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Persistent Cardiac Magnetic Resonance Imaging Findings in a Cohort of Adolescents with Post-Coronavirus Disease 2019 mRNA Vaccine Myopericarditis

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We describe the evolution of cardiac magnetic resonance imaging findings in 16 patients, aged 12-17 years, with myopericarditis after the second dose of the Pfizer mRNA coronavirus disease 2019 vaccine. Although all patients showed rapid clinical improvement, many had persistent cardiac magnetic resonance imaging findings at 3- to 8-month follow-up. (*J Pediatr* 2022;245:233-7).

Myopericarditis has emerged as an important adverse event following coronavirus disease 2019 (COVID-19) mRNA vaccination, particularly in adolescents.¹ Patients typically exhibit chest pain and an elevated serum troponin level in the days following the COVID-19 mRNA vaccine. They usually are hemodynamically stable, and symptoms and cardiac biomarkers normalize within a few days.² Cardiac magnetic resonance imaging (MRI) studies, when performed early, frequently demonstrate abnormalities such as edema and late gadolinium enhancement (LGE), meeting Lake Louise criteria for diagnosing myocarditis noninvasively.^{3,4} In classical myocarditis, LGE can be predictive of a poor outcome.⁵ Little is known about the prognostic value or expected evolution of these cardiac MRI abnormalities associated with post-COVID-19 mRNA vaccine myopericarditis. In this case series, we report the evolution of cardiac MRI compared with initial, acute-phase, cardiac MRI in our cohort of patients with myopericarditis post-COVID-19 mRNA vaccine.

Methods

This case review includes patients younger than 18 years of age presenting to Seattle Children's Hospital with chest pain and elevated serum troponin level from April 1, 2021, to January 7, 2022, within 1 week of receiving the second dose of the Pfizer COVID-19 mRNA vaccine. Institutional review board approval was obtained. All patients were evaluated by a pediatric cardiologist, underwent electrocardiogram (ECG) and echocardiogram, and were admitted

for observation with telemetry, serial troponin measurements, and repeat cardiac testing as needed. All patients underwent cardiac MRI within 1 week of initial presentation and had repeat cardiac MRI at 3-8 months' follow-up. Cardiac MRI was performed on a 1.5-T Siemens scanner (Siemens AG). Cardiac MRI analysis was performed using CVI42 (version 5.11.4; Circle Cardiovascular Imaging Inc). Patients were excluded if they did not undergo cardiac MRI or did not have a follow-up cardiac MRI. Initial and follow-up cardiac MRI data for each patient were reviewed and compared using paired Student *t* tests. Statistical significance was defined as a *P* < .05. Statistical analysis was performed using SPSS 27 (IBM Corp).

Results

A total of 35 patients with the diagnosis of myopericarditis associated with Pfizer COVID-19 mRNA vaccine were followed at our institution. Twelve patients were excluded, as they never had cardiac MRI scans due to delayed presentation after initial symptoms resolved or admission to other centers. Six patients were excluded, as they did not have a follow up cardiac MRI, either because they followed up out of state or a study is still pending. One patient was excluded, as initial cardiac MRI was performed 3 weeks after presentation. Sixteen patients who had both acute-phase and follow-up cardiac MRIs available for review comprised the final cohort. This group had a median age of 15 years (range, 12-17 years), were mostly male (*n* = 15, 94%), White, and non-Hispanic (*n* = 14, 88%). One patient was Asian, and 1 patient was American Indian. Median time to presentation from the second dose of the Pfizer COVID-19 mRNA vaccine was 3 days

COVID-19	Coronavirus disease 2019
ECG	Electrocardiogram
IVIG	Intravenous immunoglobulin
LGE	Late gadolinium enhancement
LV	Left ventricle
LVEF	Left ventricular ejection fraction
MRI	Magnetic resonance imaging
NSAID	Nonsteroidal anti-inflammatory drug

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(range 2-4 days). All patients had chest pain. The most common other presenting symptoms were fever (n = 6, 37.5%) and shortness of breath (n = 6, 37.5%). All patients had elevated serum troponin levels (median 9.15 ng/mL, range 0.65-18.5, normal <0.05 ng/mL). Twelve patients had C-reactive protein measured with median value 3.45 mg/dL, range 0-6.5 mg/dL, normal <0.08 mg/dL.

Ten (62.5%) patients had an abnormal ECG, with the most common finding being diffuse ST-segment elevation. All patients had an echocardiogram on admission; 14 of 16 patients had normal left ventricular (LV) systolic function; 2 patients demonstrated mildly reduced LV systolic function with no dilation. Left ventricular ejection fraction (LVEF) for these 2 patients was 45% and 53% (normal >55%). Median left LVEF was 59% (range 45%-69%). No patients had pericardial effusion.

The initial cardiac MRIs were performed within 1 week of presentation (median 2, range 0-7 days). All were abnormal; all showed evidence of edema by T2 imaging, and 15 of 16 had LGE in a patchy subepicardial to transmural pattern with predilection for the inferior LV free wall. Distribution of LGE can be seen in **Figure 1**.⁶ LV regional wall motion abnormalities were noted in 2 patients. Cardiac MRI median LVEF% was 54%, range 46%-63%. Cardiac MRI LVEF was mildly decreased in 7 patients. Cardiac MRI global longitudinal strain (%) measurements were abnormal in 12 patients (median -16.1%, range -13.2% to -18.1%, normal <-18%).

All patients were treated with nonsteroidal anti-inflammatory drugs (NSAIDs): 75% (n = 12) received

scheduled dosing (mostly, 10 mg/kg ibuprofen every 8 hours), with the remaining 4 receiving NSAIDs as needed for pain. The median time from vaccination to NSAID initiation was 2.5 days (range 0-4 days) and from symptom onset to NSAID initiation was 1 day (range 0-4 days). The 2 patients who presented with echocardiographic LV dysfunction were treated with intravenous immunoglobulin (IVIG) plus a corticosteroid per our institutional pathway for treatment of myocarditis. One additional patient received IVIG without corticosteroids. Median hospital length of stay was 2 days (range 1-4 days) with no intensive care unit admission and no significant morbidity or mortality. All patients had resolution of chest pain and down-trending serum troponin level before discharge.

All patients underwent follow-up cardiac MRI at 3-8 months after their initial study (median 3.7 months, range 2.8-8.1 months). The results are compared in the **Table**. Follow-up cardiac MRI LVEF (57.7 ± 2.8%) was significantly improved from initial (54.5 ± 5.5%, P < .05), and none of the patients had regional wall motion abnormalities. LVEF by echocardiogram was normal for all patients at the time of follow-up. Eleven patients (68.8%) had persistent LGE, although there was a significant decrease in the quantifiable LGE% (8.16 ± 5.74%) from the initial study (13.77 ± 8.53%, P < .05). Cardiac edema resolved in all but 1 patient. Global longitudinal strain (%) remained abnormal in most patients (75%, mean -16.4 ± 2.1%) at follow-up without significant change from the initial study (-16.0 ± 1.7, P = .6). Examples of initial and follow-up cardiac MRI images are shown in

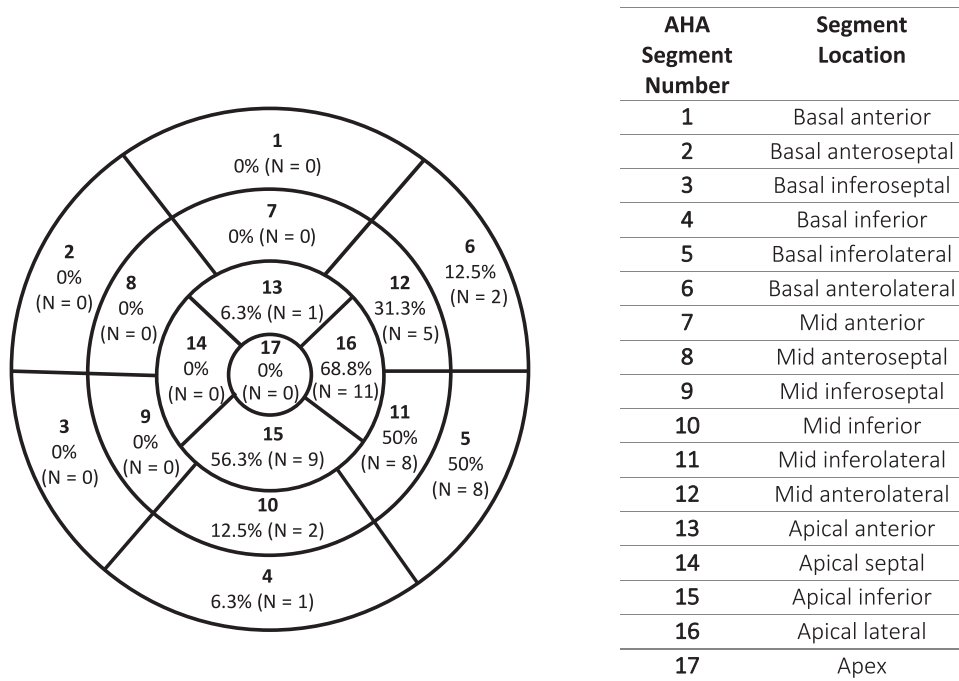


Figure 1. Distribution of LGE in AHA myocardial segments.⁶ Shown is the number and percentage of patients with LGE in each segment. AHA, American Heart Association.

Table. COVID-19 vaccine-associated myopericarditis findings in 16 patients

Diagnostic assessment	Initial, mean \pm SD	Follow-up, mean \pm SD	P value
Echocardiographic LVEF %	59.4 \pm 6.0	62.6 \pm 2.8	<.05
Electrocardiogram			
Abnormal	10 (62.5%)		
Normal	6 (37.5%)		
Peak serum troponin, ng/mL	9.0 \pm 5.2		
Cardiac MRI LVEF %	54.5 \pm 5.5	57.7 \pm 2.7	<.05
Cardiac MRI LGE % (n = 15*)	13.5 \pm 8.3	7.7 \pm 5.7	<.001
Cardiac MRI global longitudinal strain % (n = 15*)	-16.0 \pm 1.7	-16.4 \pm 2.1	.5

Bold formatting indicates $P < .05$, or statistically significant.

*Initial source images were not available for reanalysis for 1 patient.

Figure 2. The patient who received IVIG alone and 1 patient who received IVIG plus corticosteroid had resolution of LGE, and the other had persistence of LGE.

Eight patients (5 of whom had persistent LGE) underwent 24-hour cardiac rhythm monitoring, all of which were normal. Six patients, all with persistent LGE, underwent exercise tests, all of which were normal. Four patients complained of intermittent chest pain at follow up with no identifiable abnormality on evaluation; no therapy or intervention was required. No patient received heart failure medication.

Discussion

We previously reported 15 patients with clinically suspected COVID-19 mRNA vaccine-induced myopericarditis. All patients had an abnormal cardiac MRI, with edema and/or LGE in addition to clinical symptoms and troponin elevation, and some had abnormal ECG or echocardiogram.⁴ We have since established a clinical protocol for serial cardiac MRI performance in these patients, consistent with the 2021 American Heart Association statement that stressed the risk of sudden cardiac death, particularly with exercise, while active inflammation is present.⁷ Our patients were restricted from exercise on discharge. Repeat cardiac MRI was performed within 3-6 months to guide next clinical decision-making steps; timing was modified in some individuals based on scanner accessibility and safety precautions during the COVID-19 pandemic. Although symptoms were transient and most patients appeared to respond to treatment (solely with NSAIDs), we demonstrated persistence of abnormal findings on cardiac MRI at follow-up in most patients, albeit with improvement in extent of LGE.

Cardiac MRI increasingly has been identified as an important diagnostic tool for myocarditis, given its ability to identify subclinical injury and fibrosis by markers of LGE and edema. Cardiac MRI also has been used in longitudinal follow-up of patients with myocarditis to help therapeutic management, although exact screening protocols remain controversial.⁷

The presence of LGE is an indicator of cardiac injury and fibrosis and has been strongly associated with worse prognosis in patients with classical acute myocarditis. In a meta-analysis including 8 studies, Yang et al⁵ found that presence of LGE is a predictor of all cause death, cardiovascular death, cardiac transplant, rehospitalization, recurrent acute myocarditis, and requirement for mechanical circulatory support. Similarly, Georgiopoulos et al⁸ found the presence and extent of LGE to be a significant predictor of adverse cardiac outcomes in an 11 study meta-analysis.

The persistence of LGE over time and its prognostic value is less well established. Małek et al⁹ found that in a cohort of 18 patients with myocarditis, nearly 70% had persistent cardiac MRI changes at a median follow-up time of 7 months. Dubey et al¹⁰ found similar findings in their cohort of 12 pediatric patients, with persistence of LGE in all patients despite resolution of edema. The prognostic meaning of LGE in vaccine associated myopericarditis requires further study.

Strain analysis by cardiac MRI also has been shown to have prognostic utility in myocarditis even in the setting of normal LV function.¹¹ Strain testing can be performed without use of contrast material and can be particularly useful in situations in which contrast administration is challenging or contraindicated. Notably, in our cohort, although there was significant reduction in LGE at follow-up, abnormal strain persisted for the majority of patients at follow-up.

This study has certain limitations. Patients who did not seek medical attention during acute illness or did not present with significant symptoms and require hospitalization were not captured, and their disease course may be different. Incomplete cardiac MRI data on other patients precludes extrapolation of our cardiac MRI findings to all who experienced mRNA vaccine-related myopericarditis. In addition, follow-up cardiac MRI timeframes varied from patient to patient, making it difficult to predict the timing of cardiac MRI changes over time. The total number of patients reported is small, limiting ability to draw conclusions about the effect of treatment modalities or to generalize regarding outcomes of vaccine-associated myopericarditis.

In a cohort of adolescents with COVID-19 mRNA vaccine-related myopericarditis, a large portion have persistent LGE abnormalities, raising concerns for potential longer-term effects. Despite these persistent abnormalities, all patients had rapid clinical improvement and normalization of echocardiographic measures of systolic function. For patients with short acute illness, no dysfunction demonstrated by echocardiogram at presentation and resolution of symptoms at follow-up, return to sports was guided by normalization of cardiac MRI alone. In patients with persistent cardiac MRI abnormalities, we performed exercise stress testing before sports clearance per myocarditis recommendations.⁷ We plan to repeat cardiac MRI at 1-year postvaccine for our cohort to assess for resolution or continued cardiac MRI changes.

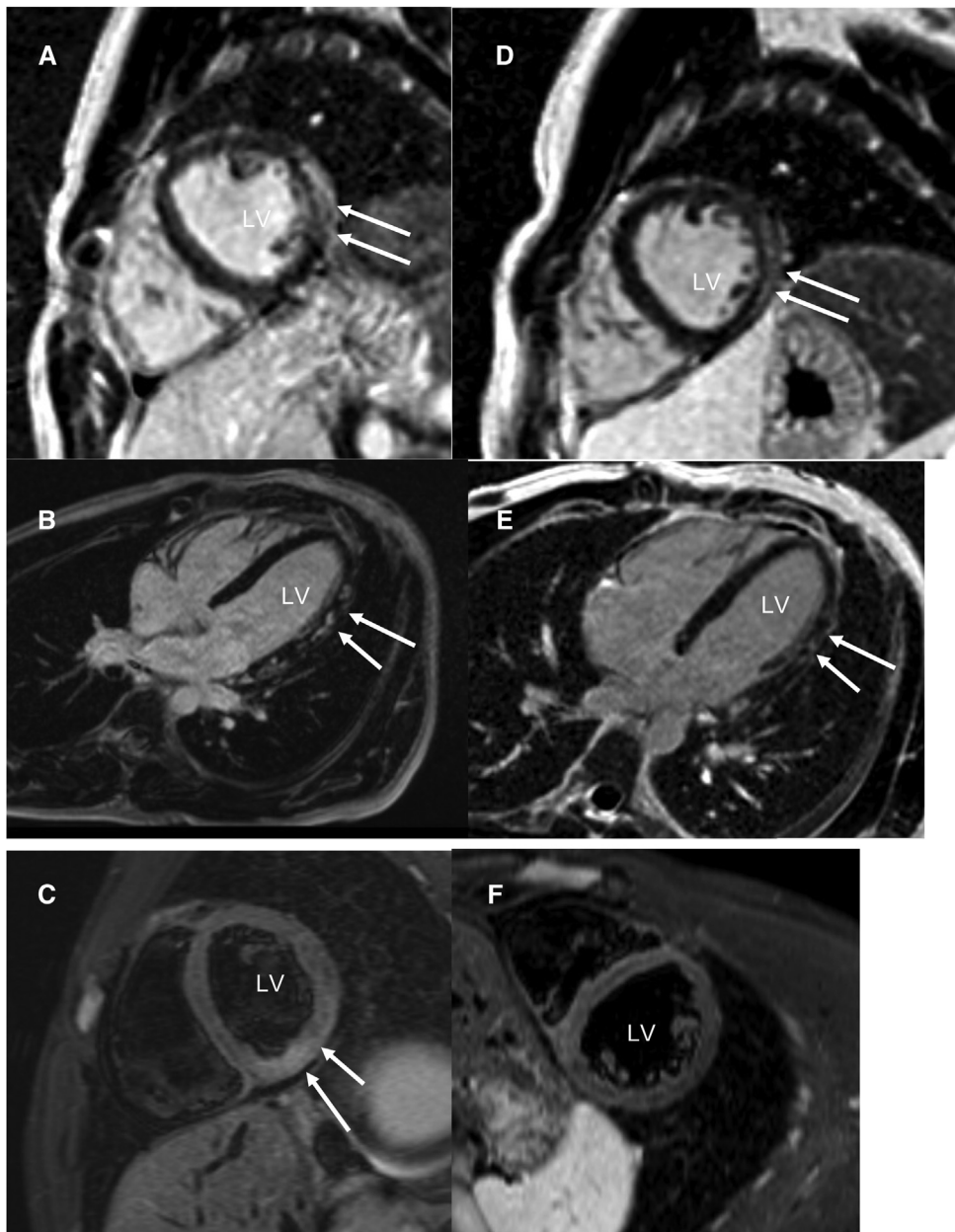


Figure 2. Cardiac MRI scans from 3 days after admission of a 16-year-old male patient who presented to the emergency department with chest pain and elevated troponin 3 days after receiving the Pfizer COVID-19 mRNA vaccine. Initial cardiac MRI. **A and B**, Subepicardial to midmyocardial LGE in inferior and inferolateral LV wall from base to apex (*arrows*). **C**, T2 hyperintensity in similar segments, consistent with edema. **D-F**, Follow-up cardiac MRI 4.4 months later. LGE is still persistent but decreased from 26% to 19.84% (*arrows*), and LVEF remained stable at 58%. There is improved T2 hyperintensity.

The Centers for Disease Control and Prevention notes that even though the absolute risk for myopericarditis following mRNA COVID-19 vaccine is small, the relative risk is greater for particular groups, including male patients aged 12-39 years. Some studies have suggested that increasing the interval between the first and second dose may reduce the incidence of myopericarditis in this population.¹² These data led to an extension in the Centers for Disease Control and Prevention–recommended dosing interval between dose 1 and dose 2 to

8 weeks. Further follow-up assessment and larger multicenter studies are needed to determine the ultimate clinical significance of persistent cardiac MRI abnormalities in patients with post-COVID-19 vaccine myopericarditis. ■

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