Editorial for "Cardiac Magnetic Resonance Follow-Up of Children After Pediatric Inflammatory Multisystem Syndrome Temporally Associated with SARS-CoV-2 (PIMS-TS) and Initial Cardiac Involvement"

During the initial peak of the 2019 coronavirus pandemic, a group of researchers in England reported a cohort of children with hyperinflammatory shock and cardiac features reminiscent of Kawasaki disease or toxic shock syndrome. The children developed symptoms 2–4 weeks after acute clinical and serologic evidence of coronavirus disease of 2019 (COVID-19) infection.[1] By May, the Centers for Disease Control and Prevention (CDC) published an online Health Advisory that summarized the manifestations of reported multisystem inflammatory syndrome in children (MIS-C). Children with this syndrome have been recognized worldwide and case definitions between the CDC, the World Health Organization, and the Royal College of Paediatrics and Child Health (RCPCH) have been similar, considering the pace of evaluation in this newly recognized disease.[2] While the acronym MIS-C remains in use, the RCPCH and many others use "pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2" (PIMS-TS).

Fever and nonspecific symptoms, including vomiting, abdominal pain, and diarrhea, have been the most common presenting symptoms of PIMS-TS, with rash and conjunctival injection occurring in about half of children. Some patients have presented with shock, and sepsis must be excluded early in management. While multisystem involvement is required for the diagnosis, cardiac features have been a prominent concern during the acute phase of PIMS-TS. Reduced ejection fraction and pericardial effusion have been the most common echocardiographic features and cardiac inflammatory markers, including troponin I and creatinine kinase subsets, have been elevated.[3]

Shortly after the description of PIMS-TS, case series began to appear with retrospective evaluations from single centers. In some of these, cardiac involvement was reported in 100% of patients with PIMS-TS,[4,5] although most noted that this was not a uniform complication. Reports varied about whether there was full resolution after discharge or whether cardiac features persisted (Table 1). In this issue of *JMRI*, Bartoszek et al report a retrospective study of 19 children, hospitalized for PIMS-TS between November 2020 and January 2021.[9] Unlike other studies, the authors described a cohort who had definitive cardiac involvement during PIMS-TS, as determined by either decreased left ventricular ejection fraction (<55% in 18 of 19 patients) or elevation in troponin I serum biomarkers. Patients underwent cardiac magnetic resonance imaging (MRI) with myocardial tissue characterization 90–100 days after the diagnosis. All patients had normal dark blood T2 imaging, normal T1/T2/extracellular volume mapping values, and no late gadolinium enhancement. Small pericardial effusion was noted in three patients (16%). These findings are similar to a recent prospective study, also on a small number of children, that similarly demonstrated no cardiac abnormalities by MRI during mid-term follow-up.[8]

Clinicians are left with the difficulty of reconciling some reports that have shown myocardial scarring after PIMS-TS[5] and even one larger survey-based study that reported late gadolinium enhancement on cardiac MRI in 14% of patients[10] with these newer data that show fewer or no long-term complications. When balancing the utility of post-hospitalization cardiac MRI and the potential risks of repeated gadolinium-based contrast exposure, we must bear in mind that early reports of new disease states tend to overrepresent severe findings. The presence of severe disease is part of what allows a new entity to be distinguished from the usual variation in existing clinical entities. This occurred early in PIMS-TS as clinicians realized that children were not presenting with sepsis or unrelated disease, but with a postinfectious inflammatory condition related to SARS-CoV-2 (severe acute

TABLE 1. Comparison of Studies Evaluating cardiac MRI After PIMS-TS

First Author, Citation	Year	*N*	Age	Cohort Description	Major Findings
Blondiaux[6]	2020	4	6–12	Retrospective cohort	75% with diffuse myocardial edema by T2-weighted imaging and abnormal native T1 mapping, with no evidence of late gadolinium enhancement at up to 15 days post-illness
Prieto[7]	2021	5	5–12	Retrospective cohort	No evidence of cardiac MRI abnormalities ~16 days post-illness
Webster[8]	2021	6	13–18	Prospective cohort, compared against existing controls	No evidence of cardiac MRI abnormalities ~60 days post-illness (no LGE imaging)
Bartoszek[9]	2021	18	8–17	Retrospective cohort	No evidence of cardiac MRI abnormalities ~90 days postinfection (including LGE imaging)
Theocharis[5]	2020	20	5–16	Retrospective cohort	35% with LV dysfunction, edema in 50%, 100% impairment in systolic strain indices ~20 days post-illness
Valverde[10]	2021	42	3–12	Internet-based retrospective survey of active PIMS-TS patients; only 15% with cardiac MRI	33% with T2 hyperintensity, 24% with pericardial effusion, 14% with late gadolinium enhancement. Timing of cardiac MRI is unclear from survey methods

LGE = late gadolinium enhancement; LV = left ventricular.

respiratory syndrome coronavirus 2) that presented similarly to Kawasaki disease or toxic shock syndrome. However, as the new case definitions were applied over a broader population, less severe manifestations were recognized and incorporated into the disease. Thus, it is not surprising that follow-up studies, such as the current one by Bartoszek et al, demonstrate lower levels of cardiac involvement (or no cardiac involvement).

In summary, the lack of positive findings on post-hospitalization MRI following MIS-C may indeed support the hypothesis that cardiac manifestations are indirect and transient and may also decrease enthusiasm for follow-up MRI, especially when contrast may be administered. These findings, however, should not be taken as a definitive conclusion that late cardiac involvement cannot occur, but only that cardiac manifestations are not as ubiquitous as originally assumed.

Gregory Webster, MD, MPH
Division of Cardiology
Ann & Robert H. Lurie Children's Hospital of Chicago
Chicago, Illinois, USA
Department of Pediatrics
Northwestern University Feinberg School of Medicine
Chicago, Illinois, USA

Joshua D. Robinson, MD
Division of Cardiology
Ann & Robert H. Lurie Children's Hospital of Chicago
Chicago, Illinois, USA
Department of Pediatrics
Northwestern University Feinberg School of Medicine
Chicago, Illinois, USA
Department of Radiology
Northwestern University Feinberg School of Medicine
Chicago, Illinois, USA
E-mail: jdrobinson@luriechildrens.org

References

1. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet 2020;395(10237):1607-1608.
2. Sperotto F, Friedman KG, Son MBF, VanderPluym CJ, Newburger JW, Dionne A. Cardiac manifestations in SARS-CoV-2-associated multisystem inflammatory syndrome in children: A comprehensive review and proposed clinical approach. Eur J Pediatr 2020;180:1-16.
3. Kelly MS, Valle CW, Fernandes ND, Cummings BM, Lahoud-Rahme M, Chiu JS. Multisystem inflammatory syndrome in children: Cardiac biomarker profiles and echocardiographic findings in the acute and recovery phases. J Am Soc Echocardiogr 2020;33(10):1288-1290.
4. Ramcharan T, Nolan O, Lai CY, et al. Paediatric inflammatory multisystem syndrome: Temporally associated with SARS-CoV-2 (PIMS-TS): Cardiac features, management and short-term outcomes at a

UK tertiary paediatric hospital. Pediatr Cardiol 2020;41(7):1391-1401.

5. Theocharis P, Wong J, Pushparajah K, et al. Multimodality cardiac evaluation in children and young adults with multisystem inflammation associated with COVID-19. Eur Heart J Cardiovasc Imaging 2020;22:896-903.
6. Blondiaux E, Parisot P, Redheuil A, et al. Cardiac MRI in children with multisystem inflammatory syndrome associated with COVID-19. Radiology 2020;297(3):E283-E288.
7. Prieto LM, Toral B, LLorente A, Coca D, Blázquez-Gamero D. Cardiovascular magnetic resonance imaging in children with pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 and heart dysfunction. Clin Microbiol Infect 2021;27:648-650.
8. Webster G, Patel AB, Carr MR, et al. Cardiovascular magnetic resonance imaging in children after recovery from symptomatic COVID-19 or MIS-C: A prospective study. J Cardiovasc Magn Reson 2021;23(1):86.
9. Bartoszek M, Małek ŁA, Barczuk-Falęcka M, Brzewski M. Cardiac magnetic resonance follow-up of children after pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) and initial cardiac involvement. J Magn Reson Imaging 2022;55:883-891.
10. Valverde I, Singh Y, Sanchez-de-Toledo J, et al. Acute cardiovascular manifestations in 286 children with multisystem inflammatory syndrome associated with COVID-19 infection in Europe. Circulation 2021;143(1):21-32.

DOI: 10.1002/jmri.27926

Level of Evidence: 5
Technical Efficacy Stage: 2