Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COVID-19-Related Multisystem Inflammatory Syndrome in Children Affects Left Ventricular Function and Global Strain Compared with Kawasaki Disease

Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 has emerged with reports comparing its clinical features with those of Kawasaki disease (KD) and varying degrees of cardiac involvement.[1-6] The purpose of this report is to present echocardiographic features in children with MIS-C and a historical control group of children with KD to examine whether there are critical differences between these two syndromes. A retrospective review of records of patients <21 years of age admitted to our institution with MIS-C (according to the Centers for Disease Control and Prevention definition) from March to June 2020 was performed.[7] A control group of patients with KD was randomly selected from January to June 2019 and matched 1:1 on age, sex, and race. Patient demographics, clinical characteristics, and biomarkers, including troponin and C-reactive protein (CRP), collected within 24 hours of echocardiography were obtained from medical records. Echocardiograms obtained during the acute hospitalizations in both populations were included. A blinded two-dimensional, color and tissue Doppler, and strain analysis was performed on deidentified echocardiographic images using vendor-neutral software (TomTec Corporation USA, Chicago, IL).

A comparison of patient demographics and echocardiographic features is shown in Table 1. All patients were previously healthy. No deaths occurred in either group. Median left ventricular ejection fraction (LVEF), fractional shortening, and global longitudinal strain (GLS) were significantly lower in patients with MIS-C compared with those with KD. The median frequency of obtaining follow-up echocardiograms while hospitalized for MIS-C was a 2-day interval.

On initial echocardiographic assessment of patients with MIS-C, LVEF was at least mildly depressed in eight patients (67%), with concurrently reduced GLS in these same eight patients and reduced global circumferential strain (GCS) in six of the eight patients (Figure 1). Of these eight patients, only one had a normal LVEF, with normal GLS and GCS by the time of hospital discharge (day 7 to day 9 of illness). Of the remaining seven patients, six showed improvement in LVEF with normal GCS but still had reduced GLS at hospital discharge. The eighth patient had a persistent moderately reduced LVEF by hospital discharge with reduced GLS but normal GCS. LVEFs were normal on initial echocardiography in four patients with MIS-C. Of those four patients, one had reduced GLS despite a normal LVEF. Three of these four patients developed decreased LVEFs with reduced GLS and GCS on the second or third day of admission. In these patients, LVEF and GCS improved to their normal ranges between hospital days 5 and 9, but GLS remained reduced. There were no significant differences in measures of right ventricular function between the two groups. Mitral regurgitation (MR) was both more common and in greater degree in patients with MIS-C compared with those with KD. Pleural effusions were noted more often in patients with MIS-C compared with those with KD, with two patients with MIS-C having moderate pleural effusions and five having small effusions.

At the time of initial echocardiography, there were negative correlations between LVEF and troponin ($r = -0.9$, $n = 6$, $P = .01$) and LVEF and CRP ($r = -0.6$, $n = 12$, $P = .03$). For all echocardiograms obtained during the MIS-C hospitalization, lower GLS correlated with higher troponin ($r = 0.5$, $n = 24$, $P = .01$) and CRP ($r = 0.6$, $n = 37$, $P = .0003$).

At latest follow-up (median, 45 days from diagnosis) for MIS-C, only one patient had residual left ventricular dysfunction. Two had residual coronary artery dilation. No patient had more than trace MR.

This study presents a comprehensive analysis of cardiac function, including strain analysis, in patients with the newly emerging coronavirus disease 2019–associated MIS-C. Unlike patients with KD, the majority of those with MIS-C had significantly reduced left ventricular function at presentation. Even though LVEF and GCS normalized by days 7 to 9 of illness in most patients, abnormalities in GLS persisted. Correlations of abnormal LVEF and GLS with cardiac inflammatory biomarkers, such as CRP and troponin, highlight the presence of myocarditis in patients with MIS-C. Other echocardiographic findings that were significantly different in patients with MIS-C compared with KD included more MR and pleural effusions, both likely related to the ongoing inflammatory response in MIS-C. The presence of these findings on the initial echocardiogram of a patient presenting with KD-like illness should raise suspicion for MIS-C and prompt closer clinical observation for the development of cardiac dysfunction. Fortunately, at the time of discharge, most patients had resolution of MR and pleural effusions and were clinically asymptomatic. Although coronary artery dimensions did not appear to be a distinguishing parameter between the two groups, this may be secondary to the small sample size and randomly selected KD population, which had a low rate of coronary artery dilation inherently. Although larger studies with longitudinal follow-up to assess cardiac function in patients with MIS-C are needed, the data from our study should encourage echocardiographers to perform comprehensive cardiac function assessment, including strain analysis in patients with MIS-C, and to use cardiac biomarkers such as troponin and CRP as an adjunct for management of these patients.

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Table 1 Comparison of patient demographics and echocardiographic features at initial presentation between patients with MIS-C and those with KD

Parameter	MIS-C (*n* = 12)	KD (*n* = 12)	*P**
Demographics			
Age, y	8 (5.5 to 11.5)	6 (4 to 7)	.09
Sex			.65
Female	3 (25)	4 (33)	
Male	9 (75)	8 (67)	
Race			.56
Black	8 (67)	8 (67)	
Other	1 (8)	0 (0)	
White	3 (25)	4 (33)	
LV systolic and diastolic function			
LVIDd *Z* score	−0.1 (−1.3 to 0.9)	−0.5 (−0.9 to 0.2)	.71
IVSd *Z* score	0.3 (−0.2 to 1.3)	0.4 (0.2 to 1)	.86
LVPWd *Z* score	0.2 (0.1 to 1.3)	−0.4 (−0.8 to 0.4)	.13
SF (2D), %	25.3 (22.1 to 29.1)	32.1 (29.0 to 33.6)	**.01**
LVEF (biplane Simpson), %	42.5 (39.6 to 56.8)	58.4 (56.8 to 64.3)	**.03**
Mitral E/A ratio	2.0 (1.3 to 2.3)	2.0 (1.5 to 2.3)	.71
Mitral E/E′ ratio	7.8 (5.9 to 8.5)	7.1 (6.0 to 7.7)	.56
Septal E/E′ ratio	8.6 (7.9 to 11.7)	8.8 (7.0 to 9.6)	.49
LV strain assessment			
Four-chamber peak systolic strain, %	−14.0 (−21.7 to −12.0)	−19.5 (−21.5 to −17.6)	.07
Two-chamber peak systolic strain, %	−12.7 (−15.8 to −11.2)	−18.3 (−21.2 to −17.4)	**<.01**
Three-chamber peak systolic strain, %	−15.2 (−16.8 to −11)	−17.8 (−23.8 to −15.8)	**.05**
GLS, %	−14.0 (−18.9 to −11.4)	−19.3 (−20.1 to −18.3)	**.02**
GCS, %	−18.3 (−27.4 to −14.5)	−22.8 (−27.9 to −19.8)	.34
RV systolic and diastolic function			
RV fractional area change, %	33.7 (27.2 to 37.1)	34.5 (30.1 to 40.0)	.51
Tricuspid E/A ratio	2.4 (1.5 to 2.9)	1.8 (1.5 to 2.0)	.31
Tricuspid E/E′ ratio	4.3 (2.3 to 5.4)	4.3 (2.5 to 4.9)	.60
Valve regurgitation and effusions			
Tricuspid regurgitation			.65
Less than mild	8 (67)	9 (75)	
Mild or greater	4 (33)	3 (25)	
MR			**.01**
Less than mild	6 (50)	12 (100)	
Mild or greater	6 (50)	0 (0.00)	
Pericardial effusion			.67
None	7 (58)	8 (67)	
Present	5 (42)	4 (33)	
Pleural effusion			**.01**
None	5 (42)	11 (92)	
Present	7 (58)	1 (8)	
Coronary arteries			
LMCA *Z* score			.31
≤2	11 (92)	12 (100)	

(*Continued*)

Table 1 (*Continued*)

Parameter	MIS-C (*n* = 12)	KD (*n* = 12)	*P**
>2	1 (8)	0 (0)	
LAD *Z* score			.14
≤2	12 (100)	10 (83)	
>2	0 (0.00)	2 (17)	
LCx *Z* score			—
≤2	8 (100)	10 (100)	
RCA *Z* score	−0.1 (−0.9 to 1.1)	0.5 (−0.8 to 1.2)	.54
Coronary artery aneurysm	0 (0)	0 (0)	—

2D, Two-dimensional; *IVSd*, interventricular septal end-diastolic dimension; *LAD*, left anterior descending coronary artery; *LCx*, left circumflex coronary artery; *LMCA*, left main coronary artery; *LV*, left ventricular; *LVIDd*, left ventricular internal end-diastolic dimension; *LVPWd*, left ventricular posterior wall end-diastolic dimension; *RCA*, right coronary artery; *RV*, right ventricular; *SF*, shortening fraction.
Data are expressed as median (interquartile range) or as number (percentage).
*Statistical significance was assessed at the .05 level using Wilcoxon rank sum tests for continuous variables and χ^2 or Fisher exact tests for categorical variables. Significant *P* values are set in bold.

Left Ventricular Ejection Fraction (%)
Days Since Admission

Patient	0	1	2	3	4	5	6	7	8	9
1			40		53			66		
2			35		58			54		52
3		40	54				62			
4		47	46		40			56		
5	45		55							
6	60	54	53	45		64				
7		39			47			55		67
8			40				39			
9				48						60
10									67	
11		57		51	52					
12		69	62	46	49		46			58

Global Longitudinal Strain (%)
Days Since Admission

Patient	0	1	2	3	4	5	6	7	8	9
1			-14.0					-20		
2			-8.5		-14.1			-15.4		-14.6
3		-9.8	-17.7				-16.8			
4		-11.4	-12.1		-10.2			-13.3		
5	-14.6		-16.7							
6	-21.4	-14.3	-13.6	-18.1		-17.2				
7		-14.9			-16.9			-14.8		-18.1
8			-12.3				-9.7			
9		-18.9		-15.3						-18.1
10									-20.0	
11		-19.6		-18.6	-18.7					
12		-12.6	-13.3	-5.5	-13.1		-14.4			-18.7

Global Circumferential Strain (%)
Days Since Admission

Patient	0	1	2	3	4	5	6	7	8	9
1			-14.5		-20.5			-28.1		
2			-8.9		-22.6			-25.8		-28.0
3			-22.5							
4		-14.3	-14.7		-13.7			-27.6		
5										
6	-27.4	-18.5	-18.7	-20.8		-22.6				
7		-16.3			-17.6			-22.4		-22.3
8			-18.3				-21.7			
9		-18.6		-18.0						-27.6
10									-23.6	
11		-35.8		-20.2	-22.3					
12		-39.1	-27.8	-13.3	-31.9		-27.3			-24.1

Figure 1 Longitudinal assessment of LVEF, GLS, and GCS in 12 patients with MIS-C during the hospital admission.

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