not be measured in all patients. The troponin values returned to normal levels in the patients on day 3 (range: 1–21 days). Additionally, in our study, initial echocardiographic findings were significantly higher in patients with an increase in troponin compared with those without.

It has been reported that the ECG of patients monitored for MIS-C may show prolongation of the PR and QTc interval, atrioventricular block, ectopic atrial rhythm, nonspecific ST and T changes, and ectopic ventricular arrhythmia. Arrhythmia has been detected in 7–60% of children diagnosed with MIS-C.[19,20] We detected sinus tachycardia in 23.1% of patients and sinus bradycardia in 15.4% of patients on ECG during hospitalisation. However, sinus tachycardia improved rapidly following treatment. The ECG evaluation of the patients with sinus tachycardia showed no additional findings. It was considered that sinus tachycardia might be due to inflammation because of its propensity to promote rapid recovery after treatment. In the current study, the patients who developed sinus bradycardia were asymptomatic and recovered without specific treatment for bradycardia. The cause of bradycardia may be intravenous immunoglobulin (IVIG) and steroid therapy. It has been previously reported that Kawasaki patients develop bradycardia after IVIG and steroid therapy.[21]

Signs of decreased LV function, coronary artery dilatation or aneurysm, mitral regurgitation, and pericardial effusion can be detected in echocardiography evaluation of patients with MIS-C. In a study of 503 patients, echocardiography findings showed that 34% had a decrease in LV function, whereas 13% had a coronary artery aneurysm. It has been reported that LV dysfunctions and coronary artery aneurysms generally return to normal within the first month and completely normalise within 90 days.[4] In our study, the mean EF value of the patients was 56.7%, and EF was low in six (23%) patients. One patient (3.8%) had severe EF impairment, whereas mild dilatation of the coronary arteries was detected in two patients (7.7%). In accordance with the previous literature, the decrease in LV function and coronary artery dilatation in all patients improved within 1 month.

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It has been reported that mitral regurgitation and pericardial effusion can be detected on echocardiography in patients with MIS-C.[17] In this study, 57.7% of the patients had mitral regurgitation, and 15.4% had tricuspid regurgitation. In all but one patient, valve regurgitation improved within the first month, whereas in control, the valve regurgitation improved by the third month. Pericardial effusion was detected in three (11.5%) patients, among whom, the effusion improved rapidly with treatment.

Ventricular extrasystoles were detected in two of the patients during follow-up. One patient was symptomatic and initially had no cardiac involvement. Since monomorphic ventricular extrasystoles were detected frequently, beta-blocker therapy was started for both patients. It has been reported that arrhythmia develops in 7–60% of children diagnosed with MIS-C.[20] In a study that evaluated 286 patients with MIS-C, death occurred because of ventricular arrhythmia in one patient, which revealed that although cardiac function improves with treatment, arrhythmia may still develop later.[17] In this regard, regular follow-up of patients should be performed.

Cardiac MRI findings include pericardial effusion, abnormal T2 myocardial values/hyperintense myocardium on T2-weighted imaging (representing myocardial oedema), early gadolinium enhancement (representing capillary leak or hyperaemia), and late gadolinium enhancement (representing myocardial necrosis or fibrosis).[22] Studies in which evaluation is performed using cardiac MRI after MIS-C in children are limited and usually include early-stage evaluations. Valverde *et al.* reported that cardiac MRI was observed in 42/286 (14.7%) patients; T2 hyperintensity was found in 14 (33.3%), pericardial effusion in 10 (23.8%), early gadolinium enhancement in 1 (2.4%) and LGE in 6 (14.3%) during the first month.[17] In a study in which cardiac MRI was used to evaluate 19 patients 3 months after MIS-C, minimal pericardial effusion was detected in only 3 patients, all of whom improved.[23]

The CMR findings suggest that MIS-C induces myocardial injury with myocarditis-like damage in the early phase of the disease, with subsequent rapid improvement within a few weeks of symptom onset, following appropriate immunomodulatory treatment.[15,24] Theocraharis *et al.* evaluated 20 patients with MIS-C with cardiac MRI at an early stage and showed that myocardial necrosis developed in one patient.[25] In the present study, 13 (50%) patients were evaluated with cardiac MRI median 6 months after discharge. The results showed that ECV values increased in two patients (43% and 41%, respectively), which may be compatible with interstitial fibrosis. Additionally, the EF of five patients were <60%. To the best of our knowledge, no previous study has evaluated the long-term results of MIS-C. Therefore, these findings are important and noteworthy, although more large-scale studies are required to fully validate our findings.

Our study had some limitations. Cardiac MRI and Holter monitoring could not be performed for some of our patients as their families refused. As cardiac MRI could not be performed at the beginning, our cardiac MRI findings for this period were unavailable.

Conclusion

Our results showed that the cardiac involvement of patients improved rapidly with treatment, as indicated by previous studies. However, during the 1-year follow-up, frequent extraventricular systole was detected in two patients, one of who initially did not show cardiac involvement. Cardiac MRI evaluation of two patients revealed possible interstitial fibrosis. In particular, we believe that these findings may be useful to evaluate critically ill paediatric patients and patients with severely low EF with cardiac MRI in their follow-up.

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