Radiology: Cardiothoracic Imaging

RESEARCH LETTER

Cardiac MRI Findings in Male Patients with Acute Myocarditis in the Presence or Absence of COVID-19 Vaccination

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Recently, cases of acute myocarditis developing shortly after receiving mRNA COVID-19 vaccines have been reported in young adults (1,2). In patients with acute viral myocarditis, certain cardiac MRI phenotypic characteristics can help prognosticate long-term complications (3). It is presently unclear if the patterns of disease in vaccine-related disease tend to be like those of other forms of myocarditis and if they can be used similarly to anticipate outcomes.

In this study, we aimed to compare the phenotypic clinical characteristics and cardiac MRI findings in patients with mRNA COVID-19 vaccine–associated myocarditis to those in patients with acute myocarditis from other causes.

Materials and Methods

This retrospective study was approved by the institutional review board of Lifespan Cardiovascular Institute of Brown University, with waiver of informed consent. We included patients presenting to the hospital with acute myocarditis within 4 days of their first or second mRNA COVID-19 vaccination (from January 2021 through September 2021). We excluded patients if they had prior COVID-19 infection or did not undergo cardiac MRI examination. The controls selected from a group, after applying exclusion criteria, consisted of male patients aged 16–37 years who were diagnosed with acute myocarditis from January 2016 to December 2019 from the same institution. Both groups underwent cardiac MRI examination within 1 week of their presentation. Acute myocarditis was diagnosed on the basis of clinical presentation (typical chest pain symptoms, electrocardiography findings, and elevated cardiac biomarkers) and presence of Lake Louise criteria on T1- and/or T2-weighted cardiac MRI studies when available (4). A follow-up evaluation of cardiac symptoms was obtained from the outpatient cardiologists' office notes after patients were discharged from the hospital. Comparisons were made using Fisher exact test for categorical variables and Wilcoxon rank sum nonparametric test when appropriate for continuous variables. A P value less than .05 was considered statistically significant.

Results

Twenty-eight male patients (median age, 21 years [IQR, 18–25 years]) were included. The Table shows clinical and cardiac MRI characteristics between the two groups. Patients in the case group had higher left ventricular (LV) ejection fraction (EF) compared with the control group (59% vs 54%, $P = .02$), as well as higher LV global circumferential strain (GCS) (−14.8% vs −12.7%, $P = .045$) and higher LV global radial strain (GRS) (22.8% vs 18.8%, $P = .048$). Septal late gadolinium enhancement (LGE) and midmyocardial LGE involvement were more common in the control group than in the case group (as shown in Figure). The control group also had more LGE by volume and mass (median LGE volume percentage, 9.4% vs 5.7%; $P = .11$ and median LGE mass, 12.9 g vs 6.6 g; $P = .08$).

Discussion

According to prior literature, cardiac MRI can help predict long-term prognosis in patients with acute myocarditis (3). The Italian Multicenter Study on Acute Myocarditis (ie, ITAMY) showed that a midwall interventricular septum pattern of LGE—compared with a lateral wall pattern of LGE—was associated with more cardiac events (5). In our study, given that most patients with acute myocarditis associated with COVID-19 vaccination had a higher predilection for LGE present in inferolateral segments and higher LVEF, GCS, and GRS than controls, a favorable prognosis may be expected. Our study had limitations. Our sample size was relatively small, with no female patients; hence, generalization to a larger population was not possible. Also, although the control group is similar in age and sex, other confounders, including some pertinent disease severity (eg, peak troponin level value, length of stay, etc) were unaccounted for.

In conclusion, patients with COVID-19 vaccination–associated acute myocarditis had higher LVEF, GCS, and GRS, and less involvement of septal and midmyocardial LGE compared with patients with acute myocarditis from other causes. Future studies are needed to replicate these findings in long-term follow-up.

Author contributions: Guarantors of integrity of entire study, **Y.R.P., A.P.**; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are

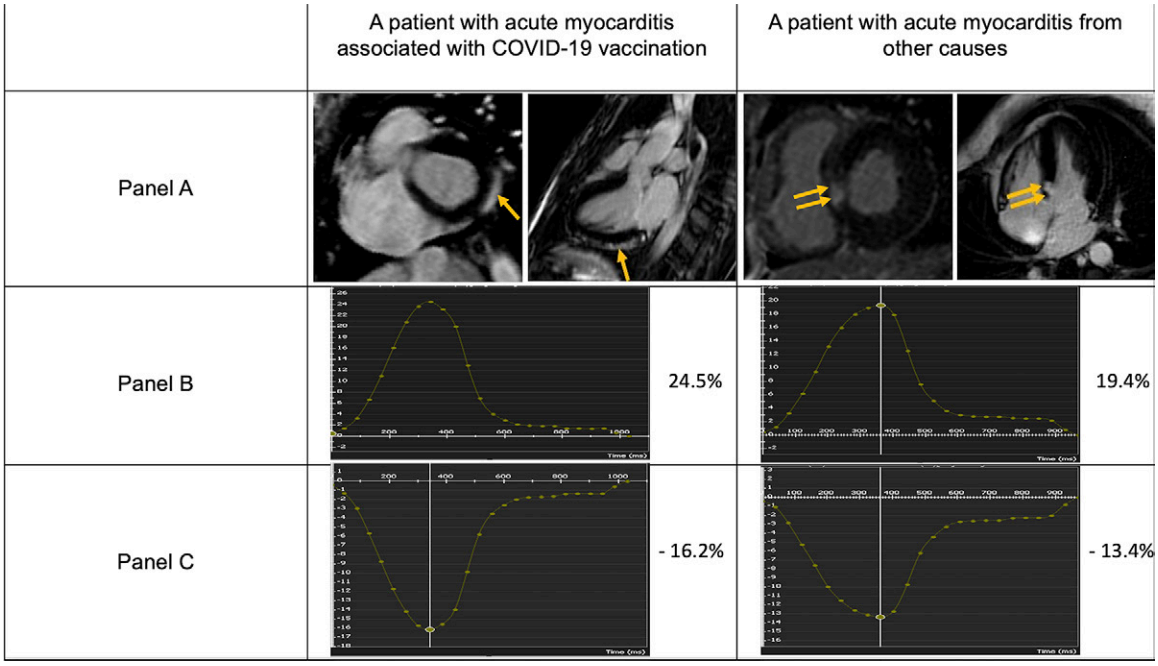

Figure: Representative cardiac MRI findings in acute myocarditis associated with COVID-19 vaccination (case, left) versus acute myocarditis from other causes (control, right). **(Panel A)** Short- and long-axis images show representative late gadolinium enhancement (LGE) (single arrow) in a 16-year-old boy with acute myocarditis associated with COVID-19 vaccination, diagnosed within 2 days of receiving his second dose of the Pfizer vaccine, and representative midmyocardial LGE (double arrow) in a 16-year-old boy with acute myocarditis from other causes. **(Panels B, C)** Global radial and circumferential strain was more impaired in the patient with acute myocarditis from other causes than in the patient with acute myocarditis associated with COVID-19 vaccination. Left ventricular ejection fraction, LGE volume percentage, and LGE mass were 61% versus 48%, 13.2% versus 19.7%, and 13.5 g versus 25.9 g, for the case and control patient, respectively.

Abbreviations

GCS = global circumferential strain, GRS = global radial strain, LGE = late gadolinium enhancement, LVEF = left ventricular ejection fraction

Summary

By comparing phenotypic clinical characteristics and cardiovascular MRI findings in 14 patients with mRNA COVID-19 vaccine–associated myocarditis to those in 14 patients with acute myocarditis from other causes, we found that patients with COVID-19 vaccination–associated acute myocarditis have higher left ventricular ejection fraction, higher left ventricular global circumferential and radial strain, and less involvement of late gadolinium enhancement in the septal segments with less involvement of midmyocardial pattern of late gadolinium enhancement, compared with patients with acute myocarditis from other causes.

Keywords

MRI, Cardiac, Left Ventricle, Inflammation, Epidemiology

appropriately resolved, all authors; literature research, **Y.R.P., K.L., S.A.**; clinical studies, **Y.R.P., S.A., R.P., M.K.A.**; statistical analysis, **Y.R.P., P.H.;** and manuscript editing, **Y.R.P., N.R.S., S.A., P.H., R.P., A.P., M.K.A.**

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Characteristics of Young Adult Men with COVID-19 Vaccine–associated Acute Myocarditis and Acute Myocarditis from Other Causes

Characteristic	Total Cohort (*n* = 28)	Acute Myocarditis from Other Causes (*n* = 14)	COVID-19 Vaccine–associated Myocarditis* (*n* = 14)	*P* Value
Clinical characteristic				
Age at diagnosis (y)				.19†
Mean	22 (6)	24 (6)	21 (6)	
Median	21 (18–25)	22 (19–26)	19 (16–24)	
Peak serum cardiac troponin I level (ng/mL)				.27†
Mean	22.3 (17)	25.6 (16.3)	18.9 (17.6)	
Median	18 (6.4–38)	23.5 (9.8–42)	14 (4.5–26)	
Brain natriuretic peptide level (pg/mL)	(*n* = 13)	(*n* = 5)	(*n* = 8)	.88†
Mean	53.6 (46.6)	50.5 (56.5)	55.5 (43.4)	
Median	57 (7–82)	29 (5–82)	60.5 (17–77)	
C-reactive protein level (mg/L)	(*n* = 23)	(*n* = 12)	(*n* = 11)	.69†
Mean	60.9 (56.1)	70.3 (67.2)	50.6 (41.6)	
Median	45 (17–102)	45 (20–108.5)	45 (11.4–96)	
Length of stay (d)				.33†
Mean	2.5 (1.3)	2.7 (1.4)	2.2 (1.1)	
Median	2 (2–3)	2 (2–4)	2 (1–3)	
ICU admission	8 (28.6)	5 (35.7)	3 (21.4)	.68‡
Cardiac events at 6 mo.	None	None	None	…
Cardiac MRI characteristic				
LVEDVi (mL/m^2)				.18†
Mean	89 (12.3)	92.6 (10.3)	85.4 (13.5)	
Median	90.5 (79–100)	94.5 (86–100)	86 (73–98)	
RVEDVi (mL/m^2)				.69†
Mean	77.9 (14.4)	77.6 (16.4)	78.1 (12.8)	
Median	79 (68.5–86.5)	81 (66–89)	77.5 (69–82)	
LVEF (%)				.02†
Mean	56.8 (5.9)	54.2 (6.9)	59.4 (3.2)	
Median	57 (55–61.5)	55 (48–58)	60 (57–62)	
RVEF (%)				.09†
Mean	58.3 (6.8)	56.1 (6.9)	60.4 (6.3)	
Median	59 (53–63)	54.5 (51–62)	60.5 (58–64)	
LV CO (L/min)				.04†
Mean	7.1 (1.3)	7.6 (1.4)	6.6 (1.1)	
Median	7.1 (6.2–8.4)	7.5 (7–8.6)	6.5 (5.9–7.3)	
LV CI (L/min/m^2)				.19†
Mean	3.7 (0.58)	3.9 (0.60)	3.6 (0.55)	
Median	3.6 (3.4–4.2)	3.7 (3.5–4.3)	3.5 (3.3–4.0)	
LV GLS (%)				.42†
Mean	−14.5 (2.1)	−14.1 (2.3)	−14.8 (1.8)	
Median	−14.9 (−16.2 to 12.7)	−14.5 (−16 to 12.4)	−15.5 (−16.5 to 12.7)	
LV GCS (%)				.03†
Mean	−13.8 (2.7)	−12.7 (3.1)	−14.8 (1.9)	
Median	−13.9 (−15.9 to 12.1)	−12.8 (−14 to 10.7)	−15.2 (−16.2 to 13.2)	

Table *(continues)*

(*continued*) Characteristics of Young Adult Men with COVID-19 Vaccine–associated Acute Myocarditis and Acute Myocarditis from Other Causes

Characteristic	Total Cohort (*n* = 28)	Acute Myocarditis from Other Causes (*n* = 14)	COVID-19 Vaccine–associated Myocarditis* (*n* = 14)	*P* Value
LV GRS (%)				.03†
Mean	20.8 (5.4)	18.8 (5.9)	22.8 (3.9)	
Median	20.7 (17.3–25.1)	18.6 (14.5–20.8)	23.2 (19.6–25.3)	
RV GLS (%)	(*n* = 27)	(*n* = 13)	(*n* = 14)	.11†
Mean	−20.0 (5.3)	−21.5 (6.7)	−18.7 (3.2)	
Median	−20.1 (−23 to 15.8)	−22.6 (−23.8 to 17)	−18.8 (−21.3 to 15.7)	
T2 W: Presence of myocardial edema on black-blood STIR image	(*n* = 20) 16 (80.0)	(*n* = 7) 4 (57.1)	(*n* = 13) 12 (92.3)	.10‡
T1 W: LGE location				
LGE in lateral segments	28 (100)	14 (100)	14 (100)	…
LGE in septal segments	4 (14.3)	3 (21.4)	1 (7.1)	.59‡
T1 W: LGE pattern				
Midmyocardial	5 (17.9)	5 (35.7)	0 (0)	.04‡
Subepicardial	28 (100)	14 (100)	14 (100)	…
Pericardial effusion (>trivial)	3 (10.7)	2 (14.3)	1 (7.1)	>.99‡
Extent of LGE (g/total myocardial mass)				.11†
Mean	9.3 (5.8)	11.0 (6.0)	7.5 (5.1)	
Median	8.4 (4.4–14.4)	9.4 (5.3–15.7)	5.7 (3.1–12.3)	
LGE (g)				.08†
Mean	12.4 (8.9)	14.6 (7.9)	10.2 (9.7)	
Median	9.7 (4.8–18.6)	12.9 (7.5–22.4)	6.6 (3.1–13.5)	
ECV (%)	(*n* = 15)	(*n* = 5)	(*n* = 10)	.32†
Mean	28.7 (4.1)	30.2 (3.8)	28.0 (4.3)	
Median	28 (26–31)	30 (28–31)	26.5 (26–31)	

Note.—Unless otherwise noted, continuous data are presented as means with SDs in parentheses or medians with IQRs in parentheses, and categorical data are presented as numbers with percentages in parentheses. Cardiac events include recurrence of symptoms, hospital readmissions, heart failure symptoms, and any arrhythmias. Cardiac MRI was performed with a 1.5-T scanner (Siemens Healthineers) using previously described acquisition parameters. Myocardial native T1 maps were obtained using a breath-hold, motion-correction, electrocardiographically triggered, modified Look-Locker inversion recovery sequence with images acquired at end diastole before and approximately 20 minutes after contrast agent injection in the midventricular short-axis plane. T2 mapping was performed using a single-shot T2-prepared steady-state free precision sequence in the midventricular short-axis plane at end diastole during breath hold with motion correction. CI = cardiac index, CO = cardiac output, ECV = extracellular volume, GCS = global circumferential strain, GLS = global longitudinal strain, GRS = global radial strain, ICU = intensive care unit, LA = left atrium, LGE = late gadolinium enhancement, LV = left ventricle, LVEDVi = LV end-diastolic volume index, LVEF = LV ejection fraction, RV = right ventricle, RVEF = RV ejection fraction, RVEDVi = RV end-diastolic volume index, STIR = short inversion time inversion recovery, SV = stroke volume, T1 W = T1 weighted, T2 W = T2 weighted.

* For mRNA COVID-19 vaccination type, 12 patients (86%) received Pfizer and two (14%) received Moderna. Dose interval for each type was 21 and 28 days, respectively. All patients developed acute myocarditis after receiving two doses of either mRNA COVID-19 vaccination type. Following vaccination, mean time prior to symptom onset was 2.9 days ± 0.5 (SD).

† Wilcoxon rank sum.

‡ Fisher exact test.