Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

JACC: CARDIOVASCULAR IMAGING VOL. 14, NO. 9, 2021

PUBLISHED BY ELSEVIER

IPIX

Possible Association Between COVID-19 Vaccine and Myocarditis

Clinical and CMR Findings

Kirsten E. Shaw, MD,[a] João L. Cavalcante, MD,[b] B. Kelly Han, MD,[b,c,d] Mario Gössl, MD[b]

AS THE CORONAVIRUS DISEASE-2019 (COVID-19) OUTBREAK SPREAD ACROSS THE GLOBE, VACCINE development efforts were expedited. The U.S. Food and Drug Administration granted an emergent use authorization for 2 vaccines: the Pfizer-Bio Tech 2-dose vaccine and the Moderna 2-dose vaccine. Our knowledge regarding adverse reactions to these vaccines continues to grow. We present cardiac magnetic resonance (CMR) imaging findings in 4 cases of acute myocarditis that were temporally related to the receipt of COVID-19 vaccine and could raise the possibility of being associated with the vaccination (**Figures 1, 2, 3, 4, and 5**). CMR imaging used a specific institutional imaging protocol (see the following text) to evaluate for the presence of myocardial edema and nonischemic myocardial injury configuring the main criteria according to the updated Lake Louise criteria (1)**.** To our knowledge, this is the largest case series to date with a comprehensive timeline description (**Figure 1**) and systematic CMR imaging evaluation of this potential adverse reaction to the COVID-19 vaccine. The fact that the 2 patients with prior COVID-19 infection developed symptoms following their first dose, and the 2 patients without prior COVID-19 infection developed symptoms following their second dose, raises interesting possibilities about a potential immune-boosting mechanism after prior immune exposure or priming.

CONCLUSIONS

It is important to note that although our small case series raises the possibility of a potential association based on the close temporal relation between a clinical and CMR picture of myocarditis and vaccination, this does not prove that the COVID-19 vaccination was the cause of myocarditis, nor does it completely exclude spontaneously occurring myocarditis in these individuals. However, documenting such findings is important given that the Centers for Disease Control and Prevention and other regulatory agencies are now actively investigating this possible adverse reaction to the Pfizer-Bio Tech and Moderna COVID-19 mRNA-based vaccines. Larger studies that vigilantly evaluate such patients using advanced imaging techniques might help clarify any possible causative association.

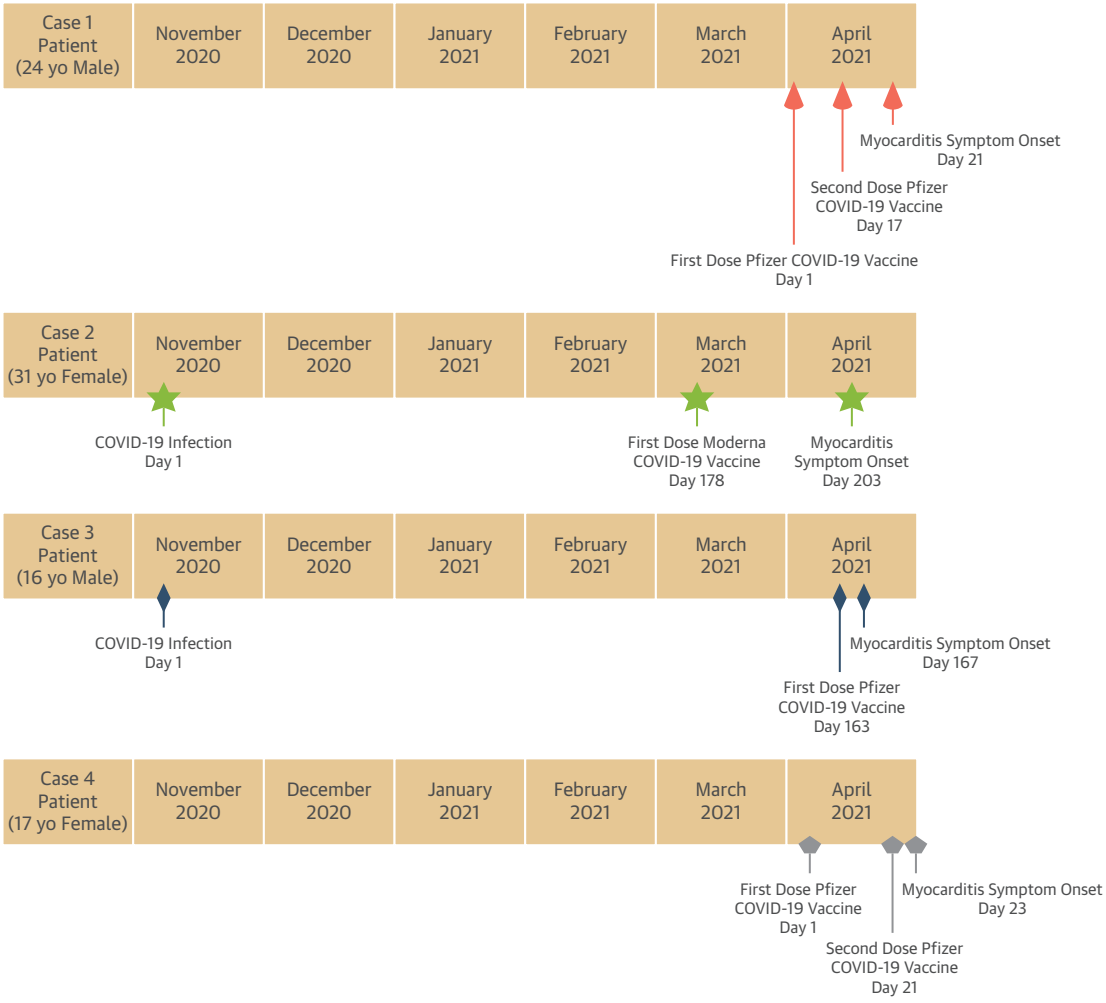
From the [a]Abbott Northwestern Hospital, Department of Graduate Medical Education, Minneapolis, Minnesota, USA; [b]Abbott Northwestern Hospital, Minneapolis Heart Institute, Minneapolis, Minnesota, USA; [c]Minneapolis Heart Institute Foundation, Minneapolis, Minnesota, USA; and the [d]Children's Minnesota Hospital, Minneapolis, Minnesota, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received May 18, 2021; revised manuscript received June 7, 2021, accepted June 7, 2021.

ISSN 1936-878X/$36.00 https://doi.org/10.1016/j.jcmg.2021.06.002

FIGURE 1 Timeline of Clinical Characteristics



Timeline of documented COVID-19 infection (cases 2 and 3), COVID-19 vaccinations, and onset of symptoms of myocarditis (all cases). All CMR studies were performed according to our institutional protocol for suspected myocarditis using a MAGNETOM Aera 1.5 Tesla magnetic resonance imaging scanner (Siemens Healthineers) including motion-corrected, inline T_1 parametric mapping using MOLLI sequence; T_2 mapping (Myomaps, Siemens Healthineers); late gadolinium enhancement imaging using free-breathing motion-corrected phase-sensitive inversion recovery sequence, 10 min-15 min after single-dose (0.1 mmol/kg) of macrocyclic Gadobutrol (Gadavist, Bayer Healthcare LLC); and extracellular volume fraction mapping (WIP 1041B, Siemens Healthineers). Breath-held steady-state free precession cine imaging was used for all long- and short-axes, with standard segmentation with semiautomated contouring. All CMR studies were independently evaluated and regions of interest drawn at the site of myocardial injury and at the remote/healthy/uninvolved myocardium for reference. CMR = cardiac magnetic resonance; COVID-19 = coronavirus disease-2019.

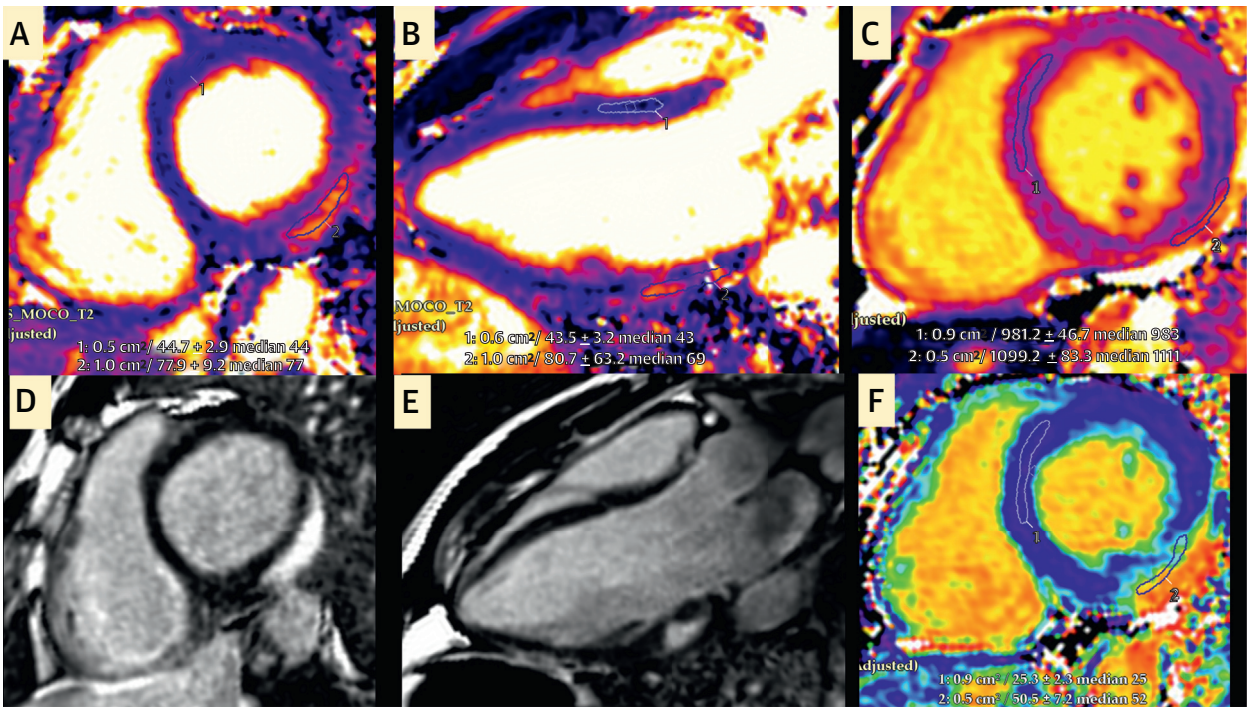
FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Cavalcante has received research support from Circle Cardiovascular Imaging and Siemens Healthineers. Dr Gössl has served as a consultant for Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Mario Gössl, Minneapolis Heart Institute at Abbott Northwestern Hospital, 920 East 28th Street, #300, Minneapolis, Minnesota 55407, USA. E-mail: mario.goessl@allina.com.

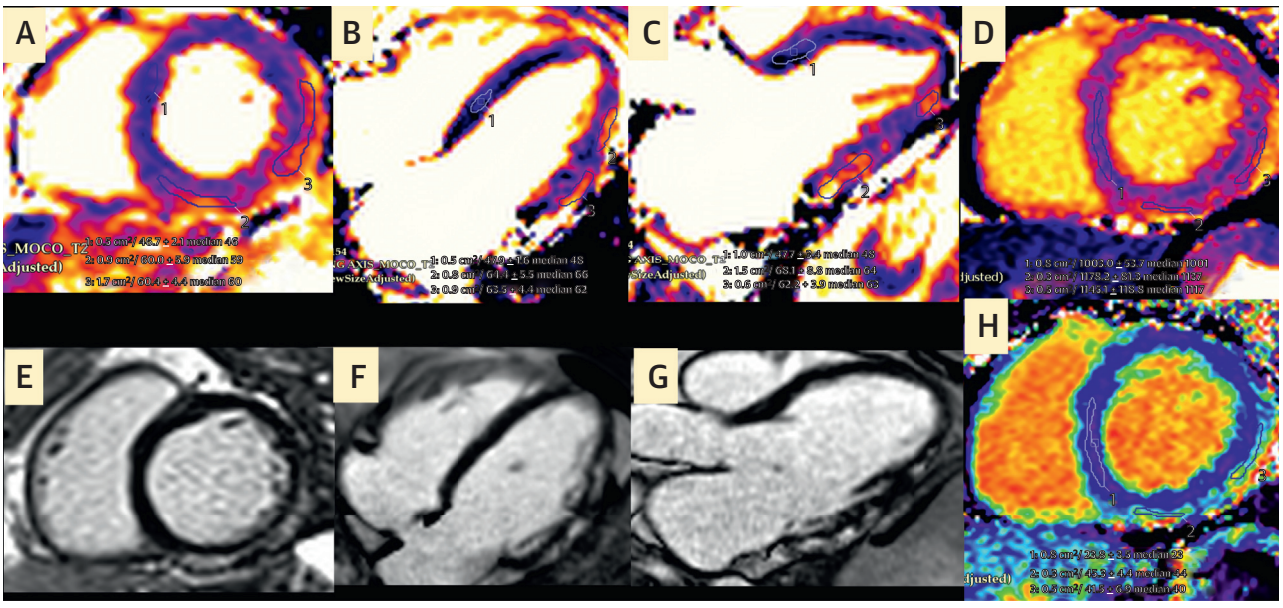
JACC: CARDIOVASCULAR IMAGING, VOL. 14, NO. 9, 2021
SEPTEMBER 2021:1856–1861

FIGURE 2 Cardiac Magnetic Resonance Imaging Demonstrating Acute Myocarditis in a 24-Year-Old Man



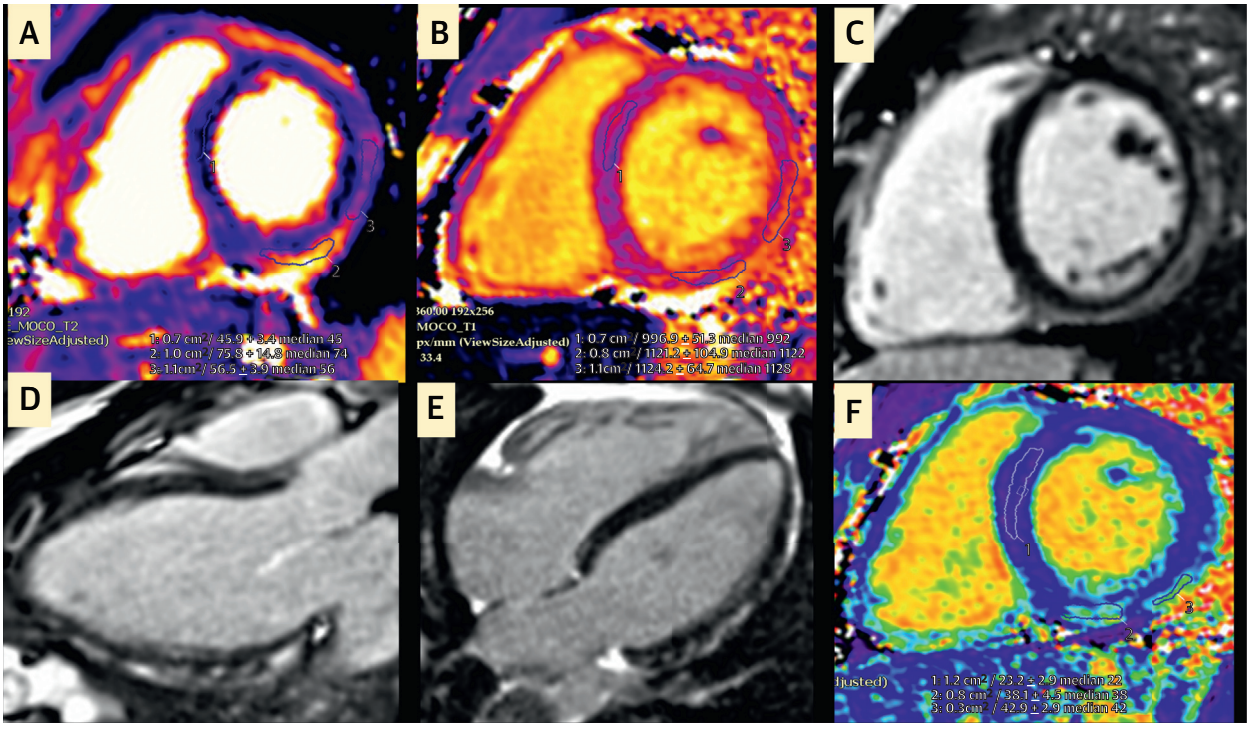
A 24-year-old man with no previous cardiac history developed chest pain 4 days following his second dose of the Pfizer coronavirus disease 2019 (COVID-19) vaccine. He had never had a prior COVID-19 infection. He presented to the emergency department where his COVID-19 antigen testing was negative, and his troponin I was elevated to 4.963 ng/mL (normal <0.034 ng/mL). An ischemic evaluation was negative. CMR demonstrated normal systolic function (left ventricular ejection fraction = 56%) with no regional wall motion abnormalities, pericardial effusion, thickening, or enhancement. On T_2 mapping **(A and B)** there was regional epicardial edema (median 69 ms-77 ms, normal <55 ms) and nonischemic myocardial injury on native T_1 **(C)** (1,111 ms, normal 950 ms-1,050 ms) localized to the basal inferolateral segment. This was confirmed as marked epicardial fibrosis on late gadolinium enhancement imaging **(D and E)**, and regional interstitial expansion **(F)** seen on extracellular volume fraction mapping (52%, normal <28%) in the basal inferolateral segment. All of these findings support acute myocarditis according to the 2018 updated Lake Louise criteria.

FIGURE 3 Cardiac Magnetic Resonance Imaging Demonstrating Acute Myocarditis in a 31-Year-Old Woman



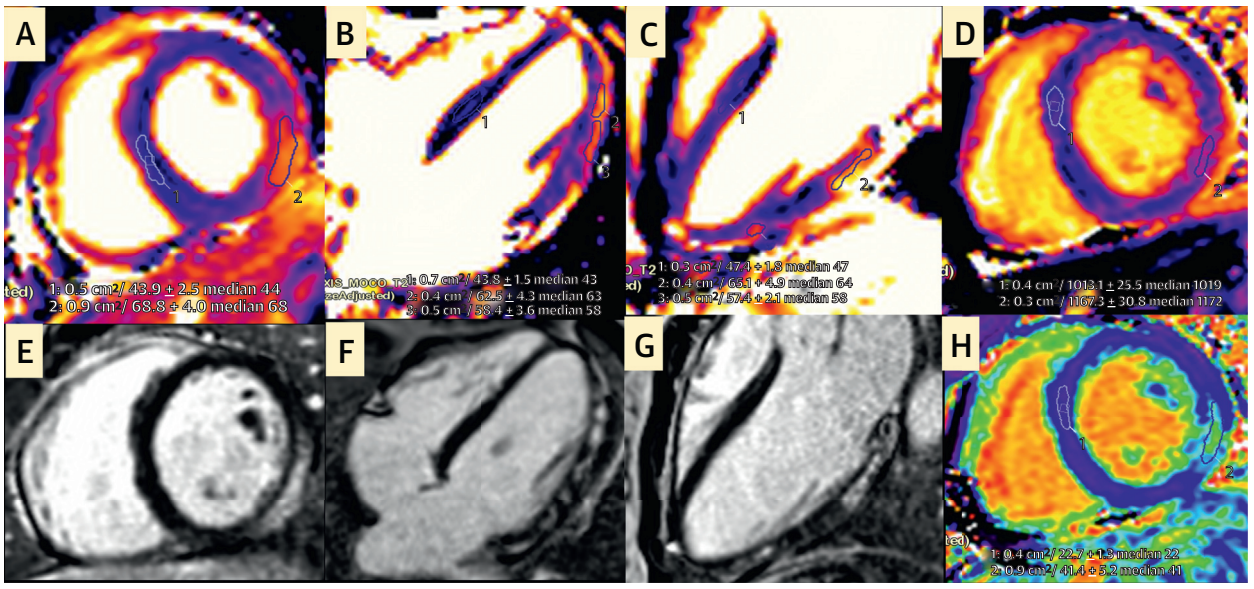
A 31-year-old woman with no previous cardiac history developed chest pressure 25 days after her first dose of the Moderna COVID-19 vaccine. She had a laboratory confirmed COVID-19 infection 7 months before. She presented to the emergency department where her COVID-19 antigen testing was negative, and her troponin I was elevated to 7.961 ng/mL (normal <0.034 ng/mL). An ischemic evaluation was negative. CMR demonstrated normal systolic function (LVEF = 57%) with no regional wall motion abnormalities, pericardial effusion, thickening, or enhancement. On T_2 mapping **(A to C)**, there were skip areas of epicardial edema involving the basal inferior, basal, mid, and apical lateral segments (59 ms-66 ms, normal <55 ms) and nonischemic myocardial injury on native T_1 mapping **(D)** (1,117 ms-1,137 ms, normal 950 ms-1,050 ms). These areas matched those where epicardial fibrosis was observed on late gadolinium enhancement imaging **(E to G)** and interstitial expansion by extracellular volume fraction mapping **(H)** (40%-44%, normal <28%). All of these findings support acute myocarditis according to the 2018 updated Lake Louise criteria. Abbreviations as in Figure 1.

FIGURE 4 Cardiac Magnetic Resonance Imaging Demonstrating Acute Myocarditis in a 16-Year-Old Man



A 16-year-old man with no previous cardiac history developed chest pain 4 d following his first dose of the Pfizer COVID-19 vaccine. He had a laboratory-confirmed COVID-19 infection 5 mo before. He presented to the emergency department where his COVID-19 antigen testing was negative, and his troponin I was elevated to 4.35 ng/mL (normal <0.034 ng/mL). CMR demonstrated normal systolic function (left ventricular ejection fraction = 64%) with no regional wall motion abnormalities, pericardial effusion, thickening, or enhancement. On T_2 mapping **(A)**, there were skip areas of epicardial edema involving the basal and mid inferior, inferolateral, and anterolateral segments (56 ms-74 ms, normal <55 ms) and nonischemic myocardial injury on native T_1 mapping **(B)** (1,122 ms-1,128 ms, normal 950 ms-1,050 ms). These areas matched those where epicardial fibrosis was observed on late gadolinium enhancement imaging **(C to E)** and interstitial expansion by extracellular volume fraction mapping **(F)** (38%-42%, normal <28%). All of these findings support acute myocarditis according to the 2018 updated Lake Louise criteria. Abbreviations as in Figure 1.

FIGURE 5 **Cardiac Magnetic Resonance Imaging Demonstrating Acute Myocarditis In A 17-Year-Old Woman**



A 17-year-old women with no previous cardiac history developed chest pain 2 d following her second dose of the Pfizer COVID-19 vaccine. She did not have a known prior COVID-19 infection. She presented to the emergency department where her COVID-19 antigen testing was negative, and her troponin I was elevated to 5.41 ng/mL (normal <0.034 ng/mL). Her electrocardiogram demonstrated subtle ST-segment elevation of the anterior limb leads. CMR demonstrated mildly decreased systolic function (left ventricular ejection fraction = 54%) with extensive skip areas of epicardial and midwall edema on T_2 mapping involving the inferolateral and anterolateral segments (58 ms-68 ms, normal <55 ms) **(A to C)**. There was corresponding nonischemic myocardial injury on T_1 mapping **(D)** (1,172 ms, normal 950 ms-1,050 ms) as well as on late gadolinium enhancement imaging **(E to G)** in a noncoronary distribution pattern, along interstitial expansion by extracellular volume fraction mapping **(H)** (41%, normal <28%). All of these findings support acute myocarditis according to the 2018 updated Lake Louise criteria.

REFERENCE

1. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. *J Am Coll Cardiol*. 2018;72(24):3158–3176.

KEY WORDS Cardiac MRI, COVID-19, myocarditis, vaccination