Six Month Follow-up of Patients With Multi-System Inflammatory Syndrome in Children

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abstract

BACKGROUND AND OBJECTIVES: Myocardial dysfunction and coronary abnormalities are prominent features of multisystem inflammatory syndrome in children (MIS-C). In this study we aim to evaluate the early and midterm outcomes of MIS-C.

METHODS: This is a longitudinal 6-month cohort study of all children admitted and treated for MIS-C from April 17 to June 20, 2020. Patients were followed ∼2 weeks, 8 weeks, and 6 months postadmission, with those with coronary aneurysms evaluated more frequently.

RESULTS: Acutely, 31 (62%) patients required intensive care with vasoactive support, 26 (52%) had left ventricular (LV) systolic dysfunction, 16 (32%) had LV diastolic dysfunction, 8 (16%) had coronary aneurysms (*z* score ≥2.5), and 4 (8%) had coronary dilation (*z* score <2.5). A total of 48 patients (96%) received immunomodulatory treatment. At 2 weeks, there was persistent mild LV systolic dysfunction in 1 patient, coronary aneurysms in 2, and dilated coronary artery in 1. By 8 weeks through 6 months, all patients returned to functional baseline with normal LV systolic function and resolution of coronary abnormalities. Cardiac MRI performed during recovery in select patients revealed no myocardial edema or fibrosis. Some patients demonstrated persistent diastolic dysfunction at 2 weeks (5, 11%), 8 weeks (4, 9%), and 6 months (1, 4%).

CONCLUSIONS: Children with MIS-C treated with immunomodulators have favorable early outcomes with no mortality, normalization of LV systolic function, recovery of coronary abnormalities, and no inflammation or scarring on cardiac MRI. Persistence of diastolic dysfunction is of uncertain significance and indicates need for larger studies to improve understanding of MIS-C. These findings may help guide clinical management, outpatient monitoring, and considerations for sports clearance.

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DOI: https://doi.org/10.1542/peds.2021-050973

Accepted for publication Jul 23, 2021

WHAT'S KNOWN ON THIS SUBJECT: Myocardial dysfunction and coronary abnormalities are prominent early features of acute multisystem inflammatory syndrome in children (MIS-C). Persistent coronary aneurysm and/or low-normal or mild left ventricular dysfunction has been reported after hospitalization.

WHAT THIS STUDY ADDS: Early and midterm prognosis after hospitalization and immunomodulation treatment of MIS-C is excellent with return to functional baseline, normalized left ventricular systolic function, and resolved coronary abnormalities. However, persistence of diastolic dysfunction in a few patients confounds our understanding of MIS-C.

To cite: Capone CA, Misra N, Ganigara M, et al. Six Month Follow-up of Patients With Multi-System Inflammatory Syndrome in Children. *Pediatrics*. 2021;148(4):e2021050973

Multisystem inflammatory syndrome in children (MIS-C) is a new postinfectious inflammatory disorder that has emerged during the coronavirus disease 2019 pandemic. Critical illness is a prominent feature, with up to 80% of patients requiring intensive care, ~50% showing features of LV systolic dysfunction and myocarditis, and 10% to 20% developing coronary artery aneurysms (z score $\geq$2.5).[1–4] For patients presenting with preserved systolic function, myocardial injury may still occur, detected by echocardiographic measures of diastolic dysfunction. Although MIS-C has many similarities to other inflammatory syndromes such as Kawasaki disease (KD), children with MIS-C tend to be older and have more intense inflammation and myocardial injury than children with KD.[3] Coronary artery involvement is the major cardiovascular sequelae of KD and coronary dilation associated with KD tends to regress within 2 years.[5,6] However, the long-term complications of MIS-C are still unknown. In this study, we describe the management and early to midterm outcomes of a cohort of pediatric patients 6 months after admission for MIS-C.

METHODS

This is a 6-month follow-up study of pediatric patients (<21 years of age) hospitalized for MIS-C between April 17, 2020, and June 20, 2020, at Cohen Children's Medical Center. This study was approved by the Northwell Health Institutional Review Board with informed consent waived. The clinical presentation and hospitalization of some patients (n = 31) included in this report have been published previously by Capone et al and/or as part of a multicenter publication.[2,4] This article differs from the aforementioned articles because it adds more patients to the acute phase analysis and more importantly longitudinal data. Furthermore, diastolic function was added to the analysis along with cardiac MRI (CMRI) results. Patients were included if they met the Centers for Disease Control and Prevention case definition for MIS-C and if they had evidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection by either detection of serum antibodies or nucleic acid from a nasopharyngeal specimen (polymerase chain reaction+).[7,8]

Patients received immunomodulatory treatment and anticoagulation as per our institutional guideline (Supplemental Fig 3). Patients were clinically followed at ~2 weeks, 8 weeks, and 6 months postadmission. Some patients were seen more frequently as clinically indicated (Table 1).

Serial echocardiograms were performed at the time of admission and then as clinically indicated or per protocol. Ventricular function and coronary dimensions were tracked serially from date of admission to 6-month follow-up. Boston Children's Hospital z score system was used for all echocardiographic measurements.[9] Left ventricular (LV) systolic dysfunction was defined as a left ventricular ejection fraction (LVEF) <55% by 5/6 area-length method and graded as mild (LVEF 45% to 54%), moderate (LVEF 35% to 44%), or severe (LVEF <35%) as previously described.[4] A patient was considered to have diastolic dysfunction (yes or no) if at least 2 parameters (E/A, e', or E/e') were abnormal. The mitral inflow E/A Doppler profile was considered abnormal if the E and A waves were fused or if the E/A ratio had a Boston Children's Hospital Z score >2.0. The e' velocity and E/e' ratio, either septal or lateral, were considered abnormal if either had a Boston Children's Hospital z score >2.0. Aneurysm and dilation of a proximal coronary artery (right coronary artery, left main coronary artery, and/or left anterior descending coronary artery) were defined by using z scores as per the latest AHA Kawasaki guidelines (dilation 2.0–2.49, small aneurysm $\geq$2.5 to <5, medium aneurysm $\geq$5 to <10, and large aneurysm $\geq$10).[5] Qualitative lack of tapering was used to describe an abnormal coronary appearance that did not meet criteria for dilation or aneurysm.

CMRI was performed 2 to 4 weeks after discharge from hospital as per our institutional protocol in follow-up of clinically diagnosed myocarditis such as patients with LV systolic dysfunction, elevated troponin, and/or EKG changes.[10] All CMRI studies were performed without general anesthesia or sedation. Image analysis was done by using Circle software (CMRI-42).

Continuous variables are summarized as mean and SD or median and interquartile range (IQR) as appropriate. Categorical variables are presented as frequency. All analyses were performed by using Excel (Office Professional +13, Microsoft, Redmond, WA).

Interrater reliability was assessed by using Cohen's κ coefficient. Multiple statistical classifications describing degree of reliability are reported in the literature. A commonly used methodology by Landis et al categorizes agreement as follows: <0.01, poor agreement; 0.01–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; 0.81–1.00, almost perfect agreement.[11] Because interrater reliability demonstrated substantial agreement for LVEF and substantial

agreement for coronary abnormalities (including lack of tapering), the data on the formal transthoracic echocardiogram report were used for analysis.

RESULTS

Acute Presentation

Fifty consecutive patients met Centers for Disease Control and Prevention criteria for MIS-C and had laboratory evidence of SARS-CoV-2 infection during this study period. Our cohort was predominantly male (56%) with a median age of 8.5 years (range 9 months to 17 years). The epidemiological characteristics and clinical profile of patients were similar to our previously reported data[4] (Table 1). Notably, C-reactive protein (CRP) was markedly elevated (median 204 mg/L; IQR: 12–291; reference <5) and the platelet count was low-normal (median 172 K/μL; IQR: 122–232) in our cohort.

Cardiac abnormalities present on admission and followed in this study are detailed in Table 2. Thirty-three patients (66%) had cardiovascular manifestations that included LV systolic dysfunction, LV diastolic dysfunction, or coronary dilation or aneurysm. Twenty-six patients (52%) had LV systolic dysfunction and required an intensive level of care with vasoactive support. Of these 26 patients, 11 also had LV diastolic dysfunction and 10 had coronary dilation or aneurysms. Two patients had aneurysms only without any type of LV dysfunction. Five patients had diastolic dysfunction only without evidence of LV systolic dysfunction or coronary dilation/aneurysm. Of note, 14 patients (28%) showed an abnormal coronary appearance (lack of tapering) that we followed to assess for longitudinal significance, if any.

Plasma brain natriuretic peptide (pro-BNP) and plasma CRP were more elevated in patients with LV systolic dysfunction than those without (pro-BNP: 9874 pg/mL [IQR: 4514–24 152] vs 3151 pg/mL [IQR: 1343–4424], $P = .005$, and CRP 233 mg/L [IQR: 142–289] vs 148 mg/L [IQR: 95–212], $P = .03$, respectively). Neither were associated with the development of coronary abnormalities. Although plasma high-sensitivity troponin T levels were elevated in patients with LV systolic dysfunction compared with those with normal function (44 ng/L [IQR: 20–110] vs 21 ng/L [IQR: 6–79] $P = .14$), this was not statistically significant. Additionally, troponin T level was not associated with the development of coronary abnormalities. Although peak levels of CRP, pro-BNP, and troponin T were more elevated in patients with

TABLE 1 Demographics, Clinical Characteristics, and Hospital Course

	Value
Demographic characteristics	
Patients, *n*	50
Age, years, median (IQR)	8.5 (5.4–11.5)
Age, range	0.9–17
Female sex, *n* (%)	22 (44)
Race, *n* (%)	
White	4 (8)
Black	15 (30)
Asian American	6 (12)
Other or multiracial	21 (42)
Unknown or declined	4 (8)
Ethnicity, *n* (%)	
Hispanic	13 (26)
Non-Hispanic	37 (74)
Clinical characteristics	
Wt status categories, *n* (%)	
Underweight (<5th percentile)	3 (6)
Normal wt (5^{th} to <85th percentile)	21 (42)
Overweight (85th to <95th percentile)	6 (12)
Obese (≥95th percentile)	20 (40)
Hospitalization	
PICU admission, *n* (%)	26 (79)
Length of stay, days, median, IQR	4 (4–8)
Discharged alive, *n* (%)	50 (100)
Laboratory results	
White blood cell count, median (IQR), K/μL	9 (7.1–12.5)
Absolute lymphocyte count, median (IQR), K/μL	1 (0.6–1.5)
Lymphopenia, *n* (%)	38 (76)
Hemoglobin, median (IQR), g/dL	11.4 (10.5–12.1)
Platelet count, median (IQR), K/μL	172 (122–232)
C-reactive protein (reference: <5), median (IQR), mg/L	204 (122–291)
D-dimer (reference: <230), median (IQR), ng/mL	2248 (1295–2829)
Ferritin (reference: 15–150), median (IQR), ng/mL	782 (366–1664)
Pro-BNP (reference: <300), median (IQR), pg/mL	5023 (2708–12 766)
Troponin T (reference: <14), median (IQR), ng/L	37 (9–109)
High troponin, *n* (%)	19 (38)
Medications for MIS-C, *n* (%)	
IVIg	48 (96)
Methylprednisolone	35 (70)
Any biologic	13 (26)
Anakinra	6 (12)
Tocilizumab	4 (8)
Infliximab	3 (6)
Aspirin	46 (92)
Enoxaparin	23 (46)

IVIg, intravenous immunoglobulin.

TABLE 2 Echocardiographic Abnormalities Present on Admission and on Follow-up at 2 Weeks, 8 Weeks, and 6 Months

Echocardiogram Findings	Acute (n = 50)	2 wk (n = 47)	8 wk (n = 42)	6 mo (n = 24)
Any coronary abnormality, *n* (%)	26 (52)	13 (27)	5 (14)	0
LMCA *z* score	0.38 ± 1.1	−0.14 ± 0.92	−0.40 ± 0.88*	−0.41 ± 0.92*
LAD *z* score	0.62 ± 1.24	−0.21 ± 1.12	−0.85 ± 0.82*	−0.84 ± 0.72*
RCA *z* score	−0.14 ± 1.25	−0.48 ± 0.84	−0.77 ± 0.76*	−0.99 ± 0.78*
LAD/*RCA* *z* score ≥2.5, *n* (%)	8 (16)	2 (4)	0	0
LAD/RCA *z* score 2–2.49, *n* (%)	4 (8)	1 (2)	0	0
Lack of tapering (*z* score <2), *n* (%)	14 (28)	10 (21)	5 (14)	0
Any LV systolic dysfunction, *n* (%)	26 (52)	1 (2)	0	0
LVEF (mean, SD)	54 ± 9	64 ± 4	62 ± 4*	62 ± 3*
Mild (LVEF 45%–54%), *n* (%)	15 (30)	1 (20)	0	0
Moderate (LVEF 35%–44%), *n* (%)	11 (22)	0	0	0
Severe (LVEF <35%), *n* (%)	0	0	0	0
Diastolic dysfunction, *n* (%)	16 (32)	5 (11)	4 (9)	1 (4)

* Significant difference ($P < .05$).

cardiac manifestations, we were not powered to assess sensitive laboratory cutoffs predictive of cardiac abnormalities. When assessed as dichotomous variable, abnormalities in initial laboratory tests were no different between those with cardiac manifestations versus those without.

Most patients exhibited rapid clinical improvement, with 48 patients (96%) having received treatment as per our institutional guideline (Supplemental Fig 3). Thirty-five patients (70%) were discharged on tapering steroids, 46 patients (92%) with aspirin and 23 patients (46%) with enoxaparin or apixaban as per our institutional guidelines (Table 1).

The median length of hospital stay for the entire cohort was 5 days (IQR: 4–7). There were no in-hospital deaths, and no patient required extracorporeal membrane oxygenation support. Of the 26 patients with LV systolic dysfunction at admission, 18 patients (69%) had normalization of the LV systolic function by discharge; 4 patients (15%) had persistent but improved LV systolic dysfunction. The remaining 4 patients had mild dysfunction during admission and did not have a discharge echo to assess. Recovery of function occurred at a median of 3 days with an IQR of 1 to 8 days. Coronary findings were unchanged at discharge.

Two-Week Follow-up

Of the 47 patients who presented for the 2-week follow-up visit, 22 (47%) reported fatigue with ordinary activity. Of these 22 patients, 18 had features of shock and myocardial systolic dysfunction at initial admission. All other patients were asymptomatic.

Platelet levels were elevated at 2 weeks compared with presentation (median 463 K/μL [IQR: 375–541] vs median 172 K/μL [IQR: 122–232], $P < .001$). All other markers had normalized, including CRP (median 0.14 mg/L [IQR: 0.1–0.7]), troponin T (median 6 ng/L [IQR: 6–7]), and BNP (median 63 pg/mL [IQR: 54–112]).

The LV systolic function was normal in all except 1 patient who had persistent mild LV systolic dysfunction (LVEF 54%) (Table 2, Fig 1). Diastolic dysfunction was noted in 5 patients (11%), all of whom who had mild LV systolic dysfunction during hospitalization, 4 of whom also had troponin elevation. Of these 5 patients with diastolic dysfunction, 3 had the dysfunction in the acute phase. The coronary abnormalities were improving: 2 (4%) had coronary aneurysms, 1 (2%) had coronary dilation, and 12 (21%) showed lack of tapering. No new coronary abnormalities were noted (Table 2, Fig 2).

All patients were tapered off steroids once inflammatory markers normalized (range: 10–21 days) and continued on anticoagulation with hematology follow-up as per institutional guidelines.

Eight -Week Follow-up

Of the 42 patients who presented for the 6–8 week follow-up visit, 5 (12%) continued to have fatigue with regular activity. All patients had normal LV systolic function and resolved coronary aneurysms and dilation (Table 2, Figs 1 and 2). However diastolic dysfunction persisted in 4 patients (9%) and qualitative coronary abnormalities were noted in 5 (12%) patients. No new coronary abnormalities were noted.

Anticoagulation with enoxaparin or apixaban was discontinued in all patients before the 8-week visit after normalization of inflammatory markers and platelet count as per institutional guidelines. Aspirin was discontinued at the 8-week visit only on normalization of the coronaries and platelet count.

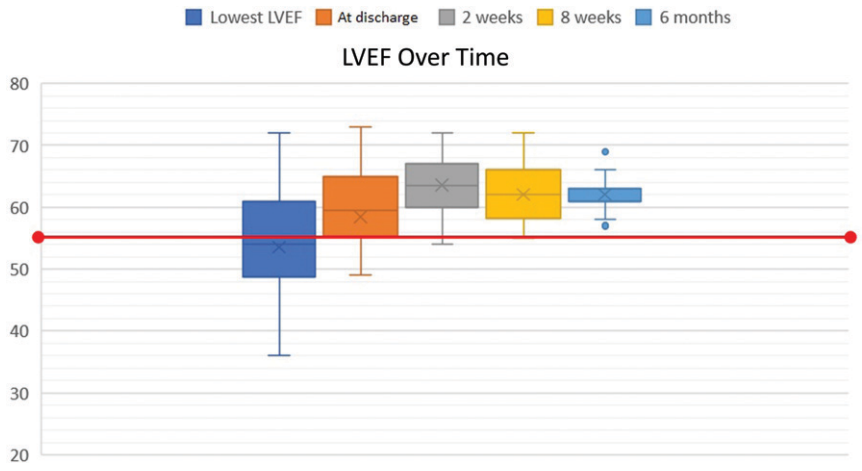

FIGURE 1

Image showing Left Ventricular Ejection Fraction (LVEF) serially improving from admission to the 6-month follow-up. Red horizontal line indicates lower limit of normal (LVEF of 55%).

CMRI was performed in 11 patients with previous LV systolic dysfunction and troponin elevation during admission. There was no evidence of persistent edema or fibrosis in any patient. No coronary artery dilation or aneurysms were seen.

Six-Month Follow-up

Of the 25 patients who presented to the 6-month follow-up visit, all were asymptomatic and at their functional baseline. Echocardiography showed normal LV systolic function and normal coronary arteries (Table 2, Figs 1 and 2). This was true for both patients who initially presented with cardiac abnormalities (12 of 25, 48%) and those that presented with normal systolic function and coronary appearance (13 of 25, 52%). One patient, although asymptomatic, continued to demonstrate LV diastolic dysfunction. Of note, this patient had LV dysfunction and troponin elevation during hospitalization; however, there was no inflammation or fibrosis on CMRI at 8 weeks. By the 6-month visit, 31 of 33 (94%) patients with initial cardiac abnormalities were seen in follow-up over the time period of the study.

DISCUSSION

In this study, we report on the early and midterm outcomes of 50 children recovering from MIS-C after hospitalization in the acute phase. The epidemiological characteristics and clinical profile of the acute phase were similar to other single-center and multicenter studies.[1–3] Children experienced intense inflammation, with most patients presenting with shock, cardiac dysfunction, and/or coronary abnormalities. For patients with cardiovascular involvement, most LV systolic dysfunction resolved within 7 to 10 days and most coronary aneurysms resolved by 2 weeks. The rapidity of resolution in our study is unlike the typical course of viral myocarditis and KD and suggests that cardiac manifestations are a result of systemic inflammation and vasodilation rather than immune infiltrate mediated damage to the myocardium.

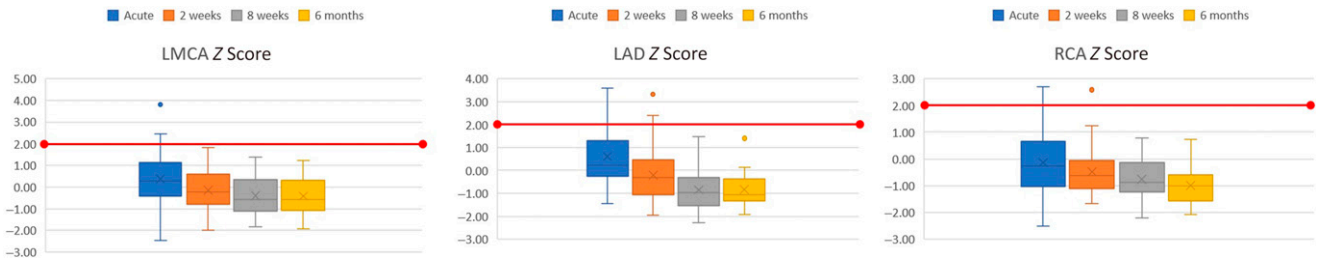

FIGURE 2

Temporal changes in mean coronary artery size (from left to right: left main coronary artery (LMCA), left anterior descending coronary artery (LAD), and right coronary artery (RCA) from admission to the 6-month follow-up. All coronaries have smaller absolute size by 8 weeks. Red horizontal line indicates upper limit of normal (z score >2).

Despite normalization of systolic function, some patients continued to have subjective symptoms of fatigue and exercise intolerance at the 2- and 8-week visit. These symptoms had resolved by 6 months in all patients. The persistent functional morbidity at 2 and 8 weeks after acute illness and normalization of LV function is likely related to a combination of acute severe inflammation, cytokine storm, and critical illness in the acute phase as well as postviral infection fatigue and subtle subclinical neurologic or cardiovascular post-coronavirus sequelae.[12,13]

There are no comparative studies evaluating the treatment protocols of MIS-C to date. Our patients were uniformly treated as per our institutional guideline which shares similarities with expert consensus recommendations from the American College of Rheumatology and other institutional protocols.[14,15] This treatment protocol was associated with rapid clinical improvement and reduction in inflammatory markers in most patients, with no mortality and with improvement in cardiac findings. None of our patients had secondary infections, showed evidence of coronary thrombosis, developed a recognized clinical thrombotic event, or had a bleeding complication from steroids or anticoagulation. The clinical improvement noted here without adverse outcome is associated with a specific treatment strategy that may assist providers in caring for patients with MIS-C while we await further guidance from multicentered and comparative effectiveness studies.

The proportion of patients with coronary abnormalities at initial diagnosis was high (52%), because of our inclusion of qualitative coronary artery abnormalities such as lack of tapering in addition to dilated or aneurysmal coronary arteries. Loss of normal tapering of coronary artery is known to be associated with KD although the exact prognostic significance is unknown.[16] We included it here as an abnormality to follow given reports of coronary aneurysms in the subacute and convalescent phase of MIS-C.[17] Fortunately, lack of tapering resolved by 6 months with no new development of coronary abnormalities noted at the 2 to 8 week follow-up, when our follow-up was highest and when expected coronary abnormalities would be seen.

Although coronary artery dilation has been described in febrile patients without KD, coronary aneurysms are not.[18] In our cohort, 16% of patients presented with aneurysmal coronary arteries (z score ≥ 2.5) in the acute phase. There was relative thrombocytopenia in the acute phase and thrombocytosis at the 2-week follow-up that resolved by 6 months. Although this could suggest a vascular pathology similar to KD, 100% of these aneurysms regressed by 8 weeks.[5] It is unclear if this regression is treatment-related or the natural progression of the vasculitis noted in MIS-C. Until this is known, continuing anticoagulation in MIS-C, particularly through the thrombocytosis phase noted on follow-up, may have important prognostic implications.

A large subset of our MIS-C cohort had LV systolic dysfunction and troponin elevation suggestive of myocyte injury. However, unlike viral myocarditis, most patients demonstrated rapid recovery. Although systolic function resolved, diastolic dysfunction, or impaired relaxation, persisted in a subset of patients. Diastolic dysfunction has been associated with impaired microvascular function and low-grade inflammation in KD and may be suggestive of subclinical myocardial injury unable to be detected by LVEF, a global marker of cardiac function.[19] The presence of diastolic dysfunction is consistent with other MIS-C studies[20]; however, its clinical importance and long-term implication are currently unknown.

Because of the extensive myocardial involvement and elevation of biomarkers reported in MIS-C, recent return-to-sports guidance has suggested restricting children for 3 to 6 months postillness as in direct infiltrative viral myocarditis. A subset of patients with direct infiltrative myocarditis will develop fibrosis/myocardial scarring as detected by late gadolinium enhancement on MRI. This finding has been associated with long-term cardiovascular dysfunction and mortality. In MIS-C, CMRIs performed in acutely hospitalized patients have found mostly myocardial edema and have not yet reported on fibrosis in or after the convalescent phase.[21,22] We performed CMRIs during the convalescent phase in 11 patients with reduced LV function and elevated troponin. Fortunately for these children, there was no evidence of persistent edema or fibrosis indicating myocardial scarring. The rapid improvement of cardiac findings and lack of reported fibrosis in the convalescent phase may have implications for sports clearance and risk of arrhythmia after recovery from MIS-C. Perhaps children may not need to be exercise-restricted for as long as they would for direct infiltrative viral myocarditis although larger studies are needed to confirm this. Given our findings, our current practice is to allow sports participation in patients with normalization of their inflammatory markers and systolic cardiac function at 8 weeks after hospital discharge.

This is a single-center case series that has several limitations. First, the MIS-C case definition is broad. Consequently, some patients included in this study may have had a different underlying cause including acute coronavirus disease 2019 with "cytokine storm" or classic KD rather than MIS-C, given the difficulty in differentiating these clinical diagnoses. Similarly, it is also possible that we underestimated the incidence of MIS-C in our patient population. As we included only cases with confirmed SARS-CoV-2 infection in our study, limited availability of molecular or serological tests may have led to exclusion of children who met clinical criteria for MIS-C but did not have a positive SARS-CoV-2 test.

Second, this is a small single-center cohort study. Although our patients with cardiac abnormalities noted during hospitalization improved, 8 patients without acute echocardiographic abnormalities were lost to follow-up at 8 weeks. These patients may have developed coronary aneurysms or other cardiac sequela. More patients were lost to 6-month follow-up, although all those with functional deficits or qualitative coronary abnormalities returned and showed improvement. It is unlikely that we are missing new coronary aneurysms at 6 months in patients with normal coronary artery *z* scores at 8 weeks.

Although interrater reliability demonstrated substantial agreement for LVEF and substantial agreement for coronary abnormalities, we did not assess interrater reliability for diastolic dysfunction. Assessment of diastolic dysfunction in children has poor interobserver agreement making these measures unreliable and may adversely affect interpretation. However, until better diastolic criteria are universally available, given the findings of Matsubara et al,[20] it is important to assess diastolic dysfunction using all available parameters as this may be important to long-term follow-up and patient care.

Finally, although our favorable outcomes were associated with our broad immunotherapy and anticoagulation, without a comparison group, small single-center cohort studies do not provide evidence for effective treatment of MIS-C.

CONCLUSIONS

This study suggests that early prognosis after hospitalization and immunomodulation treatment of MIS-C is excellent. All 50 children treated at our institution survived, with return to functional baseline, normalized LV systolic function, and resolved coronary abnormalities. None of our patients had treatment complications such as secondary infections or bleeding from anticoagulation. CMRI in select high-risk patients revealed no persistent inflammation or scarring. This suggests an uncomplicated course of myocarditis in MIS-C with favorable outlook on long-term prognosis. However, there was persistence of echocardiographic diastolic dysfunction in a few patients of uncertain significance. Larger studies are needed to aid in improved understanding of this syndrome. Meanwhile, these findings may provide guidance to clinicians particularly in relation to clinical management, outpatient monitoring, and considerations for sports clearance.

ABBREVIATIONS

CMRI: cardiac MRI
CRP: C-reactive protein
IQR: interquartile range
KD: Kawasaki disease
LV: left ventricular
LVEF: left ventricular ejection fraction
MIS-C: Multisystem inflammatory syndrome in children
pro-BNP: plasma brain natriuretic peptide
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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