

# Editorial for “Cardiac Magnetic Resonance Imaging Findings in COVID-19 Vaccine-Related Myocarditis: A Pooled Analysis of 468 Patients”

Myocarditis is a rare adverse event following administration of messenger RNA (mRNA)-based Coronavirus disease 2019 (COVID-19) vaccines, with highest risk in adolescent and young adult men.<sup>1</sup> Cardiac MRI plays an important role in the assessment of acute myocarditis with unparalleled ability for noninvasive characterization of myocardial tissue. In the setting of suspected myocarditis, the revised Lake Louise Criteria (LLC) are typically used for evaluation of cardiac MRI findings.<sup>2</sup> Several recent case series have described cardiac MRI findings in patients with myocarditis following COVID-19 vaccination.<sup>3,4</sup> However, these are limited by relatively small sample sizes.

In this issue of JMRI, Samimisedeh et al<sup>5</sup> advance our understanding of the pattern of cardiac MRI abnormalities in myocarditis following COVID-19 vaccination by reporting the results of a systematic review and meta-analysis. The authors identified 102 publications including individual case reports and cases series with a total of 468 patients with suspected myocarditis following COVID-19 vaccination. Among these patients, 79% met LLC for non-ischemic myocardial inflammation on cardiac MRI. Myocardial edema based on the presence of a T2-based abnormality was identified in 72% of patients overall, while late gadolinium enhancement (LGE) was identified in 93%. In the setting of acute myocarditis, LGE typically reflects myocardial injury. Overall, only 4% of patients had impaired global systolic function (defined as left ventricular ejection fraction <50%). The median interval from vaccination to MRI was 6 days, although data on timing was only available in 68 patients.

Confirming the results of a prior narrative review,<sup>1</sup> the most common pattern of LGE was subepicardial (88%) and the most frequent location was the basal to mid inferolateral wall (61%). A prior case series found that the pattern of myocardial injury in patients with myocarditis after COVID-19 vaccination was similar to other causes of myocarditis, but with less severity.<sup>3</sup>

The majority of patients were male (90%) with mean age of 27 years. Median interval between vaccine administration

and symptom onset was 3 days with 95% of patients presenting with chest pain. Troponin was elevated in 99%. Overall, 78% presented after the second vaccine dose, consistent with prior reports indicating that the risk of myocarditis is higher after the second dose compared to first and third doses.<sup>6,7</sup> An important finding was that no deaths were reported among 263 patients with available survival data.

Myocarditis following COVID-19 vaccination is typically associated with a transient, mild course, with complete resolution of symptoms within a few weeks. However, there is limited longitudinal cardiac MRI data to date. Small case series have demonstrated resolution of myocardial edema, normalization of left ventricular function and interval decrease in LGE extent at intermediate term follow-up.<sup>8</sup> However, minimal persistent LGE without corresponding edema at follow-up has been reported in some patients, likely reflecting myocardial fibrosis.

Relatively mild imaging abnormalities in conjunction with no adverse cardiac events, raises the possibility that myocarditis following COVID-19 vaccination might have a favorable prognosis despite the persistence of minimal LGE. However, longer-term follow-up in larger cohorts of patients is needed. Importantly, COVID-19 illness is associated with even higher risk of myocarditis, which should be balanced against the risk of vaccine-related complications.<sup>9</sup>

Limitations of this analysis include heterogeneity in MRI protocols and differences in inclusion criteria. Of note, the results of this analysis do not reflect the entire spectrum of patients with suspected myocarditis after vaccination as there is a strong positive publication bias. Many of the publications only included patients meeting defined clinical or imaging criteria for myocarditis, whereas others included patients with suspected disease. Importantly, parametric mapping values vary substantially depending on the technique (including the specific sequence and field strength), and therefore pooling multi-site data is of limited value. One approach to combining data is to convert T1 and T2 values to z-scores using site-specific reference values.<sup>10</sup>

Additional data are needed on longitudinal imaging changes, baseline risk factors, and long-term prognosis in patients with myocarditis after COVID-19 vaccination. Understanding the pattern and extent of myocardial injury and its implications will allow for improved care of these patients and may help to address vaccine hesitancy. The publication by Samimisedeh et al is an important step in that direction.

### Conflict of Interest

Dr. Hanneman has received speaker's honorarium from Sanofi-Genzyme, Amicus, and Medscape. Dr. Thavendiranathan has received speaker's honorarium from Amgen, BI, and Takeda.

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### References

1. Sanchez Tijmes F, Thavendiranathan P, Udell JA, Seidman MA, Hanneman K. Cardiac MRI assessment of nonischemic myocardial

inflammation: State of the art review and update on myocarditis associated with COVID-19 vaccination. *Radiol Cardiothorac Imaging* 2021;3:e210252.

2. Marschner CA, Shaw KE, Sanchez Tijmes F, et al. Myocarditis following COVID-19 vaccination. *Cardiology Clinics* 2022. doi:10.1016/j.ccl.2022.05.002.
3. Fronza M, Thavendiranathan P, Chan V, et al. Myocardial injury pattern at MRI in COVID-19 vaccine-associated myocarditis. *Radiology* 2022; Feb 15;212559. doi:10.1148/radiol.212559. Online ahead of print.
4. Starekova J, Bluemke DA, Bradham WS, Grist TM, Schiebler ML, Reeder SB. Myocarditis associated with mRNA COVID-19 vaccination. *Radiology* 2021;301(2):E409-E411.
5. Samimisedeh P, Afshar EJ, Hassani NS, Rastad H. Cardiac MRI findings in COVID-19 vaccine-related myocarditis: A pooled analysis of 468 patients. *J Magn Reson Imaging* 2022. Epub ahead of print.
6. Ling RR, Ramanathan K, Tan FL, et al. Myopericarditis following COVID-19 vaccination and non-COVID-19 vaccination: A systematic review and meta-analysis. *Lancet Respir Med* 2022 Apr 11;S2213-2600(22)00059-5. doi:10.1016/S2213-2600(22)00059-5. Online ahead of print.
7. Sanchez Tijmes F, Zamorano A, Thavendiranathan P, Hanneman K. Imaging of myocarditis following mRNA COVID-19 booster vaccination. *Radiol Cardiothorac Imaging* 2022;4:e220019.
8. Fronza M, Thavendiranathan P, Karur GR, et al. Cardiac MRI and clinical follow-up in COVID-19 vaccine associated myocarditis. *Radiology* 2022; May 3;220802. doi:10.1148/radiol.220802. Online ahead of print.
9. Barda N, Dagan N, Ben-Shlomo Y, et al. Safety of the BNT162b2 mRNA Covid-19 vaccine in a nationwide setting. *N Engl J Med* 2021; 385:1078-1090.
10. Thavendiranathan P, Zhang L, Zafar A, et al. Myocardial T1 and T2 mapping by magnetic resonance in patients with immune checkpoint inhibitor-associated myocarditis. *J Am Coll Cardiol* 2021;77:1503-1516.

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