Multimodality cardiac evaluation in children and young adults with multisystem inflammation associated with COVID-19

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Aims
Following the peak of the UK COVID-19 epidemic, a new multisystem inflammatory condition with significant cardiovascular effects emerged in young people. We utilized multimodality imaging to provide a detailed sequential description of the cardiac involvement.

Methods and Results
Twenty consecutive patients (mean age 10.6 ± 3.8 years) presenting to our institution underwent serial echocardiographic evaluation on admission (median day 5 of illness), the day coinciding with worst cardiac function (median day 7), and the day of discharge (median day 15). We performed cardiac computed tomography (CT) to assess coronary anatomy (median day 15) and cardiac magnetic resonance imaging (CMR) to assess dysfunction (median day 20). On admission, almost all patients displayed abnormal strain and tissue Doppler indices. Three-dimensional (3D) echocardiographic ejection fraction (EF) was <55% in half of the patients. Valvular regurgitation (75%) and small pericardial effusions (10%) were detected. Serial echocardiography demonstrated that the mean 3D EF deteriorated (54.7 ± 8.3% vs. 46.4 ± 8.6%, P = 0.017) before improving at discharge (P = 0.008). Left main coronary artery (LMCA) dimensions were significantly larger at discharge than at admission (Z score –0.11 ± 0.87 vs. 0.78 ± 1.23, P = 0.007). CT showed uniform coronary artery dilatation commonly affecting the LMCA (9/12). CMR detected abnormal strain in all patients with global dysfunction (EF <55%) in 35%, myocardial oedema in 50%, and subendocardial infarct in 5% (1/20) patients.

Conclusions
Pancarditis with cardiac dysfunction is common and associated with myocardial oedema. Patients require close monitoring due to coronary artery dilatation and the risk of thrombotic myocardial infarction.

Keywords
Hyper-inflammatory syndrome • Kawasaki • PIMS-TS • MIS-C • COVID-19 • SARS-CoV-2

Introduction
During the COVID-19 pandemic, our group1,2 and others in Europe3–5 and the USA6 have described cohorts of children and young adults presenting as a hyperinflammatory syndrome with multiorgan involvement, with features similar to Kawasaki disease shock syndrome (KDSS), toxic shock syndrome (TSS), haemophagocytic lymphohistiocytosis (HLH), and macrophage activation syndrome (MAS) induced by a cytokine storm.5,3 This new condition has arisen after the peak of the SARS-CoV-2 pandemic in the respective countries. The novel syndrome has been named paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2

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infection (PIMS-TS) in a case definition published by the Royal College of Paediatrics and Child Health (RCPCH) or multisystem inflammatory syndrome in children (MIS-C). Very similar case definitions have been published in the UK, in the USA, and by the World Health Organization.

Cardiac involvement has been reported in those with PIMS-TS. However, a detailed description of cardiac manifestations of this syndrome is lacking. We present the comprehensive results of sequential multimodality cardiac imaging with echocardiography, computed tomography (CT), and cardiac magnetic resonance imaging (CMR) in the first 20 unselected sequential patients with this syndrome at our centre.

Methods

This was a retrospective single institution study of the cardiac imaging manifestations in consecutive patients presenting to the Evelina London Children’s Hospital (ELCH) with features of PIMS-TS as defined by the RCPCH, UK. Imaging was performed with local ethical approval (08/H0810/058).

Clinical and laboratory evaluation

Demographic data and SARS-CoV-2 case contacts were collected from hospital notes. Vital signs and cardiac biomarkers including troponin-T and N-terminal probrain natriuretic peptide (NT-proBNP) were collected prospectively.

Cardiac imaging evaluation protocol

All patients had echocardiographic evaluation on admission. Echocardiograms were performed daily during the acute phase of the disease, and on alternate days during the recovery phase. We defined three time points for analysis: echocardiogram on admission; echocardiogram based on worst three-dimensional (3D) ejection fraction (EF) during the hospital admission; and discharge echocardiogram. As this is an emerging disease with evolving cardiac involvement of an unknown extent and course, we performed further cross-sectional cardiac imaging (CT and CMR) to determine: coronary artery dimensions; myocardial characterization; and functional parameters.

Echocardiography

Philips IE33 and EPIQ 7C echocardiography systems (Philips Medical Systems, Andover, MA, USA) were used to obtain imaging with offline processing using Philips IntellSpace Cardiovascular (ISCV) and analysis using QLAB, Version 10.8.5 (Philips Medical Systems).

The echocardiogram included extensive functional assessment. Left ventricular (LV) function was quantified in accordance with published guidelines, and Z scores were calculated where appropriate. Peak pulsed wave tissue Doppler imaging (TDI) systolic and diastolic velocities of the basal septal and lateral segments of the left ventricle were analysed according to published standards. The LV diastolic function and LV filling pressures were assessed. The four-chamber, three-chamber, and two-chamber views were used for 2D based speckle-tracking myocardial deformation echocardiographic analysis. 3D echocardiography was used to calculate LV volumes and EF.

The dimensions of the coronary arteries were expressed as Z scores in accordance with the published reference standard. Coronary artery dilation was defined by the presence of a Z score >2 in the affected segment.

All echocardiographic measurements and reports were reviewed prospectively by consultants with subspecialty expertise in echocardiography (PT, JW, KP, and OM).

Cardiac computed tomography

Prospectively ECG-gated coronary CT angiography was performed using a Somatom Force scanner (Siemens Healthcare AG, Erlangen, Germany). Scans were performed urgently in the presence of echocardiographic evidence of rapidly evolving coronary dilatation. Imaging was acquired at end-systole defined by the end of the T-wave. Intravenous contrast (OmnipaqueTM 350) was administered at 1.5–2.0 mL/kg and monitoring slices were used to determine maximal contrast density in the descending aorta. The mean dose-length product was low at 46.2 mGy-cm for cohort mean body surface area (BSA) of 1.4 m². Images were analysed using SECTRA-PACS (Sectra AB, Linköping Sweden). Intraluminal diameters of the coronary artery segments were measured in two dimensions using multplanar reconstruction (MPR) by two blinded observers (J.W. and S.M.). The mean value was recorded, and Z scores were calculated as per Dallaire et al., in keeping with the literature on extrapolating coronary CT measurements from echocardiographic datasets.

Cardiac magnetic resonance

Retrospectively ECG-gated balanced state-free precession (bSSFP) cine imaging was acquired in short- and long-axis orientations of the heart including two-chamber, three-chamber, and four-chamber views. Field of view was optimized to cover the chest wall. Typical imaging parameters were: parallel imaging factor (SENSE) 2; in-plane resolution 2 × 2 mm; slice thickness 8 mm in the long axis and 8–10 mm in the short axis; and temporal resolution 30 phases. Myocardial inflammation was assessed in accordance with the Lake Louise CMR criteria. Due to the lack of consistent reference normal values in native T1 mapping and T2 relaxation times in children, myocardial oedema was characterized by increased signal intensity on T2-weighted imaging and myocardial injury was characterized by the presence of non-ischaemic patterns of late gadolinium enhancement (LGE). Evidence of myocardial oedema with T2 hyperintensity was defined as:

\[
T2 \text{ ratio} > 2
\]

where: T2 ratio = signal intensity myocardium/signal intensity skeletal muscle.

A Look-Locker sequence was performed to assess inversion time 5 min after administration of 0.1 ml/kg i.v. gadobutrol (Gadovist, Bayer Schering Pharma, Germany). Phase-sensitive inversion recovery (PSIR) was used to assess for LGE. CMR 42 (Circle Cardiovascular Imaging, Canada) was used to measure LV volumes, feature tracking global strain indices (short axis for circumferential strain; mean long-axis values for longitudinal strain; radial strain) was not assessed due to poor interuser variability), and assess for evidence of myocardial necrosis and fibrosis.

Statistical analysis

Statistical analysis was performed using SPSS v. 26. Interobserver variability of CMR LV volume segmentation and CT coronary artery measurements were quantified using an intraclass coefficient two-way model with absolute agreement. Measurements were sampled for 10 subjects by two authors (J.W. and K.P. for CMR data; J.W. and S.M. for CT data). Variables were tested for normality using the Kolmogorov–Smirnov test. Repeated measures analysis of variance (RM ANOVA) was performed to evaluate changes of all echocardiographic parameters assessed on admission, during hospitalization, and at discharge. The results for variables with normal distribution were reported as mean ± SD, while the non-normally distributed parameters were reported as median (range). Statistical significance was defined as a two-tailed p-value of <0.05.
Ethics
This study complies with the Declaration of Helsinki. Local ethical approval was received (08/H0810/058).

Results

Demographics
The first 20 patients fulfilling diagnostic criteria for PIMS-TS treated during a 22-day period (16 April–8 May 2020) were included. Demographics are outlined in Table 1. Median duration of symptoms at time of presentation was 5 days (range 2–7 days). Mean age was 10.6 ± 3.8 years (range 4–16 years). Fifteen (75%) patients were male and 19 (95%) tested positive for either IgM or IgG antibodies to COVID-19. Two of the 19 antibody-positive patients had positive SARS-CoV-2 PCR from oropharyngeal swab sampling. Worst cardiac function, as determined by 3D echo EF, occurred on a median of 7 days (range 4–12 days) after the onset of the illness. Median patient discharge occurred after 15 days (range 11–25 days) of the illness and clinically corresponded to defervescence and normalization of inflammatory markers.

Admission echocardiography findings
On admission, five patients (25%) demonstrated subjectively increased echogenicity of the interventricular septum when compared with the rest of the myocardium, while all had increased pericardial brightness (Figure 1; Supplementary material online, Video 1). Eight patients (40%) presented with impaired LV systolic performance [M-mode-derived LV fractional shortening (FS) <30%]. 3D echocardiography assessment revealed that 10 (50%) patients presented with reduced LV systolic function (3D LVEF <55%). However, LV systolic performance, assessed by TDI and strain echocardiography, was reduced in 18 (90%) patients. Mean 2D-derived global longitudinal strain (GLS) was –13.2 ± 2.9% (range –7.0% to –18.8%). TDI echocardiography showed that nine (45%) patients had an E/e’ >8 in keeping with evidence of increased LV filling pressures; this did not correlate with serum NT-proBNP levels. On admission, 10 (50%) patients had mild mitral regurgitation (MR) and 12 (60%) had mild tricuspid regurgitation (TR). Two patients presented with moderate to severe MR and three patients with moderate to severe TR. One patient had trivial aortic regurgitation (AR) and two were found to have pericardial effusion on admission. Echocardiographic coronary assessment revealed that three patients (15%) had already developed coronary artery dilatation.

Serial echocardiography assessment
All patients underwent serial echocardiographic assessments during their hospital stay. While LV systolic function, assessed by M-mode-derived FS, did not change during the hospitalization period compared with the admission echocardiography (P = 0.95 and P = 0.92, respectively), there was a subsequent significant improvement noted on the discharge echocardiogram (FS 29.6 ± 10.1% vs. 39.2 ± 7.0%.

| Table 1 | Demographic data including day of presentation with illness, day of worst dysfunction, and timing of imaging |
|---------|---------------------------------------------------------------------------------------------------------------|
| ID | Age (years) | Gender | Ethnicity | Day of presentation | Day of worst dysfunction | Day of discharge | Day CT performed | Day MRI performed |
| 1 | 8 | M | 1 | 3 | 12 | 25 | 12 | 25 |
| 2 | 13 | F | 1 | 5 | 6 | 14 | 15 | 19 | 21 |
| 3 | 6 | M | 2 | 4 | 12 | 15 | 19 | 21 |
| 4 | 6 | F | 1 | 6 | 8 | 11 | 23 | 25 |
| 5 | 12 | M | 1 | 5 | 8 | 17 | 16 | 17 |
| 6 | 8 | F | 1 | 4 | 5 | 15 | 21 | 23 |
| 7 | 12 | F | 1 | 3 | 4 | 13 | 6 | 16 |
| 8 | 11 | M | 2 | 5 | 8 | 13 | 27 | 28 |
| 9 | 5 | M | 4 | 6 | 7 | 15 | 27 | 18 |
| 10 | 14 | M | 1 | 2 | 8 | 10 | 26 | 25 |
| 11 | 14 | M | 4 | 5 | 8 | 13 | 14 | 21 |
| 12 | 9 | M | 2 | 5 | 8 | 14 | 12 | 17 |
| 13 | 4 | F | 1 | 2 | 6 | 14 | 9 | 21 |
| 14 | 15 | M | 1 | 6 | 7 | 15 | 10 | 18 |
| 15 | 7 | M | 5 | 5 | 7 | 12 | 22 | 20 |
| 16 | 16 | M | 5 | 4 | 6 | 13 | 9 | 21 |
| 17 | 11 | M | 2 | 4 | 7 | 16 | 23 | 16 |
| 18 | 11 | M | 1 | 2 | 4 | 9 | 8 | 19 |
| 19 | 16 | M | 1 | 4 | 10 | 17 | 22 | 29 |
| 20 | 15 | M | 1 | 3 | 4 | 9 | 4 | 11 |
| Median | 11 | 15M:5F | 1 (n = 12), 2 (n = 4), (n = 0), (range) 4 (n = 2), 5 (n = 2) | 5 | 7 | 15 | 15 | 20 |
| (range) | (4–16 years) | (2–6 days) | (4–12 days) | (11–25 days) | (4–27 days) | (11–29 days) |

Ethnicity key: 1, Black/African/Caribbean/Black British; 2, Asian/Asian British; 3, mixed/multiple ethnic groups, 4, White (UK); 5, White (other).

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P = 0.002). The observations regarding LV systolic performance were confirmed by TDI echocardiography and 2D-derived GLS. In keeping with FS remaining unchanged between admission and during hospitalization, the recorded septal and lateral TDI velocity Z scores (s’sep and s’lat) also did not differ significantly (P = 0.34 and P = 0.60, respectively). Similarly the GLS recorded on admission did not change significantly (P = 0.40) during hospitalization. Overall there was significant improvement of the systolic septal and lateral TDI velocities and the 2D-derived GLS from admission to discharge (s’sep TDI 6.9 ± 1.4 cm/s vs. 8.1 ± 1.6 cm/s, P = 0.014; s’lat TDI 8.0 ± 1.6 cm/s vs. 9.4 ± 2.1 cm/s, P = 0.007; and GLS –11.9 ± 7.6% vs. –17.0 ± 2.9%, P = 0.018). 3D echocardiography appeared to be more sensitive to identify a significant change from baseline assessment during the admission period (54.7 ± 8.3% vs. 46.4 ± 8.6%, P = 0.017) and a subsequent significant improvement on discharge (46.4 ± 8.6% vs. 68.6 ± 7.5%, P = 0.008). LV diastolic function, assessed by E/A and E/e’ ratios, did not significantly change during serial echocardiographic assessments. However, TDI echocardiography demonstrated that the late diastolic velocities of the lateral aspect of the mitral annulus (a’lat) during admission were significantly reduced, which was a sustained finding throughout hospitalization (Table 2).

On admission echocardiography, two patients (10%) had left anterior descending (LAD) dilatation (Z score >2) and one patient (5%) had right coronary artery (RCA) dilatation. Eight patients developed coronary dilatation during the hospital admission (Figure 2; Supplementary material online, Video 2). On discharge, coronary

**Table 2**  Serial echocardiographic measurements

|                         | Admission echo (1) | In-hospital echo (2) | P (echo 1 vs. echo 2) | Echo at discharge (3) | P (echo 2 vs. echo 3) |
|-------------------------|--------------------|----------------------|----------------------|-----------------------|----------------------|
| FS (M-mode), %          | 30.2 ± 9.1         | 29.6 ± 10.1          | 0.928                | 39.2 ± 7.0            | 0.002                |
| 3D LVEF, %              | 54.7 ± 8.3         | 46.4 ± 8.6           | 0.017                | 68.6 ± 7.5            | 0.008                |
| GLS                    | –13.2 ± 2.9        | –11.9 ± 7.6          | 0.406                | –17.0 ± 2.9           | 0.018                |
| MV E/A                 | 1.77 ± 0.30        | 2.08 ± 0.98          | 0.377                | 1.76 ± 0.40           | 0.419                |
| E/e’                   | 8.3 ± 2.1          | 8.5 ± 3.4            | 0.807                | 7.1 ± 1.0             | 0.120                |
| s’sep, cm/s             | 7.4 ± 1.6          | 6.9 ± 1.4            | 0.366                | 8.1 ± 1.6             | 0.014                |
| s’lat, Z score          | –0.56 ± 1.25       | –0.90 ± 0.99         | 0.340                | –0.03 ± 1.20          | 0.014                |
| e’lat, Z score          | 8.7 ± 2.5          | 8.0 ± 1.6            | 0.502                | 9.4 ± 2.1             | 0.007                |
| a’lat, Z score          | –0.74 ± 0.95       | –0.87 ± 0.59         | 0.603                | –0.35 ± 0.68          | 0.021                |
| TAPSE, mm               | 19.0 ± 4.5         | 18.6 ± 4.4           | 0.772                | 23.0 ± 2.3            | 0.009                |
| LMCA, Z score           | –0.11 ± 0.87       | 0.23 ± 1.37          | 0.242                | 0.78 ± 1.23           | 0.108                |
| LAD, Z score            | 0.65 ± 1.22        | 1.16 ± 2.42          | 0.409                | 1.58 ± 2.71           | 0.183                |
| LCx, Z score            | –1.15 ± 0.79       | –0.69 ± 1.32         | 0.149                | –0.88 ± 1.07          | 0.597                |
| RCA, Z score            | –0.11 ± 1.24       | 0.51 ± 1.41          | 0.026                | 0.16 ± 1.53           | 0.062                |

FS, fractional shortening; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; MV, mitral valve; TAPSE, tricuspid annular plane systolic excursion; LMCA, left main coronary artery; LAD; left anterior descending; LCx, left circumflex; RCA, right coronary artery.
Cardiac computed tomography

All patients underwent cardiac CT imaging, at a median time of 15 days (range 4–27 days) after the onset of illness. Mean indexed left ventricular end-diastolic volume (iLVEDV), indexed left ventricular end-systolic volume (iLVESV), and indexed left ventricular stroke volume (iLVSV) were within normal range corrected for BSA. Global function measured by LVEF demonstrated 13 patients with normal function (EF >55%), 3 patients with borderline dysfunction (EF 50–55%), and 4 patients with mild LV dysfunction (EF <50%). There was mild right ventricular (RV) dysfunction in one patient.

Myocardial oedema was present in 10 patients (50%). Global increase in T2-weighted imaging was most commonly observed (n = 6) followed by the basal septal segments (n = 3). Strikingly, global MR strain analysis demonstrated that every patient had impairment in systolic strain indices in at least one axis compared with normal values. Those with the worst function (EF and strain) did not correlate with persistent myocardial oedema, scarring, age, or timing of presentation. Intraclass coefficient (95th confidence interval) was 0.97 (0.80–0.99) for EDV, 0.95 (0.80–0.98) for ESV, 0.95 (0.82–0.98) for SV, and 0.89 (0.58–0.97) for EF.

Table 3  CT-derived coronary artery measurements

| ID | Right coronary artery | Left main coronary artery | Left anterior descending | Left circumflex |
|----|-----------------------|---------------------------|--------------------------|-----------------|
| 1  | 5.0                   | 5.5                       | 12.2                     | 3.0             |
| 2  | 0.6                   | 3.2                       | 3.5                      | –               |
| 3  | 0.7                   | 0.5                       | 1.6                      | 0.7             |
| 4  | –1.1                  | 0.5                       | 0.3                      | 0.6             |
| 5  | –1.0                  | 1.2                       | 1.5                      | 0.8             |
| 6  | –1.2                  | 2.0                       | 1.6                      | –0.1            |
| 7  | 0.2                   | 3.5                       | 3.5                      | 1.7             |
| 8  | 0.5                   | –0.1                      | 0.1                      | –0.9            |
| 9  | 2.0                   | 0.9                       | 1.8                      | –1.8            |
| 10 | –1.9                  | –0.8                      | 0.1                      | 0.2             |
| 11 | –0.6                  | 2.3                       | 2.6                      | 0.3             |
| 12 | 0.3                   | –0.2                      | 1.4                      | 0.2             |
| 13 | 1.0                   | 3.8                       | 4.1                      | 2.2             |
| 14 | 0.8                   | 1.0                       | 3.0                      | 0.3             |
| 15 | –0.7                  | 1.4                       | 1.8                      | 0.6             |
| 16 | 0.9                   | 2.1                       | 3.2                      | 0.9             |
| 17 | –1.1                  | 2.4                       | 2.0                      | –0.4            |
| 18 | 0.1                   | 1.7                       | 2.4                      | 0.1             |
| 19 | –0.9                  | 0.6                       | 0.9                      | –1.9            |
| 20 | 0.9                   | 1.7                       | 4.3                      | 0.5             |

Z score values are extrapolated from echocardiography.

Cardiac magnetic resonance

All patients underwent CMR, with seven of these under general anaesthetic (Table 4). Median time to MRI was 20 days (range 11–29 days) after the onset of illness. Maximal indexed left ventricular end-diastolic volume (iLVEDV), indexed left ventricular end-systolic volume (iLVESV), and indexed left ventricular stroke volume (iLVSV) were within normal range corrected for BSA. Global function measured by LVEF demonstrated 13 patients with normal function (EF >55%), 3 patients with borderline dysfunction (EF 50–55%), and 4 patients with mild LV dysfunction (EF <50%). There was mild right ventricular dysfunction in one patient.

Discussion

This novel multisystem inflammatory syndrome has been differentiated from KD and KDSS and is thought to be a new disease entity temporally associated with prior exposure to SARS-CoV-2 infection. A striking feature is the high degree of cardiovascular compromise, often with circulatory shock, myocardial depression, and coronary involvement. Using multimodality analysis, we show that the extent of cardiac involvement is greater than first reported, with LV dysfunction, myocardial oedema, and coronary artery changes persisting even after clinical defervescence and normalization of inflammatory markers.

While coronary involvement in KD occurs in 23–50% of cases, in this cohort of patients we found a higher incidence (60%) of cases with enlarged coronary arteries and a distinctive pattern of involvement: (i) the LCx and RCA were never affected in isolation; (ii) the orifice of the LMCA was frequently ectatic; and (iii) dilatation of the proximal vessels (with no segmental distribution) appeared to lend itself to a description of ectasia rather than aneurysm (Table 3). One patient had congenital absence of the LCx.

The intraclass coefficient (95th confidence interval) for measurement of all coronary arteries was 0.951 (0.925–0.971), P <0.0001.
vessel was always uniformly ectatic. This is in contrast to KD where involvement is diffuse, the LMCA orifice is typically spared, and there are often normal interposing segments between aneurysms. The observed coronary changes in this new condition may be a prominent response to fever and an underlying cytokine storm—reflected in the elevated inflammatory markers occurring with PIMS—rather than changes within the arterial wall that occur in KD. It might be postulated that with resolution of inflammation there should be recovery of any findings temporally related to the inflammation.

The incidence of coronary involvement was higher on CT compared with echocardiography, a consistent finding from other studies where 56% of aneurysms may be missed by echocardiography alone. Existing data suggest that CT is an excellent tool for assessing coronary aneurysms in KD, with good correlation to established echocardiographic parameters and permitting better detection particularly of smaller lesions which have been noted in this patient group.

There was echocardiographic evidence of cardiac involvement affecting LV systolic and diastolic performance in all patients studied, which is greater than with previous studies. In a study of a similar inflammatory syndrome, 60% had some form of cardiac involvement; however, only 2D EF or the presence of coronary abnormalities was recorded. In our study, a significant proportion of patients had abnormal LV systolic function on admission, and serial echocardiograms demonstrated that LV dysfunction evolved, typically worsening by day 7 of the illness on a range of echocardiographic modalities. Even though LV dysfunction, by means of M-mode FS, was identified in a significant proportion of patients, this is likely to be an underestimate of the true extent of the overall LV systolic dysfunction. The use of 3D echocardiography revealed that a higher proportion of the patients had affected LV systolic function on admission, which significantly worsened during hospitalization in line with deterioration of their clinical status. Similarly, at discharge, the 3D-derived LVEF normalized in almost all patients in keeping with their clinical improvement. The above findings were confirmed by the low GLS and the altered systolic TDI velocities in a significant proportion on admission, indicating that 3D LVEF may be a more sensitive marker for dysfunction in this group. In general, serial detailed echocardiographic assessment determined that functional cardiac involvement was more extensive than first thought. The process was not static and involved a pancarditis affecting the valves, the myocardium and causing pericardial effusions (25% on CMR). KD rarely causes such a frequency of cardiac impairment, with valvular dysfunction occurring in 25% and ventricular dysfunction occurring in only 20%.

LV dysfunction persisted in 35% of patients assessed by CMR-derived EF. However, we identified further subtle signs of ongoing dysfunction with abnormal strain patterns in all patients persisting beyond 2 weeks of the onset of the illness. Positive T1 and T2 criteria were present in 10 patients, suggesting that the extent of active

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**Table 4** Cardiac magnetic resonance imaging data showing volumetric, functional, and late gadolinium enhancement pattern

| ID | iLVEDV (mL/m²) | iLVESV (mL/m²) | iLVSV (mL/m²) | LVEF (%) | iWall mass (g/m²) | T2-weighted signal | LGE pattern | Pericardial effusion | Peak circumferential strain (%) | Peak longitudinal strain (%) |
|----|----------------|----------------|----------------|----------|------------------|-------------------|-------------|---------------------|-------------------------------|-----------------------------|
| 1  | 97             | 52             | 45             | 47       | 57               | –                 | –           | –                   | –15.0                         | –13.5                       |
| 2  | 72             | 31             | 41             | 57       | 46               | Septum           | –           | –                   | –16.7                         | –15.9                       |
| 3  | 91             | 37             | 54             | 60       | 48               | Septum           | –           | –                   | –16.7                         | –16.5                       |
| 4  | 64             | 27             | 37             | 58       | 35               | –                 | Small       | –                   | –16.7                         | –11.9                       |
| 5  | 101            | 45             | 56             | 56       | 52               | Lateral wall     | –           | –                   | –16.1                         | –13.6                       |
| 6  | 58             | 28             | 30             | 52       | 34               | –                 | –           | –                   | –17.6                         | –12.5                       |
| 7  | 48             | 17             | 31             | 65       | 52               | Global           | Speckling    | –                   | –19.1                         | –13.9                       |
| 8  | 61             | 34             | 27             | 45       | 46               | Global           | Speckling    | –                   | –18.3                         | –14.0                       |
| 9  | 93             | 43             | 52             | 55       | 45               | –                 | Small       | –                   | –18.5                         | –11.5                       |
| 10 | 78             | 38             | 40             | 51       | 52               | –                 | –           | –                   | –16.7                         | –13.7                       |
| 11 | 97             | 47             | 51             | 52       | 65               | –                 | –           | –                   | –18.3                         | –17.1                       |
| 12 | 75             | 18             | 56             | 76       | 35               | –                 | Small       | –                   | –22.4                         | –18.5                       |
| 13 | 79             | 32             | 47             | 59       | 53               | –                 | Small       | –                   | –18.8                         | –16.1                       |
| 14 | 71             | 36             | 35             | 49       | 48               | –                 | Small       | –                   | –18.3                         | –16.0                       |
| 15 | 81             | 32             | 49             | 60       | 64               | Global           | –           | –                   | –18.5                         | –18.5                       |
| 16 | 100            | 34             | 67             | 66       | 53               | Global           | –           | –                   | –19.0                         | –16.2                       |
| 17 | 71             | 16             | 55             | 78       | 36               | Septum           | Small       | –                   | –19.8                         | –19.5                       |
| 18 | 69             | 29             | 40             | 58       | 47               | Global           | –           | –                   | –20.8                         | –17.0                       |
| 19 | 83             | 42             | 40             | 48       | 43               | Global           | Speckling    | –                   | –15.1                         | –11.1                       |
| 20 | 94             | 33             | 61             | 64       | 69               | –                 | Infarct     | –                   | –19.8                         | –17.2                       |
| Mean| 79.1           | 33.5           | 45.7           | 57.8     | 49.1             | –                 | –           | –                   | –18.1                         | –15.2                       |
| SD  | 15.3           | 9.6            | 10.9           | 8.9      | 9.9              | –                 | –           | –                   | 1.8                           | 2.5                         |

iLVEDV, indexed left ventricular end-diastolic volume; iLVESV, indexed left ventricular end-systolic volume; iLVSV, indexed left ventricular stroke volume; LVEF, left ventricular ejection fraction; LGE, late gadolinium enhancement.
myocardial inflammation was prominent but resolving and in keeping with the rapid clinical and echocardiographic recovery seen in patients following resolution of inflammation. It would be worth mentioning that one patient presented with a typical acute coronary syndrome caused by a subendocardial infarction. This demonstrates the need for high vigilance in this group of patients.

In conclusion, the major findings are that the extent of cardiac involvement is greater than first reported, with evolving cardiac impairment and coronary changes. Ongoing dysfunction, oedema, and coronary artery changes can persist despite defervescence and normalization of inflammatory markers. We propose that all patients who present with this novel multisystem inflammatory syndrome should be screened with basic and then advanced, echocardiography supplemented by structured multimodality imaging.

Limitations and further work
This is a newly described condition and the data presented are retrospectively reviewed. We propose further collaborative work between institutions to streamline treatment pathways. A large number of patients had ongoing dysfunction and enlarged coronary arteries indicating the need for ongoing assessment and review of medium- to long-term outcomes.

Supplementary material
Supplementary material is available at European Heart Journal – Cardiovascular Imaging online.

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