



BNT162b2 (Pfizer- BioNTech) and mRNA 1273 (Moderna) vaccines were the first messenger RNA (mRNA)-based vaccines ever approved. In both vaccines, a mRNA sequence determines the structure and assembly of the immunogen, the SARS-CoV-2 spike (S) glycoprotein. The mRNA is protected from degradation by lipid nanoparticles (LNPs) and taken up by the cells as an LNP-mRNA complex through simple endocytosis. Previous studies have documented cases of myocarditis mainly in males less than 30 years of age following immunization with mRNA COVID-19 vaccination. In this study, the authors from Canada used 18Fluorine-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET), magnetic resonance imaging (MRI), and values of circulating biomarkers to investigate possible cardiac sequelae in participants diagnosed with acute myocarditis early after mRNA COVID-19 vaccination.

The findings like elevated troponin serum levels, abnormal ST-elevations in the electrocardiogram, altered ventricle movement in echocardiogram, or late gadolinium enhancements (LGE) at cardiac MRI, indicate the development of myocarditis. Symptoms usually occur within the first 3 days after the second dose of mRNA COVID-19 vaccines. Most reported cases had a clinically mild course, and symptoms resolved without treatment. However, some patients required intensive care support or even died of acute heart failure. Arrhythmic failure, either by cardiac arrest or by ventricular fibrillation, is considered to be the mechanism leading to death.

The etiology of vaccine-associated myopericarditis remains unknown. *Postmortem* heart histopathological examination demonstrated an inflammatory infiltrate, mostly of T lymphocytes and macrophages mixed with eosinophils, B lymphocytes, and plasma cells. Early hypotheses suggested that the SARS-CoV-2 S protein, which could be detectable in the blood, may induce cardiac-targeted autoantibodies through molecular mimicry. Other hypotheses are hypersensitivity myocarditis or autoimmune myocarditis driven by T-helper type 17 responses, but there is no evidence to support this pathology yet. Some arguments suggest that aberrant immune responses, both innate and adaptive, were triggered by the mRNA and/or LNPs.

Cardiac MRI is important for assessing alterations in myocardial tissue, while cardiac 18F-FDG PET provides complementary physiological information about changes in myocardial metabolism.



### ***About the study***

The study involved 54 participants aged 17 years or older who had been vaccinated against COVID-19. The diagnostic criteria for acute myocarditis that developed after mRNA COVID-19 vaccination were: 1. the onset of symptoms within 14 days of vaccine administration without any other identified cause, 2 fulfillment of clinical presentation and diagnostic testing criteria for clinically suspected myocarditis proposed by the European Society of Cardiology, and 3. fulfillment of the diagnostic criteria for myocarditis following COVID-19 vaccination proposed by the Center for Disease Control and Prevention.

All participants had cardiac PET and MRI, 12-lead electrocardiography (ECG), and clinical evaluation on the same day, approximately two months after the COVID-19 vaccination. Circulating levels of biomarkers such as interleukin 6, interleukin 8, high-sensitivity C-reactive protein, myeloperoxidase, high-sensitivity troponin I, and B-type natriuretic peptide were assessed.

The researchers evaluated adverse outcomes that developed after COVID-19 vaccination, including resuscitated sudden cardiac death, new-onset sustained atrial or ventricular arrhythmia, stroke, myocardial infarction, and heart failure that required medical care.

### ***Results***

54 participants were divided into three groups. 17 participants who developed new cardiac symptoms within 14 days of vaccination and met diagnostic criteria for acute myocarditis were included in the first group (symptomatic myocarditis). Four of 17 patients met



probable criteria, and 13/17 met confirmed criteria for myocarditis at baseline.

53% of patients (9 patients) developed myocarditis after the mRNA-1273 (Moderna) vaccine and 47% (8 patients) after the BNT162b2 (Pfizer-BioNTech) vaccine. Eleven patients were hospitalized after vaccination, and the median length of hospitalization was three days. Five patients were treated with anti-inflammatory therapy stopped at least two weeks before the research visit.

The second group included 17 participants with new cardiac symptoms who did not meet the criteria for myocarditis (symptomatic without myocarditis). The third group included 20 participants who did not have cardiac symptoms within 14 days of vaccination and did not meet diagnostic criteria for acute myocarditis (asymptomatic).

PET and MRI examination detected persistent myocardial inflammation and edema in a small proportion of participants (5/17) diagnosed with acute myocarditis after mRNA COVID-19 vaccination (PET detected in two and MRI in three participants). Abnormal ECG findings with T-wave changes were found in one of 17 participants with symptomatic myocarditis.

Other ECG parameters or circulating blood biomarkers did not differ between the groups. None of the participants experienced adverse cardiac events beyond myocarditis.

### *Conclusion*

PET and MRI visualization of myocardial tissue has shown localized myocardial inflammation and edema in a small proportion of patients with symptomatic myocarditis approximately two months after COVID-19 vaccination.

Although these results demonstrate low rates of adverse events in patients with myocarditis after mRNA COVID-19 vaccination, the authors stated that more participants might have had focal FDG uptake or other cardiovascular abnormalities if they had been imaged sooner after the vaccination. They emphasized a need for long-term follow-up, especially in patients with persistent LGE on MRI.

The study was published in *Radiology: Cardiothoracic Imaging*.

### *Journal Reference*

Marschner CA. et al. Myocardial Inflammation at FDG PET/MRI and Clinical Outcomes in Symptomatic and Asymptomatic Participants after COVID-19 Vaccination. *Radiology*:



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