



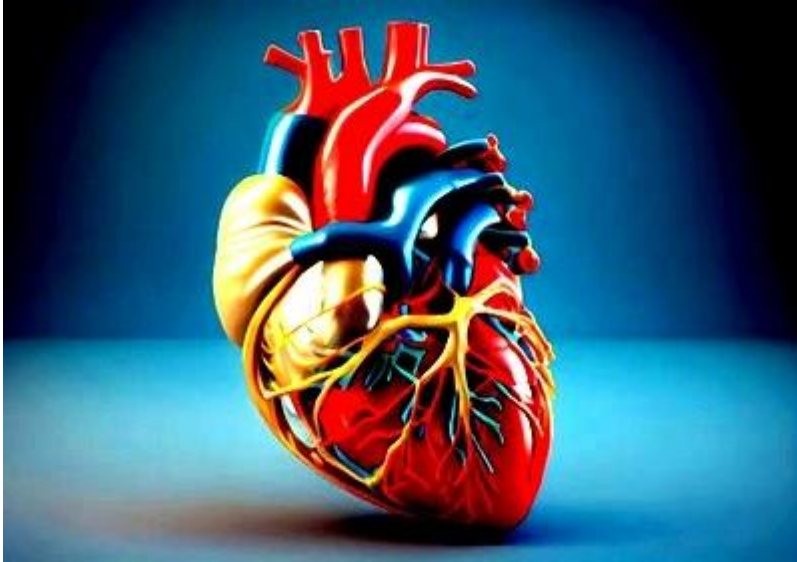
Higher ¹⁸F-FDG uptake was detected in the myocardium, axilla, liver, and spleen of asymptomatic vaccinated individuals up to 6 months after the second mRNA COVID-19 vaccination (PET/CT study) | 1

In messenger RNA (mRNA)-based COVID-19 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 vaccination. The findings like elevated troponin serum levels, abnormal ST-elevations in the electrocardiogram, altered ventricle movement in echocardiogram, or late enhancement in cardiac magnetic resonance imaging (MRI), suggested the development of myocarditis. In this study, the Japanese authors used positron emission tomography (PET)/computed tomography (CT) imaging to investigate myocardial changes and ¹⁸Fluorine-fluorodeoxyglucose (¹⁸F-FDG) uptake in asymptomatic individuals vaccinated with the mRNA COVID-19 vaccines who underwent imaging for reasons unrelated to myocarditis.

Cardiac MRI and ¹⁸F-FDG PET/CT imaging are routinely used as noninvasive diagnostic procedures for myocardial inflammation of diverse origins. PET/CT, compared to cardiac MRI, provides information about inflammation in the whole body.

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About the study

This retrospective study included vaccinated and unvaccinated individuals who underwent ¹⁸F-FDG PET/CT for reasons unrelated to myocarditis. The first group received one or two doses of mRNA COVID-19 vaccine (the BNT162b2 mRNA, Pfizer-BioNTech, or the mRNA-1273, Moderna) with clear vaccine documentation. Most vaccinated individuals (77.6%) received the BNT162b2 mRNA vaccine, and 21% received the mRNA-1273 vaccine. Participants in the second group were unvaccinated.

The median interval between the first vaccination and PET imaging was 13 days, whereas the median interval from the second vaccination to PET imaging was 88 days. Individuals were categorized into seven groups based on the interval between vaccination and imaging: imaging after the first dose, ≤30 days, 31-60 days, 61-120 days, 121-180 days, and >180 days after the second dose.

The exclusion criteria were as follows: blood glucose level higher than 100 mg/dl at the time of ¹⁸F-FDG injection, hematologic diseases such as lymphoma and leukemia, cardiac sarcoidosis, thyroid disease, cardiac surgery, chemotherapy that may result in cardiac dysfunction, chest irradiation in past 6 months, treatment with anti-inflammatory drugs, and a history of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

The ¹⁸F-FDG uptake in the myocardium, axilla, liver, and spleen was quantitatively assessed using the maximum standardized uptake value (SUV_{max}). The following scale was used to measure myocardial visual score: 0 (minimal uptake), 1 (mostly minimal or mild uptake), 2



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(mostly intense or moderate uptake), and 3 (homogeneously uptake).

Results

The study included 1003 subjects, 303 unvaccinated (157 women, 146 men), and 700 vaccinated (356 men, 344 women). At the time of PET/CT imaging, 40 participants received one mRNA COVID-19 vaccine (BNT162b2 mRNA, Pfizer-BioNTech, or mRNA-1273, Moderna), while 660 received two doses. Vaccinated participants were older (mean age, 56.8 years) than unvaccinated (mean age, 52.9 years). 53.1% of vaccinated participants (372/700) and 49.5% of unvaccinated participants (150/303) were not diagnosed with cancer.

18F-FDG PET/CT results

Asymptomatic vaccinated participants had higher myocardial 18F-FDG (SUVmax) uptake in the myocardium, axilla, liver, and spleen than unvaccinated participants (for myocardium median SUVmax was 4.8 vs. 3.3). In the cohort not diagnosed with cancer, median myocardial 18F-FDG uptake and SUVmax were also higher in vaccinated individuals than in unvaccinated.

When participants were categorized by gender, myocardial 18F-FDG uptake was higher in vaccinated men (median SUVmax, 4.9) than in unvaccinated men (median SUVmax, 3.9), as well as in vaccinated women (median SUVmax, 4.7) than in unvaccinated women (median SUVmax, 3.2).

When individuals were categorized by age into three groups, less than 40 years, 41 to 60 years, and more than 60 years, the vaccinated individuals in each age group had higher 18F-FDG uptake in the axilla and myocardium than unvaccinated.

When myocardial 18F-FDG uptake was evaluated by the time interval between vaccination and PET/CT, individuals who underwent PET/CT imaging up to 180 days after the second dose of mRNA vaccine had higher myocardial 18F-FDG uptake than unvaccinated individuals. However, this difference was not seen if imaging was done more than 180 days after the second vaccination. The authors stated that increased myocardial 18F-FDG uptake up to 180 days after the second vaccination could reflect a relatively minor inflammation and not severe myocardial abnormalities.

18F-FDG uptake in the axilla was also significantly higher in participants who underwent imaging up to 120 days after the second vaccination (median SUVmax range, 1.5-2.0) than



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in unvaccinated participants (median SUV_{max}, 1.2). This difference was not observed in subjects who underwent imaging more than 120 days after the second vaccination.

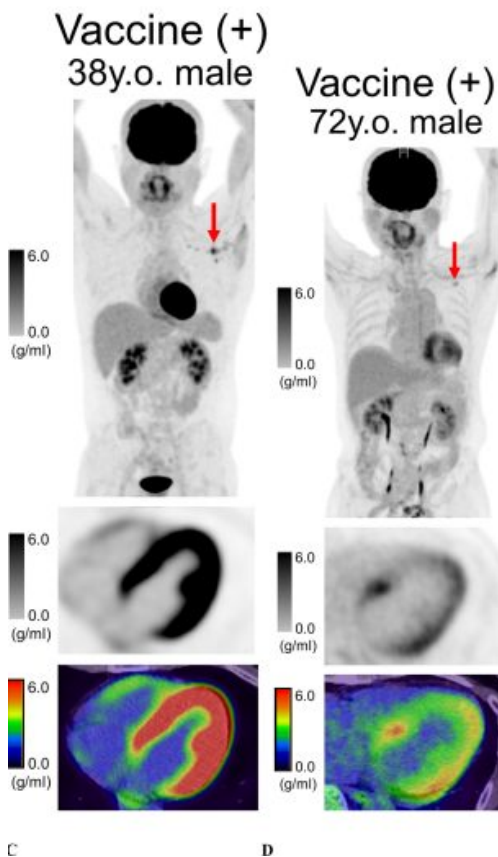
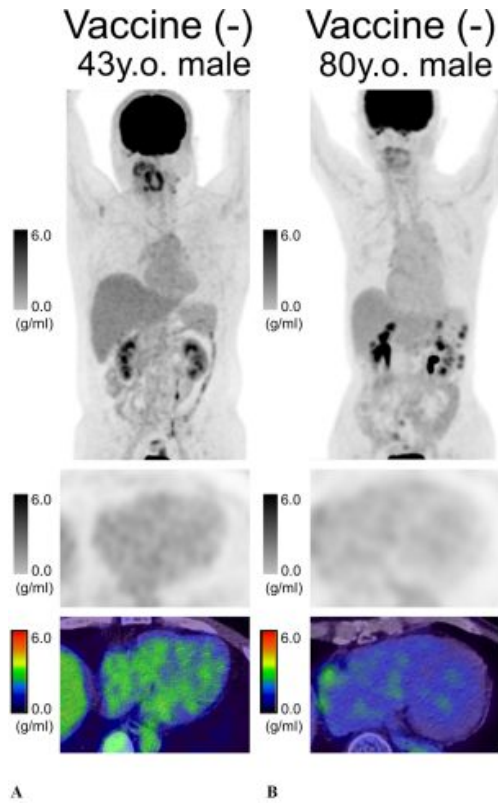
There was no difference in ¹⁸F-FDG uptake between types of mRNA vaccine (the BNT162b2 mRNA, Pfizer-BioNTech, or the mRNA-1273, Moderna).



Higher ^{18}F -FDG uptake was detected in the myocardium, axilla, liver, and spleen of asymptomatic vaccinated individuals up to 6 months after the second mRNA COVID-19 vaccination (PET/CT study) | 5

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Higher 18F-FDG uptake was detected in the myocardium, axilla, liver, and spleen of asymptomatic vaccinated individuals up to 6 months after the second mRNA COVID-19 vaccination (PET/CT study) | 7

Image from the original article by Nakahara T et al, Radiology 2023.

Conclusion

This study has shown that asymptomatic vaccinated subjects who underwent PET/CT up to 180 days after their second mRNA COVID-19 vaccination had increased 18F-FDG uptake in the myocardium, axilla, liver, and spleen as compared to unvaccinated participants. Higher myocardial 18F-FDG uptake on PET/CT was found in vaccinated participants regardless of gender, age, or type of mRNA vaccine.

This increase was not seen in subjects who underwent imaging more than 180 days after vaccination. The authors suggested that future research should validate these findings.

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Journal Reference

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