Radiology: Cardiothoracic Imaging

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

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Summary statement

By comparing phenotypic clinical characteristics and cardiovascular magnetic resonance (CMR) findings in 14 patients with COVID-19 mRNA vaccine-associated myocarditis to 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 to patients with acute myocarditis from other causes.

Keywords: myocarditis; COVID-19 infection; COVID-19 vaccination; cardiovascular magnetic resonance

Abbreviations

LV = left ventricular, LGE = late gadolinium enhancement, GCS = global circumferential strain, GRS = global radial strain

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 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 COVID-19 mRNA vaccine-associated myocarditis to 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 four 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 males aged 16-37 years who were diagnosed with acute myocarditis from January 2016 to December 2019 from the same institution. Both groups had a cardiac MRI examination performed within one week of their presentation. Acute myocarditis was diagnosed based on clinical presentation (typical chest pain symptoms, electrocardiogram, and elevated cardiac biomarkers) and presence of Lake Louise criteria on T1- and/or T2-weighted cardiac MRIs 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's exact test for categorical variables, and Wilcoxon rank-sum non-parametric test when appropriate for continuous variables. $P < .05$ was considered statistically significant.

Results

Twenty-eight males (median age, 21 years [interquartile range, 18-25]) were included. Table 1 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 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 was more common in the control group than in the case group. 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

Based on prior literature, cardiac MRI can help predict long term prognosis in patients with acute myocarditis (3). The Italian study in Myocarditis registry (ITAMY) showed that a mid-wall 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 LV EF 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 (e.g. peak troponin value, length of stay, etc.) were unaccounted for.

In conclusion, patients with COVID-19 vaccination-associated acute myocarditis had higher LV EF, 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.

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References

1. Patel YR, Louis DW, Atalay M, Agarwal S, Shah NR. Cardiovascular magnetic resonance findings in young adult patients with acute myocarditis following mRNA COVID-19 vaccination: a case series. J Cardiovasc Magn Reson 2021;23(1):101. doi: 10.1186/s12968-021-00795-4

2. Truong DT, Dionne A, Muniz JC, McHugh KE, Portman MA, Lambert LM, Thacker D, Elias MD, Li JS, Toro-Salazar OH, Anderson BR, Atz AM, Bohun CM, Campbell MJ, Chrisant M, D'Addese L, Dummer KB, Forsha D, Frank LH, Frosch OH, Gelehrter SK, Giglia TM, Hebson C, Jain SS, Johnston P, Krishnan A, Lombardi KC, McCrindle BW, Mitchell EC, Miyata K, Mizzi T, Parker RM, Patel JK, Ronai C, Sabati AA, Schauer J, Sexson-Tejtel SK, Shea JR, Shekerdemian LS, Srivastava S, Votava-Smith JK, White S, Newburger JW. Clinically Suspected Myocarditis Temporally Related to COVID-19 Vaccination in Adolescents and Young Adults. Circulation 2021. doi: 10.1161/CIRCULATIONAHA.121.056583

3. Aquaro GD, Perfetti M, Camastra G, Monti L, Dellegrottaglie S, Moro C, Pepe A, Todiere G, Lanzillo C, Scatteia A, Di Roma M, Pontone G, Perazzolo Marra M, Barison A, Di Bella G, Cardiac Magnetic Resonance Working Group of the Italian Society of C. Cardiac MR With Late Gadolinium Enhancement in Acute Myocarditis With Preserved Systolic Function: ITAMY Study. J Am Coll Cardiol 2017;70(16):1977-1987. doi: 10.1016/j.jacc.2017.08.044

4. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, Kindermann I, Gutberlet M, Cooper LT, Liu P, Friedrich MG. Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation: Expert Recommendations. J Am Coll Cardiol 2018;72(24):3158-3176. doi: 10.1016/j.jacc.2018.09.072

5. Aquaro GD, Ghebru Habtemicael Y, Camastra G, Monti L, Dellegrottaglie S, Moro C, Lanzillo C, Scatteia A, Di Roma M, Pontone G, Perazzolo Marra M, Barison A, Di Bella G, Cardiac Magnetic Resonance" Working Group of the Italian Society of C. Prognostic Value of Repeating Cardiac Magnetic Resonance in Patients With Acute Myocarditis. J Am Coll Cardiol 2019;74(20):2439-2448. doi: 10.1016/j.jacc.2019.08.1061

Table 1: Characteristics of Young Adult Men with COVID-19 vaccine-associated Acute Myocarditis and Acute Myocarditis from Other Causes

	Total cohort (N=28)	Acute myocarditis from other causes (n=14)	COVID-19 vaccine-associated myocarditis* (n=14)	*P* value
Clinical Characteristics				
Age at diagnosis (y) Mean (SD) Median (IQR)	 22 (6) 21 (18-25)	 24 (6) 22 (19-26)	 21 (6) 19 (16-24)	.19[1]
Peak serum cardiac troponin I (ng/ml) Mean (SD) Median (IQR)	 22.3 (17) 18 (6.4-38)	 25.6 (16.3) 23.5 (9.8-42)	 18.9 (17.6) 14 (4.5-26)	.27[1]
Brain natriuretic peptide (pg/ml) Mean (SD) Median (IQR)	(n=13) 53.6 (46.6) 57 (7-82)	(n=5) 50.5 (56.5) 29 (5-82)	(n=8) 55.5 (43.4) 60.5 (17-77)	.88[1]
C-reactive protein (mg/l) Mean (SD) Median (IQR)	(n=23) 60.9 (56.1) 45 (17-102)	(n=12) 70.3 (67.2) 45 (20-108.5)	(n=11) 50.6 (41.6) 45 (11.4-96)	.69[1]
Length of stay (days) Mean (SD) Median (IQR)	 2.5 (1.3) 2 (2-3)	 2.7 (1.4) 2 (2-4)	 2.2 (1.1) 2 (1-3)	.33[1]
ICU admission	8 (28.6)	5 (35.7)	3 (21.4)	.68[2]
Cardiac events at six months	none	none	none	…
Cardiac MRI Characteristics				
LVEDVi (ml/m^2) Mean (SD) Median (IQR)	 89 (12.3) 90.5 (79-100)	 92.6 (10.3) 94.5 (86-100)	 85.4 (13.5) 86 (73-98)	.18[1]
RVEDVi (ml/m^2) Mean (SD) Median (IQR)	 77.9 (14.4) 79 (68.5-86.5)	 77.6 (16.4) 81 (66-89)	 78.1 (12.8) 77.5 (69-82)	.69[1]
LVEF (%) Mean (SD) Median (IQR)	 56.8 (5.9) 57 (55-61.5)	 54.2 (6.9) 55 (48-58)	 59.4 (3.2) 60 (57-62)	.02[1]
RVEF (%) Mean (SD) Median (IQR)	 58.3 (6.8) 59 (53-63)	 56.1 (6.9) 54.5 (51-62)	 60.4 (6.3) 60.5 (58-64)	.09[1]
LV CO (l/min) Mean (SD) Median (IQR)	 7.1 (1.3) 7.1 (6.2-8.4)	 7.6 (1.4) 7.5 (7-8.6)	 6.6 (1.1) 6.5 (5.9-7.3)	.04[1]
LV CI (l/min/m^2)				

Mean (SD) Median (IQR)	3.7 (0.58) 3.6 (3.4-4.2)	3.9 (0.60) 3.7 (3.5-4.3)	3.6 (0.55) 3.5 (3.3-4.0)	.19[1]
LV GLS (%) Mean (SD) Median (IQR)	 -14.5 (2.1) -14.9 (-16.2 - -12.7)	 -14.1 (2.3) -14.5 (-16 - -12.4)	 -14.8 (1.8) -15.5 (-16.5 - -12.7)	.42[1]
LV GCS (%) Mean (SD) Median (IQR)	 -13.8 (2.7) -13.9 (-15.9 - -12.1)	 -12.7 (3.1) -12.8 (-14 - -10.7)	 -14.8 (1.9) -15.2 (-16.2 - -13.2)	.03[1]
LV GRS (%) Mean (SD) Median (IQR)	 20.8 (5.4) 20.7 (17.3-25.1)	 18.8 (5.9) 18.6 (14.5-20.8)	 22.8 (3.9) 23.2 (19.6-25.3)	.03[1]
RV GLS (%) Mean (SD) Median (IQR)	(n=27) -20.0 (5.3) -20.1 (-23 - -15.8)	(n=13) -21.5 (6.7) -22.6 (-23.8 - -17)	(n=14) -18.7 (3.2) -18.8 (-21.3 - -15.7)	.11[1]
T2W: Presence of myocardial edema on STIR sequence	(n=20) 16 (80.0)	(n=7) 4 (57.1)	(n=13) 12 (92.3)	.10[2]
T1W: LGE location				
LGE lateral segments	28 (100)	14 (100)	14 (100)	…
LGE septal segments	4 (14.3)	3 (21.4)	1 (7.1)	.59[2]
T1W: LGE pattern				
Midmyocardial	5 (17.9)	5 (35.7)	0 (…)	.04[2]
Subepicardial	28 (100)	14 (100)	14 (100)	…
Pericardial effusion (> trivial)	3 (10.7)	2 (14.3)	1 (7.1)	>.99
% LGE (gm/total myocardial mass) Mean (SD) Median (IQR)	 9.3 (5.8) 8.4 (4.4-14.4)	 11.0 (6.0) 9.4 (5.3-15.7)	 7.5 (5.1) 5.7 (3.1-12.3)	.11[1]
LGE (g) Mean (SD) Median (IQR)	 12.4 (8.9) 9.7 (4.8-18.6)	 14.6 (7.9) 12.9 (7.5-22.4)	 10.2 (9.7) 6.6 (3.1-13.5)	.08[1]
ECV (%) Mean (SD) Median (IQR)	(n=15) 28.7 (4.1) 28 (26-31)	(n=5) 30.2 (3.8) 30 (28-31)	(n=10) 28.0 (4.3) 26.5 (26-31)	.32[1]

Notes.—Unless otherwise noted, continuous data are presented as mean (standard deviation) and median (interquartile range), and categorical data are presented as number (%). CI = cardiac index, CO = cardiac output, ECV = extra cellular volume, GLS = global longitudinal strain, GCS = global circumferential strain, GRS = global radial strain, ICU = intensive care unit, LGE = late gadolinium enhancement, LA = left atrium, LV = left ventricle, LVEDVi = left ventricular end diastolic volume indexed, LVEF = left ventricular ejection fraction, RV = right ventricle, RVEF = right ventricular ejection fraction, RVEDVi = right ventricular end diastolic volume indexed, STIR = short inversion time inversion recovery black-blood technique, SV = stroke volume, T1W = T1-weighted, T2W = T2-weighted

* For mRNA COVID-19 vaccination type, 12 patients (86%) had Pfizer and 2 (14%) had Moderna. Dose interval for each type was 21 and 28 days, respectively. All patients developed acute myocarditis after receiving two doses of each mRNA COVID-19 vaccination type. Following vaccination, mean ± standard deviation days prior to symptom onset was 2.9 ± 0.5.
[1]Wilcoxon rank-sum; [2]Fisher's exact test
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, electrocardiogram triggered, modified Look-Locker inversion recovery sequence with images acquired at end-diastole before and approximately 20 minutes after contrast injection in the mid ventricular short axis plane. T2 mapping was performed using a single-shot T2 prepared steady-state free precision in the mid ventricular short axis plane at end-diastole during breath-hold with motion correction.

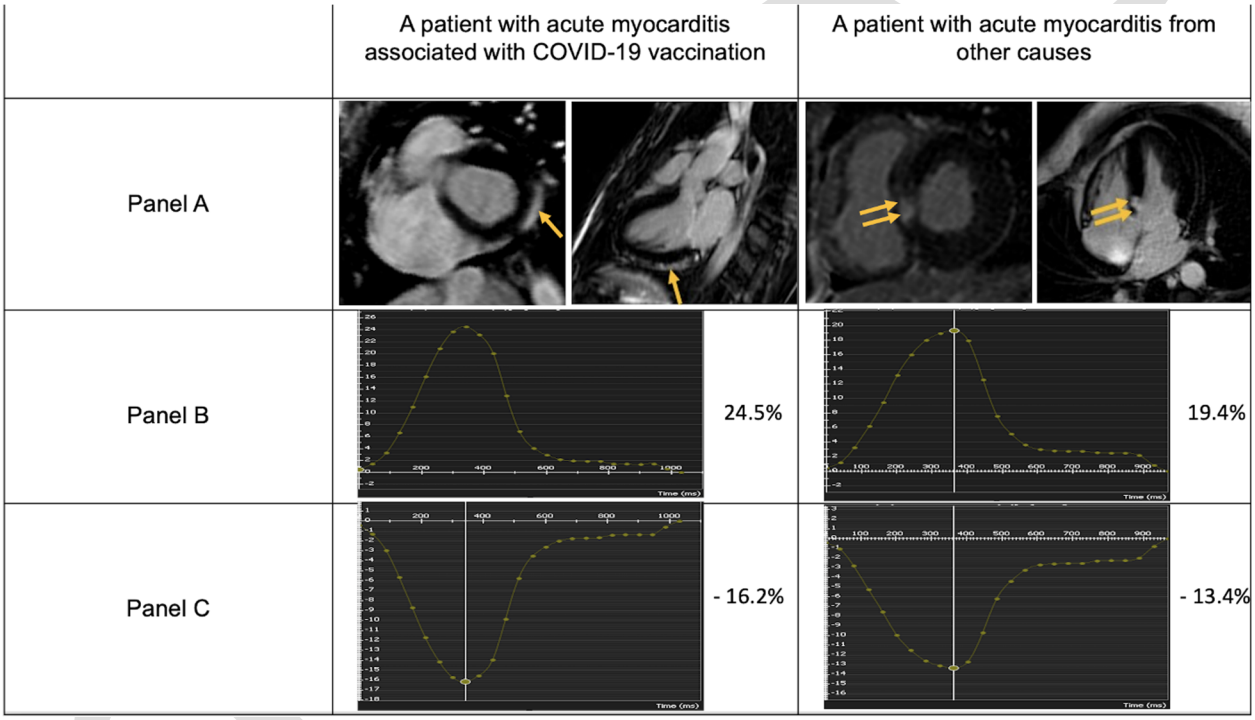

Figure 1. Representative cardiac MRI findings in acute myocarditis associated with COVID-19 vaccination (case, left) versus acute myocarditis from other causes (control, right). (Panel A) Short and long axis images showing representative late gadolinium enhancement (LGE) (single arrow) in a 16-year-old male with acute myocarditis associated with COVID-19 vaccination, diagnosed within two days of receiving his second dose of the Pfizer vaccine, and representative

mid-myocardial LGE (double arrow) in a 16-year-old male with acute myocarditis from other causes. (Panel 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. LVEF, LGE volume percentage, and LGE mass were 61% vs 48%, 13.2% vs 19.7%, and 13.5g vs 25.9g, for the case and control patient, respectively).