BNT162b2 (Pfizer- BioNTech) and mRNA 1273 (Moderna) vaccines were the first messenger RNA (mRNA)-based vaccines ever approved. In both vaccines, an mRNA sequence determines the structure and assembly of the immunogen, the SARS-CoV-2 spike (S) glycoprotein. Previous studies have documented cases of myocarditis mainly in males less than 30 years of age following immunization with mRNA COVID-19 vaccines. In this study, the authors from Canada used 18Fluorine-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET), magnetic resonance imaging (MRI), and circulating biomarkers to investigate possible cardiac sequelae in participants diagnosed with acute myocarditis early following 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. A recent Norwegian nationwide registry-based study has shown increased risks of adverse events, including anaphylactic reaction, lymphadenopathy, and myocarditis/pericarditis in older adolescents aged 12–19 years, after the second mRNA COVID-19 vaccination. https://discovermednews.com/norwegian-nationwide-study-adverse-events-in-older-adolescents-after-anti-sars-cov-2-vaccination/

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* histopathological examination of heart samples 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, detectable in the blood, may induce cardiac-targeted autoantibodies through molecular mimicry. Other hypotheses are hypersensitivity 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, could be 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 and** Results*

The study enrolled 54 participants aged 17 years or older who were vaccinated against COVID-19 and categorized into three subgroups. The subgroup of symptomatic myocarditis included 17 participants who developed new cardiac symptoms within 14 days of vaccination and met diagnostic criteria for acute myocarditis. Diagnostic criteria for acute myocarditis 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. Four of 17 patients met probable criteria, and 13/17 met confirmed criteria for myocarditis at baseline. The second subgroup included 17 participants with new cardiac symptoms who did not meet the criteria for myocarditis. The third subgroup included 20 participants who did not have cardiac symptoms within 14 days of vaccination and did not meet diagnostic criteria for acute myocarditis.

53% of patients (9 patients) developed myocarditis after vaccination with the mRNA-1273 (Moderna) vaccine, and 47% (8 patients) after vaccination with the BNT162b2 (Pfizer-BioNTech) vaccine.

Eleven patients were hospitalized after vaccination, and the median length of hospitalization was three days. Five patients received anti-inflammatory therapy at least 2 weeks before the

research visit. 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 (IL)-6, IL-8, high-sensitivity C-reactive protein, myeloperoxidase, high-sensitivity troponin I, and B-type natriuretic peptide were assessed.

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

PET and MRI scans showed persistent myocardial inflammation and edema in a small proportion of participants (5/17) with acute symptomatic myocarditis after mRNA COVID-19 vaccination. PET detected myocardial inflammation and edema in two and MRI scans in three patients. One out of 17 patients with symptomatic myocarditis had abnormal ECG findings with T-wave changes. Other ECG parameters did not differ between the groups.

None of the participants experienced adverse cardiac events beyond myocarditis.

Conclusion

PET and MRI have shown localized myocardial inflammation and edema in a small proportion of patients with symptomatic myocarditis within 14 days of 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: Cardiothoracic Imaging 2023; 5(2):e220247. Published Online: Mar 9 2023 (Open Access) https://doi.org/10.1148/ryct.220247


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