Cardiac MRI Findings of Myocarditis After COVID-19 mRNA Vaccination in Adolescents

Lydia Chelala, MD[1], Jean Jeudy, MD[2], Rydhwana Hossain, MD[2], Geoffrey Rosenthal, MD[2], Nicholas Pietris, MD[2], Charles S. White, MD[2]

Cardiothoracic Imaging · Original Research

Keywords

COVID-19, MRI, myocarditis, vaccination

Submitted: Sep 15, 2021
Revision requested: Sep 24, 2021
Revision received: Oct 8, 2021
Accepted: Oct 17, 2021
First published online: Oct 27, 2021

The authors declare that they have no disclosures relevant to the subject matter of this article.

BACKGROUND. A possible association has been reported between COVID-19 messenger RNA (mRNA) vaccination and myocarditis.

OBJECTIVE. The purpose of our study was to describe cardiac MRI findings in patients with myocarditis after COVID-19 mRNA vaccination.

METHODS. This retrospective study included patients without known prior SARS-CoV-2 infection who underwent cardiac MRI between May 14, 2021, and June 14, 2021, for suspected myocarditis within 2 weeks of COVID-19 mRNA vaccination. Information regarding clinical presentation, hospital course, and events after hospital discharge were recorded. A cardiothoracic imaging fellow and cardiothoracic radiologist reviewed cardiac MRI examinations in consensus. Data were summarized descriptively.

RESULTS. Of 52 patients without known prior SARS-CoV-2 infection who underwent cardiac MRI during the study period, five underwent MRI for suspected myocarditis after recent COVID-19 mRNA vaccination. All five patients were male patients ranging in age from 16 to 19 years (mean, 17.2 ± 1.0 [SD] years) who presented within 4 days of receiving the second dose of a COVID-19 mRNA vaccine. Troponin levels were elevated in all patients (mean peak troponin I value, 6.82 ± 4.13 ng/mL). Alternate possible causes of myocarditis were deemed clinically unlikely on the basis of medical history, physical examination findings, myocarditis viral panel, and toxicology screening. Cardiac MRI findings were consistent with myocarditis in all five patients on the basis of the Lake Louise criteria, including early gadolinium enhancement and late gadolinium enhancement (LGE) in all patients and corresponding myocardial edema in four patients. All five patients had a favorable hospital course and were discharged from the hospital in stable condition with improved or resolved symptoms after hospitalization (mean length of hospital stay, 4.8 days). Two patients underwent repeat cardiac MRI that showed persistent, although decreased, LGE. Three patients reported mild intermittent self-resolving chest pain after hospital discharge, and two patients had no recurrent symptoms after discharge.

CONCLUSION. In this small case series, all patients with myocarditis after COVID-19 vaccination were male adolescents and had a favorable initial clinical course. All patients showed cardiac MRI findings typical of myocarditis from other causes. LGE persisted in two patients who underwent repeat MRI. These observations do not establish causality.

CLINICAL IMPACT. Radiologists should be aware of a possible association of COVID-19 mRNA vaccination and myocarditis and recognize the role of cardiac MRI in the assessment of suspected myocarditis after COVID-19 vaccination.

COVID-19 has been associated with more than 170 million confirmed cases and more than 3.7 million deaths worldwide since its initial recognition [1]. As national and global responses have sought to contain the spread of COVID-19, significant resources have been applied to the development of a safe and effective vaccine [2, 3]. Within 1 year of release of the SARS-CoV-2 genome, two messenger RNA (mRNA) vaccines were approved for emergency use in several countries [4]. Advancements in vaccine development over the past decades—most notably, the advent of mRNA vaccination—fostered this achievement. Compared with conventional vaccines (i.e., vaccines involving live attenuated and inactivated pathogens), the new mRNA vaccines facilitate rapid development and large-scale deployment, serving as an attractive alternative in the setting of a global emergency [5].

doi.org/10.2214/AJR.21.26853
AJR 2022; 218:651–658
ISSN-L 0361–803X/22/2184–651

[1]Department of Diagnostic Radiology, University of Chicago Medicine, 5841 S Maryland Ave, Chicago, IL 60637. Address correspondence to L. Chelala (LChelala@radiology.bsd.uchicago.edu).

[2]Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland Medical Center, 22 S Greene St, Baltimore, MD 21201.

More than 6 billion doses of mRNA vaccine had been administered globally as of October 10, 2021 [1], and health authorities have closely monitored vaccine safety. As vaccination rates continue to rise, rare side effects have been reported. For example, concern for a possible association between COVID-19 mRNA vaccination and myocarditis in young individuals was first raised by researchers in Israel [6–9]. Subsequently, in the United States occurrences of myopericarditis in adolescents and young adults after COVID-19 mRNA vaccination have also been reported by the Vaccine Adverse Event Reporting System (VAERS) [6–8, 10]. This possible association warrants further investigation, particularly given the expansion on May 10, 2021, of the emergency approval of the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech; hereafter referred to as the Pfizer-BioNTech vaccine) by the U.S. FDA to include adolescents 12–15 years old. Thus, the aim of this study was to describe cardiac MRI findings in patients with myocarditis after COVID-19 mRNA vaccination.

HIGHLIGHTS

Key Finding

- *This retrospective case series identified five patients who underwent cardiac MRI for suspected myocarditis after COVID-19 mRNA vaccination. All patients were male adolescents and had a favorable initial clinical course. All patients showed cardiac MRI findings typical of myocarditis of other causes. LGE persisted in two patients who underwent repeat MRI.*

Importance

- *Radiologists should recognize the possible association of COVID-19 mRNA vaccination and myocarditis and the role of cardiac MRI in this clinical context.*

Methods

Patients

The institutional board review granted an exemption after review of this single-institution HIPAA-compliant retrospective study. The requirement for informed consent was waived. The records of all patients who underwent cardiac MRI at our institution between May 14, 2021, and June 14, 2021, were reviewed to identify those who underwent the examination because of a clinical suspicion for myocarditis. Patients were then excluded if they had a known history of SARS-CoV-2 infection or if they had not undergone COVID-19 vaccination within 2 weeks before MRI. The remaining patients formed the study sample, representing patients who underwent cardiac MRI for suspected myocarditis in the setting of recent COVID-19 vaccination.

A cardiothoracic imaging fellow (L.C.) reviewed the electronic medical records (EMRs) to identify included patients' demographic characteristics, medical history, results of biochemical laboratory testing, ECG results, and findings from echocardiography, which were recorded in a secure database (Table 1). This investigator also recorded information regarding patients' hospital course, condition at hospital discharge, and clinical events (including recurrent symptoms and follow-up cardiac imaging) after discharge.

Cardiac MRI Acquisition and Interpretation

All cardiac MRI examinations were performed using a 1.5-T magnet (Magnetom Sola, Siemens Healthcare). The protocol included the following sequences: axial and multiplanar cine precontrast SSFP, T1- and T2-weighted spectral adiabatic inversion recovery (SPAIR), perfusion imaging, early postcontrast short-axis SSFP, time inversion scout, and multiplanar T1-weighted inversion recovery segmented breath-hold late gadolinium enhancement (LGE) imaging. The LGE imaging was performed using IV administration of gadobenate dimeglumine. T1 and T2 parametric imaging was acquired at the discretion of the protocoling radiologist. For the scanner that performs cardiac MRI at our institution (University of Maryland Medical Center), normal reference native T1 parametric values were determined to be less than 1100 milliseconds, and normal T2 parametric values were determined to be less than 55 milliseconds.

The images from the cardiac MRI examinations were retrospectively reviewed in consensus by the previously noted cardiothoracic imaging fellow (L.C.) and by a cardiothoracic radiologist with 5 years of experience (R.H.); independent interpretations were not performed given the very small sample size. The readers initially compared cardiac functional assessment between MRI and echocardiography. The readers then assessed for individual findings associated with the diagnosis of myocarditis based on the updated 2018 Lake Louise criteria (LLC), which incorporate a combination of T1- and T2-based criteria [11]. The T1-based criteria encompassed the presence of early gadolinium enhancement (EGE), presence of LGE, and increased T1 relaxation times. The T2-based criteria encompassed the presence of focal myocardial edema, increased myocardial T2 signal intensity ratios, and increased T2 relaxation times.

The readers also recorded the presence of a pericardial effusion and of pericardial enhancement. A pericardial effusion with the pericardial fluid width measuring less than 4 mm was characterized as trace, and a pericardial effusion with the pericardial fluid width measuring 4–5 mm was characterized as small [12]. In addition, the readers evaluated the lung parenchyma and pleura for abnormalities on the axial SSFP sequence. Finally, the readers determined if the cardiac MRI examination was overall consistent with a diagnosis of myocarditis in consideration of the LLC. In patients who underwent a follow-up cardiac MRI examination after hospital discharge, the two investigators reviewed the follow-up MRI in a similar fashion. Imaging findings were summarized descriptively.

Results

Patient Demographics and Clinical Presentation

During the study period, 52 patients underwent cardiac MRI. Of these patients, 41 were excluded because of the following indications for MRI other than myocarditis: familial cardiomyopathy (n = 1), personal history of congenital heart disease (n = 5), cardiomyopathy (n = 31), and valvular disease (n = 4). The remaining 11 patients were referred for cardiac MRI because of a clinical suspicion for myocarditis based on the presence of chest pain or discomfort, elevated troponin values, and possible ECG abnormality. Of these 11 patients with suspected myocarditis, four were excluded because of a known history of SARS-CoV-2 infection and two were excluded because they had not received a COVID-19 vaccine within the 2 weeks before MRI. The remaining five patients formed the study sample.

The demographic characteristics, clinical information, and imaging findings for the five included patients are summarized in Table 1. All five patients were male. Patient age ranged from 16 to 19 years (mean age, 17.2 ± [SD] 1.0 years). All patients were referred to our institution after presenting to an outside hospital with acute chest pain. All patients reported the onset of symptoms within 4 days of receiving the second dose of a COVID-19 mRNA vaccine. Four patients received the Pfizer-BioNTech vaccine, and one patient received the mRNA-1273 COVID-19 vaccine (Moderna; hereafter referred to as the Moderna vaccine). No patient had known contact with a patient positive for SARS-CoV-2 infection. The SARS-CoV-2 nasal polymerase chain reaction (PCR) test was negative in all five patients. No patient reported significant cardiovascular risk factors or a history of previous cardiovascular events. Medications included ergocalciferol in one patient and buspirone and desvenlafaxine in one patient.

Initial Clinical Workup

ECG performed at presentation was normal in three patients. Diffuse ST segment elevation was present in one patient, and sinus bradycardia was present in one patient. Troponin levels were elevated at initial presentation in all patients. Mean initial and

TABLE 1: Patient Demographics, Clinical Presentation, Biochemical Laboratory Findings, and Imaging Findings

Characteristic	Patient A	Patient B	Patient C	Patient D	Patient E
Demographics					
Age (y)	16	17	17	19	17
Sex	Male	Male	Male	Male	Male
Clinical presentation and laboratory results					
mRNA COVID-19 vaccine manufacturer	Pfizer-BioNTech[a]	Pfizer-BioNTech[a]	Pfizer-BioNTech[a]	Moderna[b]	Pfizer-BioNTech[a]
No. of vaccine doses received	2	2	2	2	2
Interval between vaccine dose and clinical symptoms (d)	4	4	3	3	4
ECG findings	Normal	Normal	Diffuse ST elevation	Normal	Sinus bradycardia
Peak troponin I value (ng/mL)	1.38	4.81	4.91	10.00	1.38
CRP value (mg/dL)	0.16	1.70	18.00	4.12	1.40
Myocarditis panel	Negative	Negative	IgG EBV antibodies	Negative	Negative
Toxicology screening	Not performed	Negative	Negative	Marijuana	Not performed
Hospitalization length of stay (d)	9	4	3	3	3
Echocardiography findings					
Biventricular size	Normal	Normal	Normal	Normal	Normal
Biventricular function	Normal	Normal	Normal	LVEF, 40–45%; global LV hypokinesis	Normal
Additional findings	None	Ectasia of RCA and LAD	Hyperechoic septum	None	None
Cardiac MRI findings					
Interval between vaccination and MRI (d)	8	5	5	6	5
LVEF (%)	57	56	60	46	62
RVEF (%)	53	54	58	50	55
LVEDV/BSA (mL/m^2)	85	86	71	91	62
RVEDV/BSA (mL/m^2)	86	86	69	74	79
Early gadolinium enhancement	Yes	Yes	Yes	Yes	Yes
Late gadolinium enhancement	Yes	Yes	Yes	Yes	Yes
Distribution of enhancement[c]	4, 6, and 12	4, 5, 10, and 11	5, 6, and 12	5, 6, 11, 12, and 16	5, 6, 11, 12, and 13
Myocardial edema	Yes	Yes	No	Yes	Yes
Pericardial effusion	Small	Trace	Trace	Trace	Small

Note—mRNA = messenger RNA, CRP = C-reactive protein, EBV = Epstein-Barr virus, LVEF = left ventricular ejection fraction, LV = left ventricle, RCA = right coronary artery, LAD = left anterior descending artery, RVEF = right ventricular ejection fraction, LVEDV = left ventricular end-diastolic volume, BSA = body surface area, RVEDV = right ventricular end-diastolic volume.
[a]Manufacturer of the BNT162b2 mRNA COVID-19 vaccine.
[b]Manufacturer of the mRNA-1273 COVID-19 vaccine.
[c]Reported using the 17-segment American Heart Association model.

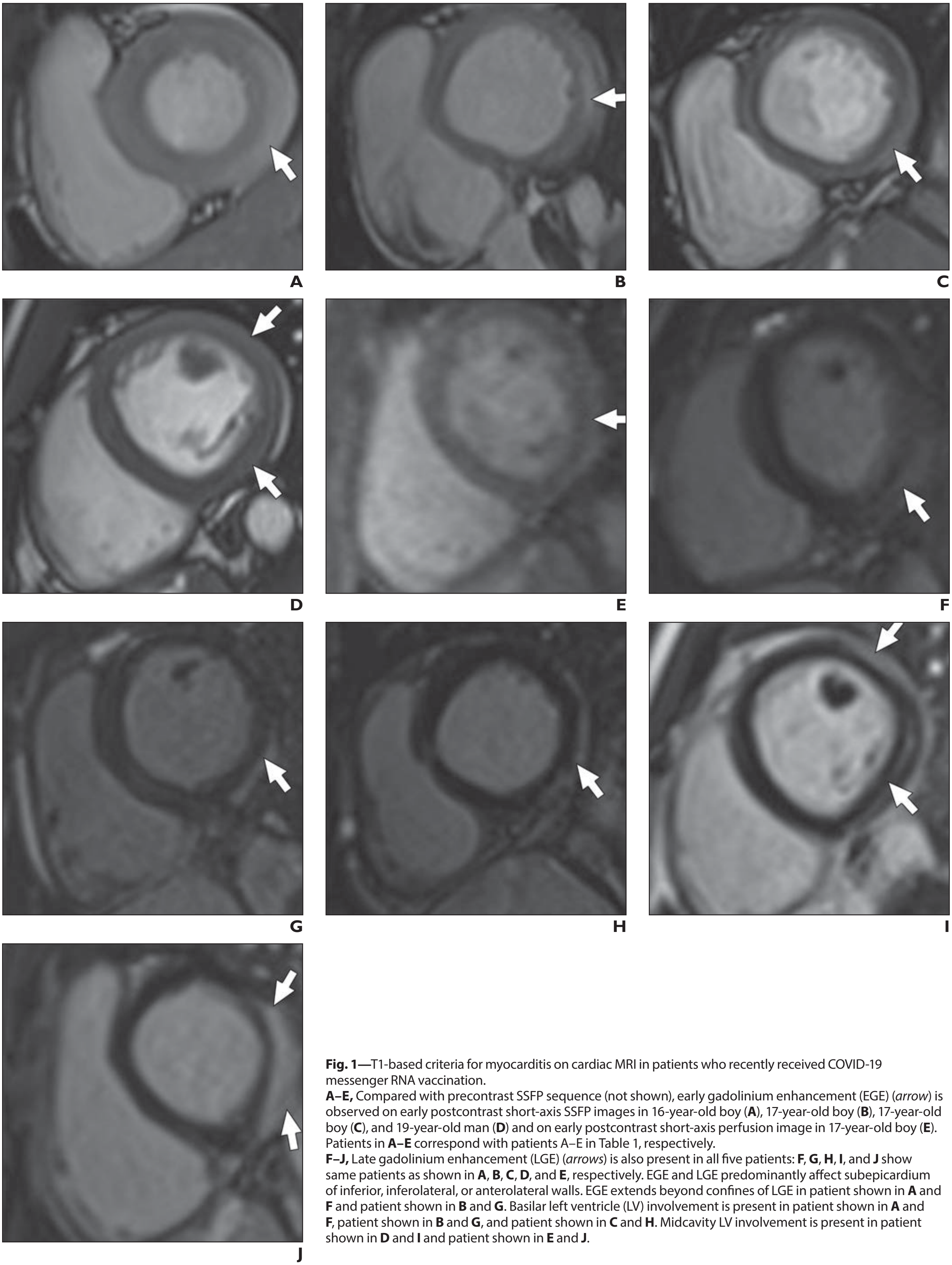


Fig. 1—T1-based criteria for myocarditis on cardiac MRI in patients who recently received COVID-19 messenger RNA vaccination.

A–E, Compared with precontrast SSFP sequence (not shown), early gadolinium enhancement (EGE) (*arrow*) is observed on early postcontrast short-axis SSFP images in 16-year-old boy (**A**), 17-year-old boy (**B**), 17-year-old boy (**C**), and 19-year-old man (**D**) and on early postcontrast short-axis perfusion image in 17-year-old boy (**E**). Patients in **A–E** correspond with patients A–E in Table 1, respectively.

F–J, Late gadolinium enhancement (LGE) (*arrows*) is also present in all five patients: **F**, **G**, **H**, **I**, and **J** show same patients as shown in **A**, **B**, **C**, **D**, and **E**, respectively. EGE and LGE predominantly affect subepicardium of inferior, inferolateral, or anterolateral walls. EGE extends beyond confines of LGE in patient shown in **A** and **F** and patient shown in **B** and **G**. Basilar left ventricle (LV) involvement is present in patient shown in **A** and **F**, patient shown in **B** and **G**, and patient shown in **C** and **H**. Midcavity LV involvement is present in patient shown in **D** and **I** and patient shown in **E** and **J**.

peak troponin I (TnI) levels measured 5.88 ± 4.26 ng/mL ($n = 4$ patients) and 6.82 ± 4.13 ng/mL ($n = 5$), respectively (normal, < 0.04 ng/mL). Mean initial and peak troponin T (TnT) levels measured 0.33 ± 0.13 ng/mL ($n = 2$ patients) and 0.65 ± 0.02 ng/mL ($n = 2$), respectively (normal, < 0.14 ng/mL). The B-type natriuretic peptide (BNP) value was normal in the four patients who underwent BNP testing (mean BNP value in these four patients, 206.5 ± 206.7 pg/mL). The C-reactive protein level was elevated in four patients (mean value in these four patients, 5.1 ± 6.6 mg/dL) and was normal in one patient.

A myocarditis viral panel excluded an acute viral infection in four patients. One patient had prior Epstein-Barr virus infection, as shown by positive IgG titers. Toxicology screening in three patients was negative aside from marijuana positivity in one patient, which was deemed unlikely to be the cause of that patient's presentation. Other potential major causes of myocarditis, aside from the recent vaccination, were deemed clinically unlikely in all patients on the basis of the absence of a significant medical history, a lack of contributory findings on physical examination, negative PCR result for SARS-CoV-2, and negative myocarditis viral panel. No patient underwent endomyocardial biopsy.

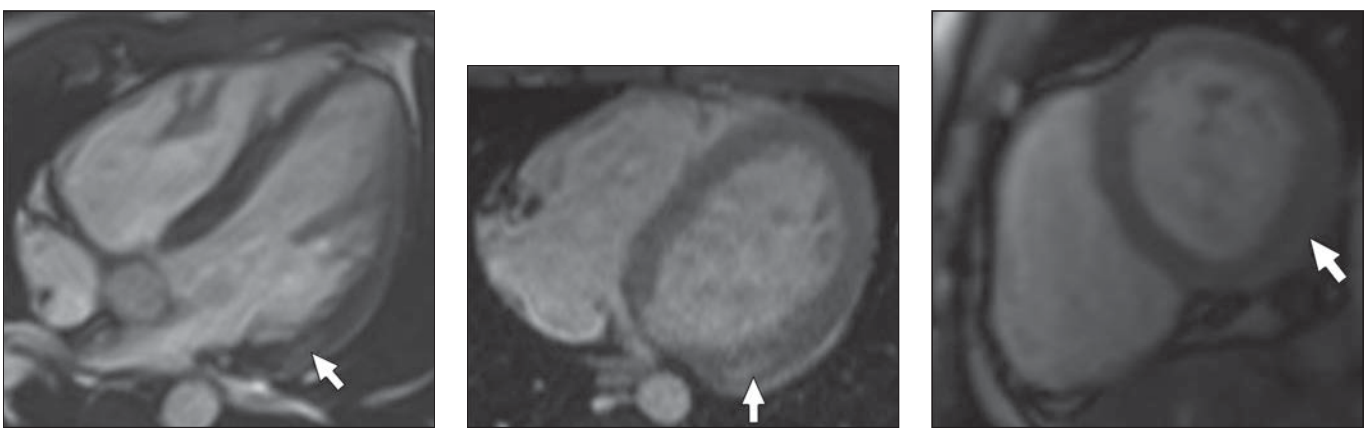
Echocardiography

All five patients underwent echocardiography because of clinically suspected myocarditis. Echocardiography was performed a mean of 5.0 ± 0.9 days after the second vaccine dose (range, 4–6 days). On echocardiography, the left ventricular ejection fraction (LVEF) was mildly to moderately decreased and associated with global hypokinesis in one patient and was normal in the remaining four patients. Biventricular size and right ventricular ejection fraction (RVEF) were normal in all patients. No patient exhibited segmental wall motion abnormalities. Ectasia of the right coronary artery and left anterior descending artery was identified in one patient.

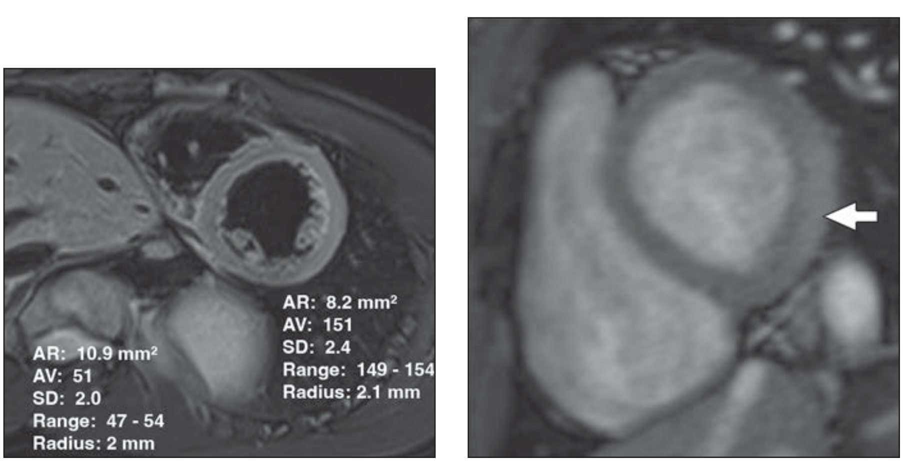
Cardiac MRI

Cardiac MRI was performed a mean of 5.8 ± 1.2 days after the second vaccine dose (range, 5–8 days), within 0.5 ± 1.5 days of the TnI peak (range, from 2 days before to 2 days after the TnI peak), and 1.3 ± 0.5 days after the TnT peak (range, 1–2 days after the TnT peak). Functional assessment on cardiac MRI was concordant with echocardiography in all patients. Specifically, cardiac MRI showed a mildly decreased LVEF of 46% and global hypokinesis in one patient and a normal functional assessment in four patients. Cardiac MRI showed no segmental wall motion abnormalities in any patient.

Cardiac MRI showed both EGE and LGE in all five patients. The LGE images showed purely subepicardial enhancement in four patients and mid-to-subepicardial enhancement in one patient (Fig. 1). All patients showed involvement of the inferior, inferolateral, or anterolateral walls. All patients showed basilar and mid-



A B C



D E

Fig. 2—Qualitative and quantitative T2-based criteria for myocarditis on cardiac MRI in patients who recently received COVID-19 messenger RNA vaccination.
A and **B,** Qualitative criterion was focal myocardial edema (*arrow*) and is shown on four-chamber precontrast SSFP images in 16-year-old boy (**A**) and 17-year-old boy (**B**).
C, Quantitative criteria included T2 parametric mapping and quantification of myocardial signal intensity ratios. Focal subepicardial edema of basilar left ventricular inferior wall (*arrow*) is shown on source image from T2 mapping in 17-year-old boy.
D, Increased myocardial signal intensity ratio of 3.0 at mid cavity is shown in 19-year-old man. AR = surface area, AV = average.
E, Qualitative focal myocardial edema (*arrow*) is also shown on short-axis precontrast SSFP image in 17-year-old boy. Patients in **A–E** correspond with patients A–E in Table 1, respectively.

cavity involvement; two patients showed apical involvement. T1 and T2 parametric imaging was performed in three patients. Two of these patients showed elevated segmental T1 relaxation times; one of these two patients showed segmental T2 relaxation times that were near the upper limit of normal, and one exhibited elevated segmental T2 relaxation times. Segmental T1 and T2 relaxation times were normal in the remaining patient. In four patients, qualitative assessment of T2-weighted sequences showed focal myocardial hyperintensity suggestive of edema that corresponded with areas of EGE and LGE on postcontrast imaging (Fig. 2). The myocardial T2 signal intensity ratio was increased (> 1.8) in all five patients. Three patients exhibited a trace pericardial effusion, and two patients exhibited a small pericardial effusion. No patient showed pericardial enhancement or lung parenchymal or pleural abnormalities on cardiac MRI. Based on the LLC, the cardiac MRI examinations were consistent with a diagnosis of myocarditis in all five patients.

Hospital Course, Condition at Hospital Discharge, and Clinical Events After Discharge

Of the five patients, one experienced nonsustained ventricular tachycardia on day 2 of hospitalization. No other patient experienced a major clinical event during or after hospital admission. All five patients showed persistent decreases in troponin levels and improvement or resolution of chest pain, and all were discharged from the hospital in stable condition. The mean hospitalization length of stay was 4.8 days (range, 3–9 days). One patient was discharged without any medications prescribed. The patient with left ventricular systolic dysfunction on imaging was prescribed at hospital discharge colchicine and metoprolol. One patient was prescribed at discharge an NSAID for pain control. An additional patient was prescribed at discharge 81 mg of aspirin daily. The remaining patient was prescribed at discharge 25 mg of metoprolol extended release daily.

The mean length of clinical follow-up after hospital discharge based on availability of records at the time of last EMR review was 95 days (range, 92–104 days). During the follow-up period, two patients underwent repeat cardiac MRI. In both patients, the repeat cardiac MRI showed stable biventricular size and function; persistent, but decreased, LGE that was similar in distribution to the initial MRI; and an absence of new areas of abnormality. In the patient with right coronary artery ectasia on echocardiography, this finding was shown to have resolved on follow-up echocardiography.

Three patients reported mild intermittent self-resolving chest pain after hospital discharge. In the first of the three patients, the recurrent symptoms occurred after discontinuation of the NSAID that had been prescribed at discharge. In the second patient, the recurrent symptoms resulted in an emergency department visit. In the third patient, symptoms consisted of mild, self-resolved intermittent chest pain. The two remaining patients had no recurrent symptoms after discharge. One of these two asymptomatic patients had persistent LGE on follow-up cardiac MRI.

Discussion

A possible causal association between COVID-19 mRNA vaccination and myocarditis has been reported [6, 9]. In this series of five patients, we describe the cardiac MRI findings of myocarditis in the setting of recent COVID-19 mRNA vaccination. The observed findings are typical of other forms of myocarditis, such as viral or idiopathic myocarditis. All patients showed EGE and LGE on cardiac MRI. The LGE was predominantly subepicardial and involved the inferior, inferolateral, or anterolateral walls in all patients. Focal myocardial edema in the areas of enhancement was observed in four patients. All patients also showed basilar involvement. Two of three patients who underwent parametric mapping showed concordant elevated T1 relaxation times and either elevated T2 relaxation times or T2 relaxation times at the top end of the normal range, supporting the diagnosis.

Myocarditis after COVID-19 vaccination is uncommon [9]. However, its prevalence may be underestimated because of the reliance on symptoms for suspecting the diagnosis. A study in young athletes with confirmed SARS-CoV-2 infection showed that a substantial proportion of individuals had subclinical myocarditis on screening cardiac MRI [13]. Subclinical myocarditis may also be possible after COVID-19 vaccination. Indeed, one patient in the present sample had persistent LGE on follow-up MRI when asymptomatic. To better understand a possible association between COVID-19 vaccination and myocarditis, the CDC has encouraged further investigation of myocarditis after COVID-19 mRNA vaccination [14].

In prior reports, patients with possible myocarditis after COVID-19 mRNA vaccination have been predominantly male and 16–24 years old, have most commonly presented within 1 week of the second vaccine dose, and have had mild disease course [9, 10]. However, the findings on cardiac MRI have not been well reported. To our knowledge, this report is the first to further describe the results of short-term follow-up in these patients, including findings on repeat cardiac MRI.

Consistent with prior reports, the patients in our series were young male patients who presented within days after receiving the second dose of COVID-19 mRNA vaccine. Patients had a favorable hospital course and were discharged in stable condition. On short-term follow-up after hospital discharge, three patients reported mild intermittent self-resolving chest pain, prompting an emergency department visit in one patient. In two patients, persistent albeit decreased subepicardial LGE was found on repeat cardiac MRI, appearing in a distribution similar to that seen on the initial MRI examination.

The pathophysiology of myocarditis in the setting of COVID-19 is believed to in part relate to the cardiotropism of the SARS-CoV-2 spike protein [15]. This protein is theorized to use the angiotensin-converting enzyme 2 receptors of cardiomyocytes for cell entry. Both the Moderna and Pfizer-BioNTech vaccines use mRNA sequences that encode the spike protein [4, 15]. If causality is established between the vaccines and myocarditis, the spike protein could potentially serve as a therapeutic target. However, myocarditis has also been described after other antiviral vaccines [16]. Coronary ectasia, as noted on echocardiography in one patient in this series, resembles descriptions of multisystem inflammatory syndrome in children (MIS-C) that has been reported in pediatric patients with COVID-19 [17]. This finding of ectasia resolved on follow-up echocardiography, and the finding's clinical significance is unclear. Nonetheless, the observation raises the possibility that myocarditis after vaccination relates to transient coronary changes. The male sex of all five patients also suggests a possible functional response to the vaccine that relates to a sex-linked gene.

This study has limitations. The presented data are descriptive and based on the retrospective assessment of only five patients. Additionally, the reported findings may be observed in myocarditis due to other causes. Comparison was not performed with a control group of patients with myocarditis in other settings to determine the findings' specificity for myocarditis after COVID-19 vaccination. Further, all patients underwent cardiac MRI due to clinical suspicion for myocarditis. Thus, the sample represents a high-risk group, which may have introduced a selection bias that contributed to the high frequency of abnormalities on cardiac MRI. Milder imaging findings may have been observed in patients with subclinical presentations. Finally, although other causes of myocarditis were excluded in all patients, it was not possible to provide definitely that the myocarditis in the five patients was caused by the COVID-19 vaccination.

In conclusion, we present cardiac MRI findings in five patients with myocarditis in the setting of recent COVID-19 mRNA vaccination. All patients were male adolescents without known prior SARS-CoV-2 infection who presented within 4 days after the second vaccine dose, and all patients had a favorable initial clinical course. All patients showed cardiac MRI findings typical of findings of myocarditis of other causes, including LGE in all five patients and corresponding myocardial edema in four patients. Short-term follow-up cardiac MRI in two patients showed persistent, albeit decreased, LGE. Additional investigation is warranted to establish causality. Nonetheless, radiologists should be aware of the possible association and recognize the role of cardiac MRI in the assessment of patients with suspected myocarditis after COVID-19 vaccination.

References

1. Johns Hopkins University of Medicine website. COVID-19 dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). coronavirus.jhu.edu/map.html. Published 2021. Accessed September 2, 2021
2. Lancet Commission on COVID-19 Vaccines and Therapeutics Task Force Members. Operation Warp Speed: implications for global vaccine security. *Lancet Glob Health* 2021; 9:e1017–e1021
3. Sharma O, Sultan AA, Ding H, Triggle CR. A review of the progress and challenges of developing a vaccine for COVID-19. *Front Immunol* 2020; 11:585354
4. Ball P. The lightning-fast quest for COVID vaccines—and what it means for other diseases. *Nature* 2021; 589:16–18
5. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines: a new era in vaccinology. *Nat Rev Drug Discov* 2018; 17:261–279
6. Marshall M, Ferguson ID, Lewis P, et al. Symptomatic acute myocarditis in seven adolescents following Pfizer-BioNTech COVID-19 vaccination. *Pediatrics* 2021; 148:e2021052478
7. Garcia JB, Ortega PP, Fernández JAB, León AC, Burgos LR, Dorta EC. Acute myocarditis after administration of the BNT162b2 vaccine against COVID-19. [in Spanish] *Rev Esp Cardiol* 2021; 74:812–814
8. Albert E, Aurigemma G, Saucedo J, Gerson DS. Myocarditis following COVID-19 vaccination. *Radiol Case Rep* 2021; 16:2142–2145
9. Ministry of Health website. Surveillance of myocarditis (inflammation of the heart muscle) cases between December 2020 and May 2021 (including). www.gov.il/en/departments/news/01062021-03. Published February 6, 2021. Accessed July 6, 2021
10. CDC website. Myocarditis and pericarditis following mRNA COVID-19 vaccination. www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html. Published November 12, 2021. Accessed September 10, 2021
11. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. *J Am Coll Cardiol* 2018; 72:3158–3176
12. Bogaert J, Francone M. Cardiovascular magnetic resonance in pericardial diseases. *J Cardiovasc Magn Reson* 2009; 11:14
13. Daniels CJ, Rajpal S, Greenshields JT, et al.; Big Ten COVID-19 Cardiac Registry Investigators. Prevalence of clinical and subclinical myocarditis in competitive athletes with recent SARS-CoV-2 infection: results from the Big Ten COVID-19 Cardiac Registry. *JAMA Cardiol* 2021; 6:1078–1087
14. CDC website. Investigating long-term effects of myocarditis: how CDC is investigating myocarditis health effects after COVID-19 vaccination. www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myo-outcomes.html. Published August 20, 2021. Accessed August 30, 2021
15. Siripanthong B, Nazarian S, Muser D, et al. Recognizing COVID-19-related myocarditis: the possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm* 2020; 17:1463–1471
16. Engler RJ, Nelson MR, Collins LC Jr, et al. A prospective study of the incidence of myocarditis/pericarditis and new onset cardiac symptoms following smallpox and influenza vaccination. *PLoS One* 2015; 10:e0118283
17. Matsubara D, Kauffman HL, Wang Y, et al. Echocardiographic findings in pediatric multisystem inflammatory syndrome associated with COVID-19 in the United States. *J Am Coll Cardiol* 2020; 76:1947–1961

(Editorial Comment starts on next page)

Editorial Comment: Cardiac MRI as a Fundamental Tool in the Evaluation of Suspected Myocarditis After COVID-19 mRNA Vaccination in Young Patients

In this study, the authors investigate the relationship between COVID-19 messenger RNA (mRNA) vaccination and myocarditis in young patients and describe the condition's key clinical and diagnostic elements. This work could have a major impact on clinical practice by providing additional insights into this emerging clinical condition, which might be misdiagnosed given its lack of clear symptoms. When assessing patients with suspected myocarditis after COVID-19 mRNA vaccination, referring clinicians and radiologists should consider the specific imaging features described in this study.

In particular, the article presents cardiac MRI as a leading tool for detecting features that help establish the diagnosis and guide appropriate clinical management. In the study, patients typically presented within 4 days after the second dose of the vaccine. As commonly observed in other forms of myocarditis, cardiac MRI techniques, including T1 and T2 parametric mapping and sequences for evaluation of myocardial edema and late gadolinium enhancement, served as useful methods for disease detection.

As all of the reported cases occurred in male patients, the authors advance the hypothesis of an association between vaccine response and sex-linked genes. Moreover, given that the Pfizer-BioNTech and Moderna vaccines (BNT162b2 and mRNA-1273, respectively) use mRNA sequences that encode for the viral spike protein, the authors suggest that myocardial tropism in vaccine-related myocarditis might result from the action of this protein. This relation may help guide the development of new therapeutic targets.

This series reports a small number of patients. Larger series, potentially obtained by combining data across institutions, could help identify differences between vaccine-related myocarditis and viral myocarditis. An additional helpful follow-up study would be to systematically evaluate patients for whom there was not a high suspicion for myocarditis to reduce this study's selection bias.

Gloria Caredda, MD
Azienda Ospedaliero Universitaria
Cagliari, Italy
careddagloria@gmail.com

The author declares that there are no disclosures relevant to the subject matter of this article.

doi.org/10.2214/AJR.21.27026