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Short-Term sequelae of Multisystem Inflammatory Syndrome in Children Assessed by CMR

Recent studies have reported a wide clinical spectrum of multisystem inflammatory syndrome in children (MIS-C) (1–3). This is the first study that describes short-term sequelae of the acute phase of MIS-C assessed by cardiac magnetic resonance (CMR) using a comprehensive imaging protocol.

A total of 44 children were referred with MIS-C (fulfilling the criteria of the U.S. Centers for Disease Control and Prevention) between April and June 2020 to our center (Royal Brompton Hospital, London, United Kingdom). A total of 20 patients were referred for CMR scanning because of myocardial involvement in the acute phase: 1) 10 (50%) patients had myocardial dysfunction (left ventricular ejection fraction ≤55%); 2) 5 (25%) patients had dilated coronary arteries (Z-score >2.5); and 3) 5 (25%) patients had increased cardiac inflammatory markers (B-type natriuretic peptide and troponin). The study was approved by the local Research Ethics Committee. The median age of the patients was 8 years (range 17 months to 14 years).

Patients under general anesthesia were scanned with a 3.0-T scanner, and the other patients were scanned with 1.5-T scanner (Vida and Aera/Avanto-FIT, Siemens, Erlangen, Germany).

Native T_1 mapping was performed using a 3(3)5 modified Look-Locker imaging single-shot balanced steady-state free precession (bSSFP) sequence at the basal and midventricular levels. T_2 mapping was also conducted on the basis of a single-shot sequence (1.5-T bSSFP, 3.0-T spoiled gradient recalled echo) measured at the basal, midventricular, and apical levels.

As required by the Society for Cardiovascular Magnetic Resonance consensus statements, normal-range data are available for all users of mapping at the Brompton Hospital. These data had been obtained and shared from healthy young and middle-aged individuals who were scanned in the 1.5-T (VE11C, Siemens Healthineers, Erlangen, Germany) and 3.0-T (VA11A, Siemens Healthineers) scanners, and the maximum value from all of them (approximately 20 healthy control subjects for each T_1 and T_2 mapping per scanner) was taken as a cutoff value to avoid overestimating the results.

Mean global T_1 and T_2 values for each slice and mean segmental T_1 and T_2 values were measured. The native T_1 normal range was 975 to 1,065 ms at 1.5-T and 1,140 to 1,395 ms at a 3.0-T scanner. T_2 values were considered abnormal if they were >60 ms at 1.5-T and >49 ms at a 3.0-T scanner. The same range was used for mean global and mean segmental values.

The results of a polymerase chain reaction nasal swab for coronavirus disease-2019 (COVID-19) were negative in the acute phase in all patients. Results of COVID-19 serological testing at the time of admission were positive in 14 (70%) patients for immunoglobulin G severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2).

The time interval between the onset of symptoms and the date of CMR was between 12 and 72 days (27 ± 14 days). Six (30%) patients required general anesthesia. Repeated echocardiogram at the time of CMR showed normal systolic function and normalized size of the coronary arteries in all but 1 patient.

All CMR conventional parameters were in the normal range (**Table 1**). Only 1 patient had mildly reduced left ventricular ejection fraction. Short tau inversion recovery images were negative in all patients. Two patients had small areas of late gadolinium enhancement.

Mean T_1 values were normal in all but 1 patient. This patient had a slightly increased mean T_1 value at the midventricular level of 1,068 ms. Altogether, 5 patients had abnormal segmental values in 1 to 5 segments. The patient with the increased T_1 values in 5 segments presented in shock with moderate systolic dysfunction. Abnormally increased T_1 values were associated with high C-reactive protein at the time of admission ($p < 0.001$).

Mean global T_2 values of basal, midventricular, and apical slices were normal in all patients. However, 1 patient showed higher T_2 values in the apical lateral segment. Both basal septal values were abnormal in another patient. Abnormal T_2 values were associated with elevated D-dimer levels at the time of admission ($p = 0.042$) and abnormal mitral annular planar systolic excursion (MAPSE) ($p < 0.001$). The number of segments with abnormal T_2 values was associated with C-reactive protein at the time of admission ($p < 0.001$) and with MAPSE ($p = 0.011$). (The Mann-Whitney *U*-test and the Kruskal-Wallis test were used as appropriate.) Three patients had dilated neck

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TABLE 1 CMR Results of the Conventional and Parametric Data

CMR Parameter	N = 20	CMR Parameter	N = 20
LV EDV index, ml/m^2	67 ± 12	RV EDV index, ml/m^2	67 ± 11
LV ESV index, ml/m^2	24 ± 6	RV ESV index, ml/m^2	26 ± 6
LV SV index, ml/m^2	44 ± 10	RV SV index, ml/m^2	42 ± 7
LV EF, %	64 ± 5	RV EF, %	62 ± 5
LV mass index, g/m^2	45 ± 8	–	
LA index, cm^2/m^2	10 ± 2	RA index, cm^2/m^2	12 ± 2
MAPSE lateral, mm	13 ± 3	TAPSE, mm	20 ± 4
CMR Parameter (1.5-T Scanner)	**N = 14**	**CMR Parameter (3.0-T Scanner)**	**N = 6**
Native T_1 at basal level, ms	1,016 ± 29	Native T_1 at basal level, ms	1,298 ± 34
Native T_1 at midventricular level, ms	1,008 ± 33	Native T_1 at midventricular level, ms	1,315 ± 35
Native T_2 at basal level, ms	45 ± 2	Native T_2 at basal level, ms	41 ± 3
Native T_2 at midventricular level, ms	46 ± 2	Native T_2 at midventricular level, ms	38 ± 2
Native T_2 at apical level, ms	49 ± 4	Native T_2 at apical level, ms	39 ± 3

Values are mean ± SD.

CMR = cardiac magnetic resonance; EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; LA = left atrial; LGE = late gadolinium enhancement; LV = left ventricular; MAPSE = mitral annular planar systolic excursion; RA = right atrial; RV = right ventricular; SV = systolic volume; TAPSE = tricuspid annular planar systolic excursion

and/or innominate veins. A splenic infarct was demonstrated in 1 of the most severely affected patients.

This study demonstrates that despite the initial life-threatening presentation of some children with MIS-C, there is rapid improvement and nearly complete normalization of all cardiac abnormalities within a few weeks after the onset of the disease. Subtle residual cardiac and extracardiac abnormalities were found in a subset of children, who will require follow-up studies.

Limitations include the large spread of patients' ages, caused by the nature of the disease and the wide range of time intervals from the onset of symptoms to CMR, that makes the interpretation of the results challenging. Statistical analysis of T_1 mapping is further limited by different field strengths used for the scanning. Extracellular volume, another parameter used for tissue characterization of acute myocarditis, was not used in this study because of a lack of institutional normal values.

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