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ORIGINAL ARTICLE

# Cardiac Assessment in Children with MIS-C: Late Magnetic Resonance Imaging Features

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## Abstract

Multisystem Inflammatory Syndrome (MIS-C) is a new entity that emerges 2–4 weeks after the SARS-CoV-2 infection in children. MIS-C can affect all systems, the most severe of which is cardiac involvement. The duration of the cardiac symptoms is still uncertain and may be persistent or prolonged. The American College of Rheumatology Clinical Guidelines recommends cardiac magnetic resonance imaging (MRI) 2–6 months after the diagnosis of MIS-C in patients presenting with significant transient left ventricular (LV) dysfunction in the acute phase of illness (LV ejection fraction 50%) or persistent LV dysfunction. There are a few studies investigating cardiac MRI findings in MIS-C patients. In this study, we aimed to evaluate cardiac MRI findings, at the earliest 3 months after diagnosis, and compare these findings with the echocardiograms in children with MIS-C. A retrospective study including 34 MIS-C patients was conducted at a tertiary-level University Hospital between June 2020 and July 2021. Centers for Disease Control and Prevention criteria were used in the diagnosis of MIS-C. Cardiac MRI was performed at least 3 months after MIS-C diagnosis. The study included 17 (50%) boys and 17 (50%) girls with a mean age of $9.31 \pm 4.72$ years. Initial echocardiographic evaluation revealed cardiac abnormality in 13 (38.2) patients; 4 (11.8%) pericardial effusion, 4 (11.8%) left ventricular ejection fraction (LVEF) < 55%, and 5 (14.7%) coronary artery dilatation. Echocardiography showed normal LV systolic function in all patients during follow-up; coronary dilatation persisted in 2 of 5 (40%) patients at the 6th-month visit. Cardiac MRI was performed in 31 (91.2%) patients, and myocardial hyperemia was not detected in any patients (T1 relaxation time was < 1044 ms in all children). However, 9 (29%) patients' MRI showed isolated elevated T2 levels, and 19 (61.3%) revealed at least one of the following findings: pericardial effusion, right ventricular dysfunction, or LVEF abnormality. In patients with MIS-C, a high rate of cardiac involvement, particularly pericardial effusion was determined by cardiac MRI performed at the earliest 2–6 months after diagnosis. Even if echocardiography does not reveal any abnormality in the initial phase, cardiac MRI should be suggested in MIS-C patients in the late period. This is the first study reporting cardiac MRI findings in the late period of MIS-C patients.

**Keywords** MIS-C · Cardiac MRI · Echocardiography

## Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), affected more than 332 million people as of January 2022 [1]. Children infected with SARS-CoV-2 appear less affected and show milder symptoms than adults [2]. However, pediatricians were faced with a new clinical syndrome, "Multisystem inflammatory syndrome in children (MIS-C)," which is similar to toxic shock and Kawasaki disease [3–5]. The post-infectious mechanisms and hyperinflammation play a role in MIS-C pathogenesis and MIS-C typically occurs 2–4 weeks after COVID-19 infection [1, 6–8]. It is unclear why only 1% of SARS-CoV-2 infected children developed MIS-C. Several studies reported a number of risk factors including overweight, asthma, ethnic origin, black or Asian, and defects in the *SOCS1*, *XIAP*, or *CYBB* genes for MIS-C [9, 10]. MIS-C may affect all systems; however, the most severe manifestation is cardiac involvement. At least one of the cardiac

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manifestations such as left ventricular dysfunction (LVD), shock, coronary artery dilatation (CAD) or aneurysms, valvulitis, pericardial effusion, arrhythmia, and conduction abnormalities occurs in approximately 80% of children with MIS-C [3, 5, 11–20].

Few studies demonstrated MIS-C-related ventricular dysfunction or CAD using standardized assessments. There are only five studies showing cardiac MRI findings in the early phase of MIS-C, and no studies on cardiac MRI findings in the late phase [21–25].

In this study, we aimed to determine long-term cardiac outcomes of MIS-C by cardiac MRI and compare MRI findings with echocardiographic findings.

## Materials and Methods

A single-center retrospective study was conducted at a tertiary-level university hospital between June 11, 2020 and July 30, 2021. The MIS-C group consisted of 34 children. The diagnosis of MIS-C was established according to the criteria defined by the Centers for Disease Control and Prevention (CDC) in May 2020 [3, 26].

The Research Ethics Committee of Ege University Faculty of Medicine and the Ministry of Health approved the study (Ethical decision No 21-5.1 T/51).

We used a standardized form to collect the epidemiological data, clinical symptoms, and laboratory findings. Laboratory findings included whole blood count [white blood cell (WBC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), hemoglobin (Hb), platelet count (PLT), monocytes], and biochemical parameters including C-reactive protein (CRP), procalcitonin, D-dimer, fibrinogen, troponin-T, and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels. Troponin-T levels were measured through a one-step enzyme immunoassay with a Dimension VistaVR system (Siemens, Munich, Germany). Reference ranges for conventional cardiac markers, Troponin-T and NT-proBNP, were accepted as $< 14$ ng/l and $< 125$ pg/ml, respectively. Combined nasopharyngeal and oropharyngeal swab specimens were collected in a viral transport medium, including VNat (Bioeksen, Turkey). All samples were analyzed by using the Bio-speedy® SARS CoV-2 Double Gene RT-qPCR (Bioeksen, Turkey) at our Molecular Virology Laboratory. This assay amplifies and detects two targets (ORF1ab and N) of the virus with a limit of detection of 200 genomes per ml. The human gene target RNAse P (RP) was measured in each sample for use in internal control. Reverse transcription-polymerase chain reaction (RT-PCR) was performed using the Rotor-Gene (Qiagen, Luxemburg). Results were considered positive if the signal was detected ($Ct < 35$) for RP, ORF1ab, and N genes.

Anti-Spike immunoglobulin G (IgG) and IgM antibodies were measured in serum samples using rapid lateral flow immunoassay (LFIA) (Colloidal Gold-Hotgen, Germany).

Echocardiographic data were recorded from clinical notes and electronic record systems. All patients underwent 2-dimensional mode and 2-dimensional M-mode echocardiography using a Vivid E9 system with a 3–7 MHz transducer. All transthoracic echocardiography was reviewed and performed by the same pediatric cardiologist. M-mode measurements were carried out with standard techniques following the recommendation of the American Society of Echocardiography [27]. The dimensions of the coronary arteries were expressed as *Z* scores by the published reference standard [28]. Coronary artery dilatation was defined as having a maximum internal diameter of $\geq 3$ mm in the absolute diameter classification and a *Z* score of $\geq 2$ in the affected segment [28]. Left ventricular (LV) dysfunction was defined as an LV ejection fraction (EF) of $< 55\%$.

The timing of echocardiography from the onset of MIS-C disease was as follows: (1) on admission; (2) at 1 month; (3) at 2–3 months; and (4) at 4–6 months.

Cardiac MRI studies were performed with a 1.5 Tesla scanner (Amira®, Siemens Healthineers, Erlangen, Germany). Patients were scanned with the electrocardiogram (ECG)-triggered using a 16-channel surface phased array of body coils. Short and long-axis images were acquired with steady-state free precession sequence (SSFP) to assess myocardial function. Short axis STIR (short Tau inversion recovery) and T1 and T2 and postcontrast T1-weighted images were obtained. Native T1 maps were acquired using a modified Look-Locker inversion recovery sequence (MOLLI). Ten minutes after injection of 0.2 mmol/kg gadolinium contrast agent, long and short axis late gadolinium enhancement (LGE) images were acquired using phase-sensitive inversion recovery sequence (PSIR).

Image analysis was performed by two radiologists (S.B. 12 years, A.C. 4 years of experience) experienced in cardiac imaging.

Cardiac volume–function data, and myocardial T1 and T2 levels were analyzed using the software; Medis medical imaging systems-Medis Suite 2.1 (Leiden, Netherlands). Native T1 maps were evaluated on basal and midventricular slices. A region of interest was drawn on septal, anterior, inferior, and lateral walls on T1- and T2-weighted images. The average of T1 and T2 levels of these segments was used to assess the mean native global T1 and T2 levels. The mean signal intensity with the highest level from any myocardial segment was determined as the segmental maximum level. T1 relaxation time levels greater than 1044 ms were considered abnormal T1 according to Pagano et al. [29]. Myocardial edema was defined as T2 relaxation time greater than 50 ms or signal intensity ratio of the myocardium to skeletal muscle equal to or greater than 2 on T2-weighted images

[30]. A small dose (25 mg/kg/dose) of chloralhydrate was used for children with some MIS-C requiring sedation, while deep sedation or anesthesia was not required in any patients. Cardiac MRI was performed 3 or 6 months after MIS-C diagnosis. MRI was not performed during the initial hospitalization period in any patient.

## Statistical Analysis

Statistical analysis was performed using SPSS statistical package (Version 25 for Windows). Data were expressed as means ± *SD* or medians (interquartile range) for continuous variables or percentages for categorical variables. Comparisons were made using the Student's *t* test for normally distributed data and the $\chi^2$ test for categorical data. The Mann–Whitney *U* test was used to compare differences in nonparametric data. Repeated measures analyses of variance were performed to evaluate changes of all echocardiographic parameters and laboratory data assessed on admission, during hospitalization, discharge, and follow-up 1, 3, 6 month. Repeated measures analysis of variance (RM ANOVA) was performed to evaluate changes in all echocardiographic parameters and laboratory data assessed on admission, first month, third, and sixth month. Statistical significance of differences and correlations were defined $p$ value of $< 0.05$.

## Results

Seventeen (50%) boys and 17 (50%) girls, with a median age of 9.31 ± 4.72 years, were included in this study. Demographic data are shown in Table 1. MIS-C was defined according to CDC criteria in all patients. None of the patients have been vaccinated.

Seventeen patients (50%) were admitted to the intensive care unit, while 11 (32.4%) patients required respiratory support. Thirteen (38.2%) PICU admitted patients required inotropes/vasopressors; 1 (2.9%) patient required hemodiafiltration for renal failure. Mortality did not occur. Length of hospital stay ranged from 3 to 29 days. Echocardiography revealed an abnormality in 18 (52.9%) patients; 4 (11.8%) mild pericardial effusion, 4 (11.8%) LV EF < 55%, and 5 (14.7%) CAD. On admission, the mean EF was 59.6 ± 8.2%, and 12 (35.3%) patients had mild mitral regurgitation, 2 (5.9%) had mild tricuspid regurgitation, 2 (5.9%) had moderate tricuspid regurgitation, 3 (8.8%) had left coronary artery (LCA) dilatation, and 2 (5.9%) had bilateral CAD (Table 2). None of the patients developed persistent heart failure.

At the 6th month of admission, none of the patients showed mitral regurgitation or tricuspid regurgitation. The echocardiography at the 6th month revealed bilateral coronary artery dilatation in 1 (5.9%) patient and the left coronary artery dilatation in 1 (5.9%) patient. Serial echocardiography findings are listed in Table 2. The right coronary artery *Z* score progressed from 3.34 to 5.96 and the left coronary artery from 4.97 to 5.61 in the first patient. The second patient's left coronary artery *Z* score progressed from 2.81 to 3.53.

In this study, LV EF was shown to be correlated with serum NT-ProBNP levels ($r = -0{,}473$, $p = 0.05$), RCA size with CRP ($r = 0.997$, $p = 0.003$), and LCA size with CRP ($r = 0.971$, $p = 0.006$), and ferritin levels ($r = 0.893$,

**Table 1** Demographic and clinical characteristics of MIS-C patients

| Patients (*n*:34) | |
|---|---|
| Gender | |
| Female (*n*, %) | 17 (50) |
| Male (*n*, %) | 17 (50) |
| Age, years, (mean ± SD) | 9.31 ± 4.72 |
| BMI, *Z* score (mean ± SD) | 0.29 ± 1.36 |
| COVID-19 IgM and/or IgG antibodies (*n*, %) | 34 (100) |
| History of previous COVID-19 disease | 3 (8.8) |
| Family history of COVID-19 | 12 (35.3) |
| The age distribution, *n* (%) | |
| 1 to < 5 years | 8 (23.5) |
| 5 to < 15 years | 21 (61.8) |
| > 15 years | 5 (14.7) |
| Underlying diseases, *n* (%) | – |
| Previously healthy | 34 (100) |
| Signs and symptoms, *n* (%) | |
| Fever | 34 (100) |
| Maculopapular rash | 19 (55.9) |
| Conjunctivitis | 17 (50) |
| Vomiting | 14 (41.2) |
| Diarrhea | 11 (32.2) |
| System involvement | |
| Cardiovascular | 24 (70.6) |
| Hematological | 22 (64.7) |
| Gastrointestinal | 21 (61.8) |
| Renal | 6 (17.6) |
| Neurological | 4 (11.8) |
| The total length of hospital stay, days, mean ± SD | 11.6 ± 5.3 |
| Length of PICU stay, days, mean ± SD | 3.6 ± 2.4 |
| Treatment, *n* (%) | |
| IVIG | 33 (97.1) |
| Steroid | 27 (79.4) |
| Anakinra | 3 (8.8) |
| Oxygen support, *n* (%) | 11 (32.4) |
| PICU admission, *n* (%) | 17 (50) |

*SD* standard deviation, *BMI* body mass index, *Ig* immunoglobulin, *IVIG* intravenous immunoglobulin, *PICU* pediatric intensive care unit

**Table 2** Echocardiographic features of MIS-C patients on admission and at 6 months of diagnosis

| | Admission ($n=34$) | 6th-month visit ($n=17$) |
|---|---|---|
| Coronary artery dilatation ($n$, %) | 5 (14.7) | 2 (11.8) |
| Right | 0 (0) | 0 (0) |
| Left | 3 (8.8) | 1 (5.9) |
| Bilateral | 2 (5.9) | 1 (5.9) |
| Pericardial effusion ($n$, %) | 4 (11.8) | 0 (0) |
| Abnormal EF ($n$, %) | 4 (11.8) | 0 (0) |
| MY ($n$, %) | 12 (35.3) | 0 (0) |
| Mild | 12 (35.3) | 0 (0) |
| Moderate | 0 (0) | 0 (0) |
| Severe | 0 (0) | 0 (0) |
| TY ($n$, %) | 4 (11.8) | 0 (0) |
| Mild | 2 (5.9) | 0 (0) |
| Moderate | 2 (5.9) | 0 (0) |
| Severe | 0 (0) | 0 (0) |
| LVEF (mean ± SD, %) | 59.6 ± 8.2 | 66.5 ± 6.3 |
| LVFS (mean ± SD, %) | 35.2 ± 3 | 40.6 ± 14.3 |

*EF* ejection fraction, *FS* fractional shortening, *MIS-C* multisystemic inflammatory syndrome in children *MY* mitral regurgitation, *TY* tricuspid regurgitation, *LVEF* left ventricular ejection fraction, *LVFS* left ventricular fractional shortening, *RVEF* right ventricular ejection fraction, *RVFS* right ventricular fractional shortening, *RCA* right coronary artery, *LCA* left coronary artery

$p=0.041$) with the total length of hospital stay ($r=0.906$, $p=0.034$).

Cardiac MRI could be performed in 31 (91.2%) patients. It could not be performed in 3 patients because they were living in other cities and did not want to come to the hospital. Cardiac MRI was performed in the 3rd month in 12 (38.7%) patients and in the 6th month in 19 (61.3%) patients. Cardiac MRI parameters are shown in Table 3. Late gadolinium enhancement was not detected in any of the patients. We did not detect myocardial hyperemia, whereas 9 (29%) patients showed abnormal T2 levels. Abnormal T2 levels were not associated with WBC, ANC, ALC, PLT, monocyte, CRP, procalcitonin, ESR, D-dimer, NT-proBNP, and Troponin-T on admission ($p>0.05$). The mean level of native T2 was correlated with NT-proBNP levels ($p=0.049$, $r=0.457$) at the 6th-month visit. The group with abnormal T2 did not show any statistical differences in system involvement, the inflammatory state in the acute phase, length of hospital stay, length of PICU stay, steroids usage, or other treatments such as inotropes and oxygen support. Cardiac MRI revealed pericardial effusion in 14 (45.2%) patients and LVD in 5 (16.1%) patients, while echocardiography did not show any abnormalities in these patients. Coronary artery dilatation was determined in 2 patients via echocardiography, whereas cardiac MRI was normal in these patients.

## Discussion

MIS-C is a new entity that develops 2–4 weeks after COVID-19. Cardiovascular system manifestations have been reported in as high as 80% of MIS-C patients [31]. Echocardiography is the first-line imaging for the detection of cardiac dysfunction. Depressed left ventricular systolic function and decreased ejection fraction, CAD, aneurysm, and pericarditis have been reported [32, 33]. Capone et al. [34] evaluated 50 MIS-C patients of which 33 (66%)

**Table 3** Cardiac MRI features of 31 MIS-C patients

| | |
|---|---|
| The length of duration after diagnosis (mean ± SD, month) | 4.8 ± 1.5 |
| LVEDV (mean ± SD, ml) | 82.7 ± 49.6 |
| LVESV (mean ± SD, ml) | 33.4 ± 18.6 |
| LVEF (mean ± SD, %) | 58.5 ± 6.1 |
| RVEF (mean ± SD, %) | 59.5 ± 8.8 |
| The diameter of pericardial effusion (mean ± SD, mm) | 5.5 ± 1.09 |
| The basal levels of native T1 (mean ± SD, ms) | 903 ± 38.6 |
| The maximum basal levels of native T1 (mean ± SD, ms) | 947.9 ± 41.9 |
| The level of midventricular native T1 (mean ± SD, ms) | 933.4 ± 47 |
| The maximum level of midventricular Native T1 (mean ± SD, ms) | 985.5 ± 55.5 |
| The basal level of native T2 (mean ± SD, ms) | 47 ± 5.13 |
| The maximum basal level of native T2 (mean ± SD, ms) | 51.09 ± 7.99 |
| Level of midventricular native T2 (mean ± SD, ms) | 48.4 ± 5.17 |
| The maximum level of midventricular native T2 (mean ± SD, ms) | 54.7 ± 8.06 |
| LVEF abnormality ($n$, %) | 5 (16.7) |
| Right ventricular dysfunction ($n$, %) | 6 (19.4) |
| Pericardial effusion ($n$, %) | 14 (45.2) |

*MRI* magnetic resonance imaging, *LVEDV* left ventricular end-diastolic volume, *LVESV* left ventricular end-systolic volume, *LVEF* left ventricular ejection fraction,

presented with cardiac manifestations which were LVD in 26 (52%) patients, and CAD in 10 (20%) patients. Theocharis et al. [20] showed that out of 11 patients with cardiac involvement, 8 (40%) had LV systolic dysfunction, 2 (10%) had left anterior descending coronary artery dilatation, and 1(5%) had right coronary artery dilatation on admission. We observed cardiovascular involvement in 13 (38.2%) patients on admission, which was lower than in the study by Capone et al. [34]. However, in our study, LVD was less frequently observed (12.9%) than in previous studies, with varying degrees of reduction in ejection fraction.

In previous studies, pericardial effusion has been shown in 9–72% of MIS-C patients [19, 35, 36]. Valverde et al. [19] reported 80 (27.9%) patients with pericardial effusion at admission, 66 (25%) of them being mild, 8 (3%) of them moderate. Pericardial effusion persisted in 20.6% of patients during hospitalization. We detected 4 (11.8%) patients with pericardial effusion on admission; all of them were mild. In the follow-up period, echocardiographic examination showed that pericardial effusion completely recovered in all patients.

A previous study determined 50% mitral regurgitation and 72% pericardial effusion via echocardiography among MIS-C patients on admission, while only 20% had small pericardial effusion and 18% had mild mitral regurgitation at discharge [36]. Valverde et al. [19] reported the rate of mitral regurgitation and tricuspid regurgitation in a large European MIS-C cohort as 42.5% and 5.9%, respectively. In this study, the initial echocardiographic evaluation showed mild mitral regurgitation in 12 (35.3%) patients and tricuspid regurgitation in 4 (11.8%) patients, and all those patients recovered within 6 months. Mitral regurgitation was less, and tricuspid regurgitation was more frequent in our cohort than in previous studies [19, 36].

The incidence of coronary artery abnormalities varies considerably across studies. Usually, mild or moderately sized coronary artery abnormalities have been reported in 9% to 26.7% of the MIS-C cases, and large/giant coronary artery aneurysms have been reported in several studies [11, 12, 14, 37, 38]. Valverde et al. [19] showed coronary artery abnormalities in 69 (24.1%) of the 286 patients and giant aneurysm in 1 (0.3%) patient. Coronary artery ectasia (*Z* score: 2.53 and 2.6 in the right coronary artery) was detected in only two patients (4%) in one of the previous studies and they recovered until discharge [36]. Similar to these studies, coronary artery abnormalities were detected in 14.7% of patients in our study.

Previous studies generally evaluated acute and early cardiac involvement of MIS-C cases [39–46]. Capone et al. [34] reported early midterm results of cardiac MRI performed in the convalescence phase 2–4 weeks after discharge in 11 of 50 MIS-C patients with initial LVD. They did not determine persistent edema or fibrosis at 8 weeks, despite higher troponin levels during hospitalization (median:37, IQR:9–109, reference < 14 ng/L) in these patients [34]. In two other studies, cardiac MRI was performed in MIS-C patients, usually within the first 1 month, and fibrosis was not reported in the acute phase [20, 47]. Bermejo et al. [40] performed cardiac MRI (between 12 and 72 days) in 20 of 44 MIS-C patients with a median age of 8 years. They detected small areas of LGE in 2 patients, abnormal mean T1 levels in 1 patient, and normal mean global T2 levels of basal, midventricular, and apical slices in all patients. Higher T2 levels in the apical lateral segment in 1 patient, and basal septal levels were abnormal in 1 patient. Blondiaux et al. [32] performed MRI 14 days after discharge in four children and found diffuse myocardial edema and hyperemia without evidence of focal myocardial necrosis/fibrosis. Dominguez et al. [21] performed cardiac MRI in 12 of 37 MIS-C patients with a median age of 8 years and detected myocardial edema in 7 patients, pericardial effusion in 5 patients, and decreased left ventricular function in 3 patients. Valverde et al. [19] reported T2 hyperintensity in 14 (33.3%) of 42 patients, pericardial effusion in 10 (23.8%), early gadolinium enhancement in 1 (2.4%) and 6 (14.3%) LGE. Studies of cardiac MRI in MIS-C patients are summarized in Table 4. However, cardiac MRI was generally performed in the acute phase, and the number of patients was, respectively, small in these studies [20, 32, 34, 39–46]. Theocharis et al. [20] detected myocardial edema in 10/20 (50%) patients. Matsubara et al. [24] reported the cardiac outcomes of 14 of 60 patients with MIS-C. Cardiac MRI was performed in five patients during the subacute phase and nine patients during the following period. Only one of nine patients had residual edema on cardiac MRI [24]. The recent study by Dove et al. [25] detected late gadolinium enhancement, T1 mapping abnormalities, and abnormal or borderline extracellular volume calculations suggesting myocardial fibrosis in two of 51 patients, and no patient had T2 mapping abnormalities corresponding with edema. In our study, echocardiography did not show any abnormality at the 6th month (except coronary dilatation), whereas cardiac MRI demonstrated cardiac involvement, particularly pericardial effusion. Sixty-one percentage of the patients still had at least one of the following findings: pericardial effusion (45.2%), right ventricular dysfunction (19.4%), and LVEF abnormality (16.7%).

Bermejo et al. [40] detected abnormal T2 levels correlated with elevated D-dimer on admission. We did not observe any correlations between T2 levels with WBC, ANC, ALC, PLT, monocyte, CRP, procalcitonin, ESR, D-dimer NT-proBNP, and troponin-T ($p > 0.05$).

Several studies have reported the short-term outcomes of cardiac complications in children with MIS-C. Cardiac complications persisted during firsty and second months at follow-up in two studies [48, 49]. Caro-Paton et al. [50] showed

**Table 4** A literature review of published studies regarding cardiac MRI findings of MIS-C patients

| Article | Age | Number of patients performed MR/number of total patients | MR findings | The time of MRI | Study design | Hospital |
|---|---|---|---|---|---|---|
| Bermejo et al.[40] | Median age: 8 years | 20/44 | 2 patients: Late gadolinium enhancement | 27 ± 14 days | | Royal Brompton Hospital Sydney Street London, UK |
| Biko et al. [41] | Mean ± SD: 9.7 ± 3.97 | 1/10 | No findings consistent with myocarditis, myocardial edema, and normal myocardial delayed enhancement and T1 mapping | Acute phase | Retrospective | Children's Hospital of Philadelphia or an affiliated hospital |
| Blondiaux et al. [32] | Mean ± SD: 9 ± 3 years | 4/8 | T1 mapping values and T2-STIR ratio suggesting myocardial hyperemia and edema | 3 patient: Acute phase, 1 patient: Recovery phase (14 days after discharge) | Retrospective | Sorbonne Université, Paris, France |
| Capone et al. [34] | Median age: 8.5 years | 11/50 | None of the patients: persistent edema or fibrosis | 2–4 weeks after discharge | Cohort study | Cohen Children's Medical Center, New York |
| Domínguez et al. [21] | Median age: 8 years | 12/37 | 7 patients: Myocardial edema, 5 patients: Pericardial effusion and 3 patients: Decreased left ventricular function | Between 5 and 100 days after symptom onset | Retrospective | Hospital Universitario Virgen del Rocío, Seville, Spain |
| Dove et al. [25] | Median age: 11.3 years | 51/51 | Two patients: Late gadolinium enhancement, 10 patients: Isolated elevated T1 values | The median time of 105 days after diagnosis | Retrospective | Emory University School of Medicine, |
| Jain et al. [46] | Mean ± SD: 8.7 ± 5.5 years | 1/3 | Myocardial edema | On day 6 | Case series | Maria Fareri Children's Hospital at Westchester Medical Center, New York |
| Matsubara et al. [24] | Mean ± SD: 10 ± 4.3 years | 15/60 | Two patients in the subacute phase who had evidence of myocardial edema (1 focal, 1 global) | Five patients: During the subacute phase (median, 8 days), 9 patients: During follow-up period (median, 162 days) | Retrospective | Institutional Review Boards of Children's Hospital of Philadelphia, and St. Peter's University Hospital |
| Minocha et al. [42] | Median age: 2.8 years | 1/33 | 1 patient: Myocarditis | Acute phase | Retrospective | Hassenfeld Children's Hospital at NYU Langone and Bellevue Hospital Center |
| Palabiyik et al. [39] | Median age: 7.68 years | 1/45 | 1 patient: Decrease in the pericardial effusion and systolic functions and an increase in cardiac dimensions | Acute phase | Retrospective | Bakirkoy Dr. Sadi Konuk Training and Research Hospital |
| Prieto et al. [43] | Median age: 7 years | 5/5 | No myocardial edema or enhancement abnormalities | Median day after admission:16 day, [9–17] | Case series | Hospital Universitario 12 de Octubre, Madrid, Spain |

**Table 4** (continued)

| Article | Age | Number of patients performed MR/number of total patients | MR findings | The time of MRI | Study design | Hospital |
|---|---|---|---|---|---|---|
| Sirico et al. [44] | Mean ± SD: 8.1 ± 4 years | 17/23 | 1 patient: LV edema, 6 patients: Left ventricle late gadolinium enhancement) 2 patients: Pericardial effusion | Within 19 days | Retrospective | Women's and Children's Health (W&CHD) of Padua University Hospital, Italy |
| Tannoury et al. [22] | Mean ± SD: 11 ± 5.5 years | 1/4 | Minimal myocarditis area in the mid inferior septum and mid inferior wall | 3.5 months | A case series | American University of Beirut Medical Center |
| Theocharis et al. [20] | Mean ± SD: 10.6 ± 3.8 years | 20/20 | 13 patients: EF normal, 3 patients: Borderline EF, 4 patients: EF < 50%, 10 patients: Myocardial edema | Median day 20 [11–29 days] | Retrospective | Evelina London Children's Hospital |
| Webster et al. [23] | Mean ± SD 13.8 ± 2.2 | 6/6 | Biventricular size and function were normal | 61 days | Prospective | Lurie Children's Hospital of Chicago |
| Valverde et al. [19] | Median age: 8.4 years | 42/286 | 14 patients (33.3%): T2 hyperintensity, 10 patients (23.8%): pericardial effusion, 6 patients (14.3%): Late gadolinium enhancement | During hospitalization | | 55 participating European hospitals |

cardiac complications in 3 (25%) patients. Pouletty et al. [51] demonstrated mild LV dysfunction persisted in only two of 7 patients admitted to the intensive care unit. A study focused on follow-up of patients with MIS-C determined only one patient with a medium CA aneurysm (*Z* score 9.8) was stable at the 6th month of initial diagnosis [52]. These reports highlighted that the majority of the cardiac manifestations resolved during the short-term follow-up period. In our study, CAD persisted in 2 (40%) of 5 patients with CAD detected by echocardiography which was higher than the literature.

MIS-C seems to be a severe acute disease with minor complications on the midterm. If we are not going to start treatment for cardiac involvement, performing cardiac MRI in general in young children who need sedation for cardiac MRI data, and in patients with mild and asymptomatic pericardial effusions or ventricular dysfunction may be a topic of discussion. However, we showed abnormalities with cardiac MRI even in asymptomatic patients or without biochemical abnormality. Therefore, we suggest performing cardiac MRI on all MIS-C patients, even echocardiography does not reveal any abnormality.

## Conclusion

Echocardiography and cardiac MRI are sensitive and specific tools to evaluate cardiac involvement in patients with MIS-C. However, this study demonstrated that cardiac MRI is more sensitive and specific in the late phase of MIS-C. Pericardial effusion was the most common finding in the late period. Cardiac MRI evaluation may be suggested for all MIS-C patients at the late phase; even echocardiography does not detect any abnormality. More extensive and prospective design studies are needed to determine cardiac residual long-term damages.

## Limitations

The first limitation of our study is its retrospective nature. Second, it is a single-center study, and a limited number of patients could be evaluated.

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## Declarations

**Conflict of interest** The authors have no conflicts of interest relevant to this article to disclose.

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