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ORIGINAL RESEARCH

IMAGING

Cardiac Magnetic Resonance Imaging in COVID-19 Vaccine-Associated Myocarditis Compared With Classical Myocarditis

Yaron Aviv, MD,[a,b,*] Arthur Shiyovich, MD,[a,b,*] Ygal Plakht, PhD,[c] Guy Witberg, MD,[a,b] Maya Weissman, MD,[a,b] Gideon Shafir, MD,[b,d] Ran Kornowski, MD,[a,b] Ashraf Hamdan, MD[a,b]

ABSTRACT

BACKGROUND Studies comparing COVID-19 vaccine-associated and classical myocarditis (CM) are lacking.

OBJECTIVES The purpose of this study was to compare cardiac magnetic resonance (CMR) imaging findings and short-term clinical outcomes in patients with messenger RNA COVID-19 postvaccination myocarditis (PVM) and CM.

METHODS This was a retrospective study of patients with myocarditis: 31 with PVM and 46 with CM. Patients underwent a CMR protocol scan including T1 and T2 sequences. Late gadolinium enhancement (LGE) was expressed as percentage of left ventricular myocardial mass and the extracellular volume was calculated based on precontrast and postcontrast T1 images. Clinical outcomes included heart failure hospitalizations and mortality.

RESULTS Study patients were predominantly male (81% in PVM vs 89% in CM, $P = 0.330$). Patients with PVM had lower T1 values compared with CM (1,064.2 ± 67.0 ms vs 1,081.6 ± 41.9 ms, $P = 0.032$), although T2 and extracellular volume values were similar in both groups. Left ventricular ejection fraction and LGE were similar in both groups. The most frequent location of LGE was the basal inferolateral wall. PVM more commonly demonstrated a mid-wall LGE pattern while CM demonstrated a subepicardial LGE pattern. Compared with CM, patients with PVM were more likely to have a pericardial effusion (42% vs 17%, $P = 0.018$) and pericardial LGE (38% vs 13%, $P = 0.009$). During short-term follow-up (median 300 days for PVM, 319 days for CM), there were no deaths or heart failure hospitalizations in either group.

CONCLUSIONS Our study shows similar CMR imaging findings and short-term outcomes in PVM and CM, although PVM was associated with milder myocardial abnormalities and more frequent pericardial involvement. (JACC Adv 2023;2:100726)

From the [a]Department of Cardiology, Rabin Medical Center, Petah Tikva, Israel; [b]Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel; [c]Faculty of Health Sciences, Department of Nursing, Soroka University Medical Center, Ben-Gurion University, Beer-Sheva, Israel; and the [d]Department of Radiology, Rabin Medical Center, Petah Tikva, Israel. *Drs Aviv and Shiyovich contributed equally to this paper.
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.

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ABBREVIATIONS AND ACRONYMS

CM = classical myocarditis

CMR = cardiac magnetic resonance

ECV = extracellular volume

HF = heart failure

LGE = late gadolinium enhancement

LVEDV = left ventricular end-diastolic diameter

LVEF = left ventricular ejection fraction

mRNA = messenger RNA

PVM = postvaccination myocarditis

In Israel, a nationwide messenger RNA (mRNA) COVID-19 vaccination campaign was initiated in 2020 and a vaccination campaign for adolescents was initiated in 2021. The vaccine has demonstrated excellent effectiveness in the short-term prevention of infection, symptomatic disease, hospitalizations, and mortality.[1] Shortly after the initiation of the vaccine campaign, reports of myocarditis as an adverse effect emerged, predominantly among young men,[2] and these findings have been consistent in larger population-wide studies.[3]

Myocarditis following COVID-19 vaccination has been reported in a number of small series. Several reports have described cardiac magnetic imaging findings of patients presenting with myocarditis following COVID-19 vaccination,[4] and reports were consistent with overall favorable short-term clinical course. Nevertheless, the management of these patients is based largely on expert opinion recommendations and evidence derived from classical myocarditis (CM), while empiric data paralleling postvaccination myocarditis (PVM) and CM as a basis for this comparison are scarce.[5,6]

Therefore, the aims of the present study were to: 1) evaluate and compare cardiac magnetic resonance (CMR) imaging findings between patients with PVM and CM; and 2) evaluate the short-term clinical outcomes of both groups.

METHODS

STUDY POPULATION. This retrospective study included PVM and CM patients who underwent CMR during the same time period, between January 2021 and January 2022. All patients with PVM and CM were adjudicated as clinical myocarditis by independent expert cardiologists, and other causes of myocardial injury were excluded. Temporal association with mRNA COVID-19 vaccination was defined as a maximum 3-week interval from any vaccine dose which was the definition used in previous studies.[2] All included patients with CM were referred to CMR due to a clinical diagnosis of myocarditis established during hospitalization in multiple centers throughout Israel, without temporal association to any vaccine dose as described above. Exclusion criteria included COVID-19-associated myocarditis. All patients were referred to 1 of 2 CMR referral centers: "Mor Inside" (1.5-T scanner), Rabin Medical Center (3.0-T scanner).

"Classical myocarditis" was defined as sporadic, non-COVID-19 related and not temporally associated to any vaccine dose. The term "classical myocarditis" was previously coined in a similar work.[5] Current guidelines do not endorse actively seeking viral etiology in patients who do not need to undergo biopsy, due to the low yield of humoral testing.[7] Thus, viral etiology in "classical myocarditis" is assumed and not proven. COVID-19 was ruled out via polymerase chain reaction testing (rather than rapid antigen testing) as those were the local health ministry's instructions for hospitalized patients during the study period. Polymerase chain reaction testing has better diagnostic accuracy than antigen testing,[8] but its sensitivity is still limited.[9] We acknowledge that during a pandemic, some patients with COVID-19 infection might have been included in the CM group, but this is inherent to any study performed during these times. Thus, there is a possibility that some patients with autoimmune or genetic etiology, as well as false negative COVID testing might be present within the CM patient group, but as with all cases of sporadic myocarditis, they represent a small minority—and their influence on the current study's results should be negligible.

This study was approved by the Clalit Health Services Institutional Review Board and performed consistently with the Helsinki Declaration. Exemption from informed consent was granted.

CMR IMAGING. CMR imaging in all patients with PVM and CM was performed using 1.5-T scanner (Ingenia, Philips Medical System), but 3 patients with PVM were scanned using 3.0-T scanner (Magnetom Vida, Siemens Healthineers). The study included only the analysis of the first CMR scans performed following clinical diagnosis.

CMR study protocol at 1.5-T included multiplanar cine imaging for acquisition of cardiac function, volumes, and mass, and late gadolinium enhancement (LGE) imaging for scar imaging. Single breath-hold modified inversion recovery Look-Locker was used for pre- and post-gadolinium T1 mapping and a navigator gated black blood prepared gradient spin-echo sequence was used for T2 mapping. CMR study protocol using the 3.0-T scanner included myocardial T1 mapping performed in short axis view using modified inversion recovery Look-Locker sequence and T2 mapping using Myomaps.

For data analysis, the complete data set was transmitted to a dedicated workstation (Philips Intellispace Portal, version 11.0). Cardiac volumes, function, and mass were measured using automated contour detection with manual correction if required. Myocardial T1 and T2 relaxation times were measured using motion-corrected images. For 1.5-T scanner,

abnormal native T1 and T2 values were defined as >1,060 ms and >57 ms; respectively,[10] and for 3.0-T scanner, abnormal native T1 values were defined as >1,105 ms.[11] LGE was defined as an image intensity level ≥2 SDs above the mean of the remote myocardium. The amount of LGE was expressed as percentage of left ventricular myocardial mass and the extracellular volume (ECV) was calculated based on precontrast and postcontrast T1 images. Myocardial segmentation (for LGE and functional comparisons) was performed according to previously reported 17-segment segmentation.[12] Pericardial LGE was considered present when enhancement involved both pericardial layers, irrespective of the presence of pericardial effusion. The diameter of pericardial effusion was measured in an end-systolic frame.

BASELINE CLINICAL DATA AND OUTCOMES. Patient's demographics (age and sex), clinical parameters (height, weight, comorbidities and risk factors, electrocardiogram), lab results [troponin T, N-terminal pro brain natriuretic peptide, hematocrit (for ECV calculation), creatine phospho-kinase, C-reactive protein], and clinical follow-up were all collected from digital patient records. Clinical outcomes of interest included heart failure (HF) hospitalizations and mortality.

STATISTICAL ANALYSIS. Baseline characteristics are presented as counts (%) for categorical variables and mean ± SD) for continuous variables, as appropriate. The results of CMR studies of patients with PVM and CM were graphically presented with boxplot charts included the following statistical parameters: mean, median (Q2, 50%), quartile 1 (Q1, 25%), quartile 3 (Q3, 75%), minimum and maximum (with no outliers). Comparisons of the investigated parameters between the study groups were performed using chi-squared test/Fisher exact test for categorical variables and Mann-Whitney U test for continuous variables.

Associations between the study group (PVM vs CM) and each of following study outcomes were evaluated: left ventricular ejection fraction (LVEF) (<60% vs ≥60%), global ECV (≥28% vs <28%), and global T1 value (≥1,060 ms vs <1,060 ms). These relationships were investigated in univariable and multivariable levels using logistic regressions. Multivariable logistic regression models included additional parameters: age, sex, body mass index, and number of days from diagnosis to CMR. The results of the models were presented as ORs/adjusted ORs (adjORs) with 95% CIs. For each test, *P* value of <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS 26 (SPSS Inc, Chicago, IL, USA) software.

TABLE 1 Baseline Characteristics of Patients With Classical and Postvaccination Myocarditis

	Classical Myocarditis (n = 46)	Postvaccination Myocarditis (n = 31)	*P* Value
Age, y	29.2 ± 8.7	35.0 ± 15.0	0.208
Male	41 (89.1)	25 (80.6)	0.334
Height, cm	174.7 ± 7.1	172.8 ± 8.2	0.092
Weight, kg	79.6 ± 16.0	74.0 ± 11.6	0.125
BMI, kg/m^2	25.9 ± 4.1	24.7 ± 4.5	0.288
Hypertension	0	2 (6.7)	0.021
Diabetes mellitus	0	1 (3.3)	0.395
Dyslipidemia	0	1 (3.3)	0.395
Smoking	9 (19.6)	2 (6.7)	0.184
Previous pericarditis	1 (2.2)	1 (3.3)	1.000
Previous myocarditis	1 (2.2)	0	1.000
Asthma	1 (2.2)	1 (3.3)	1.000
Known coronary disease	0	0	-
Peak troponin T, pg/mL	1,347 ± 2,552	1,688 ± 2,601	0.890
Peak CRP, ng/mL	10.3 ± 7.1	9.7 ± 14.9	0.144
Time from diagnosis to CMR, d	97.0 ± 152.6	81.3 ± 71.8	0.141
Electrocardiogram findings			0.415
Normal	11 (28.2)	12 (50.0)	
Diffuse ST-segment elevation	12 (30.8)	6 (25.0)	
Localized ST-segment elevation	4 (10.3)	2 (8.3)	
T-wave changes	10 (25.6)	4 (16.7)	
ST-segment depression	2 (5.1)	0	

Values are mean ± SD, or n (%).
BMI = body mass index; CMR = cardiac magnetic resonance; CRP = C-reactive protein.

Interobserver variability was tested in 20 randomly patients, in which values were separately estimated for the 5 following study parameters: LVEF, left ventricular end-diastolic diameter (LVEDV), left ventricular end-systolic diameter, LV mass, and LGE. We used the 1-way random models based on the assumption that the values for the first ("original") measurements were assigned routinely by different clinicians. For each study parameter, the intraclass correlation coefficients (ICCs) (single and average levels) with 95% CIs and *P* values were calculated. Intraobserver variability was evaluated in the same 20 patients, 9 weeks apart. These measurements were separately estimated for the 5 study parameters using Pearson correlation. For each study parameter, correlation coefficient with 95% CIs and *P* value were calculated.

RESULTS

PATIENT CHARACTERISTICS. Overall, the study included 77 consecutive patients (31 patients with PVM and 46 patients with CM; age 35 ± 15 and 29.2 ± 8.7 years; respectively, *P* = 0.21). A total of 27 out of 31 patients (87%) with PVM were diagnosed

TABLE 2 Cardiac Magnetic Resonance Imaging in Patients With Classical and Postvaccination Myocarditis

	Classical Myocarditis (n = 46)	Postvaccination Myocarditis (n = 31)	*P* Value
LVEF, %	59.3 ± 5.1	60.4 ± 5.9	0.525
LVEF, <60%	28 (60.9)	18 (58.1)	0.806
LVEDV, ml	140.3 ± 28.8	130.7 ± 26.6	0.199
LVESV, ml	58.1 ± 17.9	50.2 ± 12.7	0.105
Septal thickness, mm	8.9 ± 1.4	9.4 ± 1.8	0.468
Lateral wall thickness, mm	8.1 ± 1.4	7.7 ± 1.8	0.259
LA area, cm^2	24.1 ± 3.6	23.3 ± 3.7	0.266
RA area, cm^2	23.6 ± 3.5	22.6 ± 3.6	0.153
LVEDV index, ml/m^2	71.8 ± 11.7	70.6 ± 12.9	0.732
LVESV index, ml/m^2	29.5 ± 7.3	31.7 ± 15.5	0.959
LV mass, gr	93.7 ± 28.1	84.3 ± 18.7	0.161
LV mass index, gr/m^2	47.6 ± 11.7	44.4 ± 8.2	0.297
Global T1 value, ms	1,081.6 ± 41.9	1,064.2 ± 67.0[a]	0.032
Global T1 value, ≥1,060 ms[b]	32 (82.1)	17 (58.6)	0.033
Global T2 value, ms	53.6 ± 5.7	52.0 ± 4.0	0.515
Global T2 value, ≥57 ms	10 (38.5)	3 (12.0)	0.030
Global ECV, %	30.2 ± 3.6	28.9 ± 3.3	0.222
Global ECV ≥28%	36 (78.3)	16 (57.1)	0.054
LGE, %	4.8 ± 4.9	3.6 ± 4.4	0.204
LGE segment sum	3.3 ± 3.9	2.9 ± 2.8	0.423
LGE pattern			
Epicardial	27 (60.0)	9 (31.0)	0.021
Mid-wall	17 (37.8)	16 (55.2)	
Epicardial and mid-wall	1 (2.2)	4 (13.8)	
LGE in pericardium	6 (13.0)	12 (38.7)	0.009
Pericardial effusion	8 (17.4)	13 (41.9)	0.018
Diameter effusion, mm	0.91 ± 1.2	1.73 ± 2.1	0.304
RWMA, regional	18 (39.1)	8 (25.8)	0.225
RWMA, segment sum	1.6 ± 3.6	1.3 ± 3.2	0.464

Values are mean ± SD, or n (%). [a]The 3 patients in the PVM group who were scanned on a 3.0-T CMR scanner were excluded from this analysis. [b]For 1.5-T CMR scanner.

CMR = cardiac magnetic resonance; ECV = extracellular volume; LA = left atrium; LGE = late gadolinium enhancement; LV = left ventricle; LVEDV = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic diameter; RA = right atrium; RWMA = regional wall motion abnormality.

following the first and second vaccine dose and 4 out of 31 (13%) patients following the third vaccine dose (booster). PVM was diagnosed after a median of 5 days (IQR: 3-8 days) after vaccination.

Patient's baseline characteristics are presented in Table 1. Both groups are comprised predominantly of young males with very low rates of comorbidities and cardiovascular risk factors. Additionally, baseline characteristics were similar between both groups, except higher rates of hypertension in the PVM group. Furthermore, no statistically significant differences were found in the presenting electrocardiogram, peak-troponin T levels, and C-reactive protein levels between both groups.

IMAGING FINDINGS. CMR imaging findings are presented in Table 2 and Figures 1 and 2. The mean time intervals between clinical diagnosis and CMR scan were similar in both groups. Mean LVEF values, left ventricular dimensions, and mass were within normal range and similar in both groups, the number of segments displaying regional wall motion abnormalities were also similar in both groups, and the extent of LGE was relatively mild and did not significantly differ between the groups—even after adjustment for sex, age, and interval between symptom onset and CMR scan. Mean global ECV levels were similarly increased in both groups while mean global T2 values were within normal range in both groups. Nevertheless, global native T1 values were significantly lower in PVM compared to CM (1,064.2 ± 67.0 ms vs 1,081.6 ± 41.9 ms, respectively, $P = 0.032$). Based on the aforementioned cutoff values, native T1 values were more likely to be normal (eg, <1,060 ms in 1.5-T scanner or <1,105 ms in 3.0-T scanner) in PVM compared with CM ($P = 0.033$) and T2 values were also more likely to be normal (eg, <57 ms) in PVM, as compared with CM ($P = 0.030$). Among CM patients, abnormal ECV (eg, >28%) tended to be more common than in PVM, with borderline statistical significance ($P = 0.054$) (Figure 2).

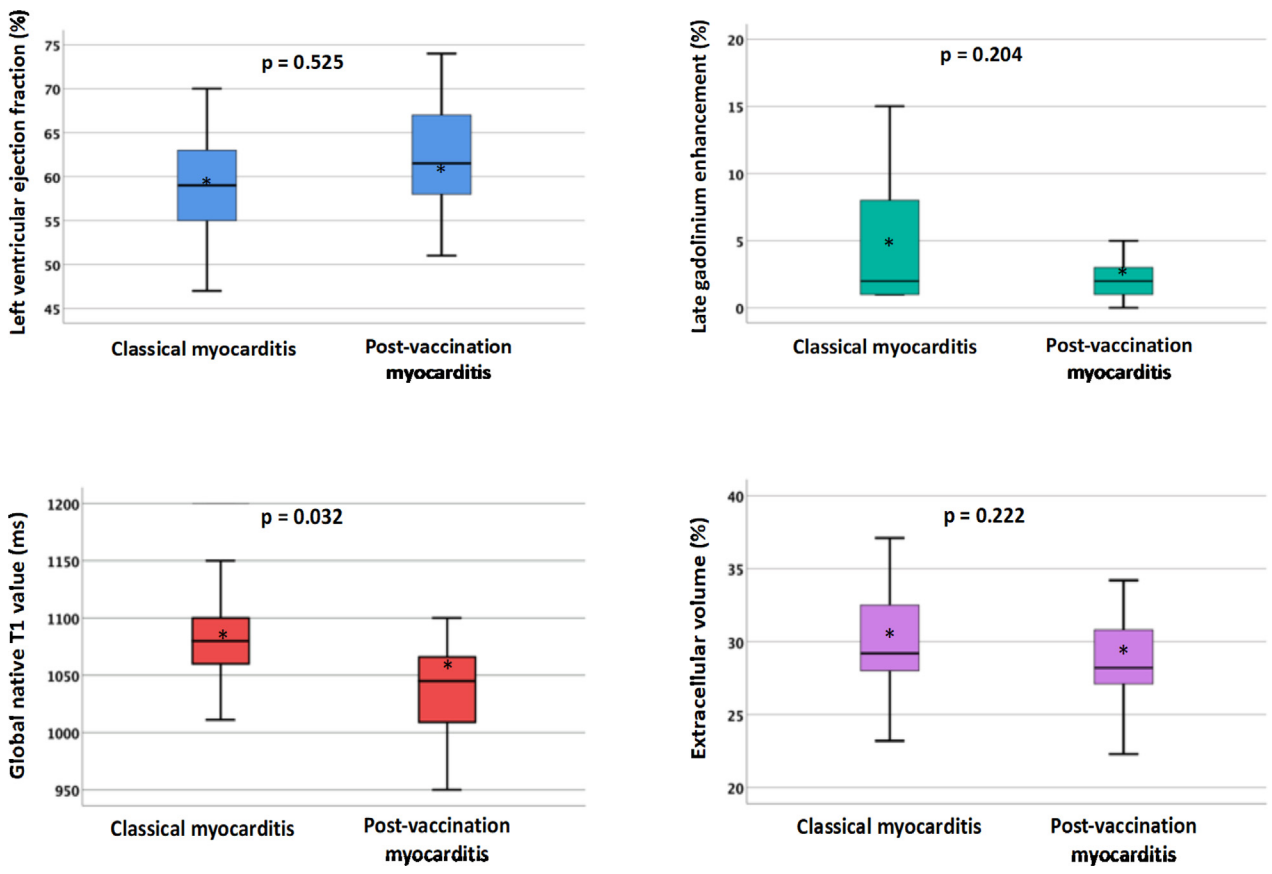
In the PVM group, 3 patients were scanned within the first week after clinical diagnosis vs 18 patients in the CM group. Of these patients scanned during the acute phase, 1 patient with PVM had elevated T2 relaxation times, vs 9 with CM. All patients with elevated T2 relaxation times were scanned within a maximum of 6 days following a clinical diagnosis, except for 1 patient in the CM group scanned 84 days following clinical diagnosis.

CM more frequently involved the epicardium, while PVM the mid-wall ($P = 0.021$). Figure 3 displays a per-segment myocardial distribution of LGE in both groups. Both groups showed a predilection for inferolateral segment involvement, most commonly involving the basal and mid-ventricular segments.

LGE of the pericardium was significantly more common in the PVM vs CM (12/31, 38% vs 6/46, 13%, respectively; $P = 0.009$). Similarly, pericardial effusion was more common in PVM as well (13/31, 42% vs 8/46, 17%, respectively; $P = 0.018$). Representative images of cases with PVM vs CM are presented in Figure 4.

The results of univariate analyses have shown no significant association between the study groups (PVM vs CM) and low LVEF (OR: 0.890, 95% CI: 0.352-2.249, $P = 0.806$). However, as compared with PVM,

FIGURE 1 CMR Structural and Functional Differences Between Postvaccination Myocarditis and Classical Myocarditis



Left ventricular ejection fraction (LVEF), late gadolinium enhancement (LGE), global T1 map values, and extra cellular volume (ECV) in patients with post-vaccination myocarditis and classical myocarditis. CMR findings demonstrated significantly lower global T1 relaxation times in PVM vs. CM, while LVEF, ECV, and LGE were similar between the groups. CM = classical myocarditis; CMR = cardiac magnetic resonance; PVM = postvaccination myocarditis.

CM was borderline associated with abnormal global ECV ≥28% (OR: 2.703, 95% CI: 0.969-7.519, $P = 0.058$) and significantly associated with abnormal global T1 values ≥1,060 ms (OR: 3.226, 95% CI: 1.072-9.709, $P = 0.037$).

The results of multivariate analyses are presented in Supplemental Table 1. After adjustment for age, sex, body mass index, and time from diagnosis to CMR scan, no significant association between the study groups (PVM vs CM) and LVEF was found. However, as compared with PVM, CM was significantly associated with abnormal global ECV ≥28% (adjOR: 3.475, 95% CI: 1.140-12.346, $P = 0.040$) and abnormal global T1 values ≥1,060 ms (adjOR: 3.663, 95% CI: 1.070-12.500, $P = 0.039$).

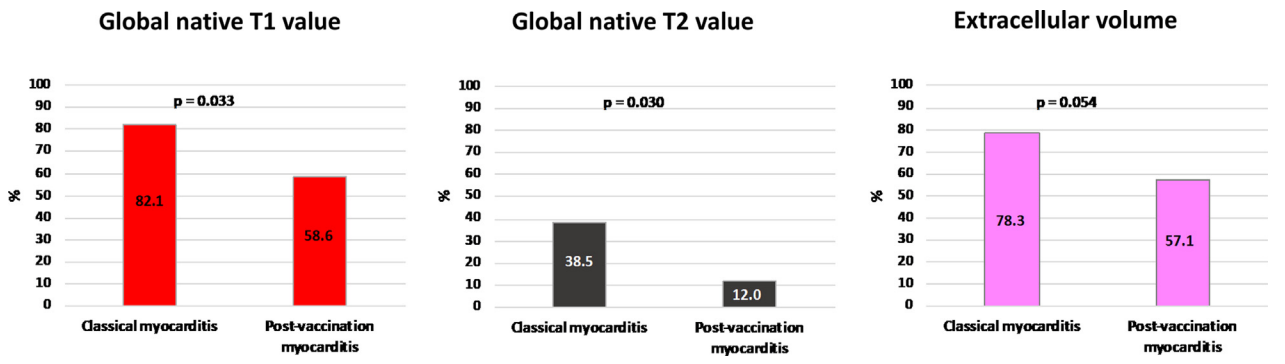
The ICC values for interobserver variability in a single level distributed between 0.882 (95% CI: 0.730-0.951) for LVEF and 0.960 (95% CI: 0.903-0.984) for LVEDV ($P < 0.001$ for each). The ICC values in an average level distributed between 0.937 (95% CI: 0.844-0.975) for LVEF and 0.979 (95% CI: 0.949-0.992) for LVEDV ($P < 0.001$ for each).

CLINICAL OUTCOMES. During follow-up time (median 300 days, IQR: 227-387 days for PVM and median 319 days, IQR: 244-401 days for CM), there were no deaths or HF hospitalizations in either group. In each group, 1 patient was hospitalized for recurrent myocarditis.

DISCUSSION

In this study, comparing CMR imaging and short-term clinical outcomes in patients with myocarditis following mRNA COVID-19 vaccination and patients with CM, we found similar LV dimensions, mass, ejection fraction, and extent of LGE in both groups.

FIGURE 2 Normal vs Abnormal Relaxation Times and ECV Between Postvaccination Myocarditis and Classical Myocarditis

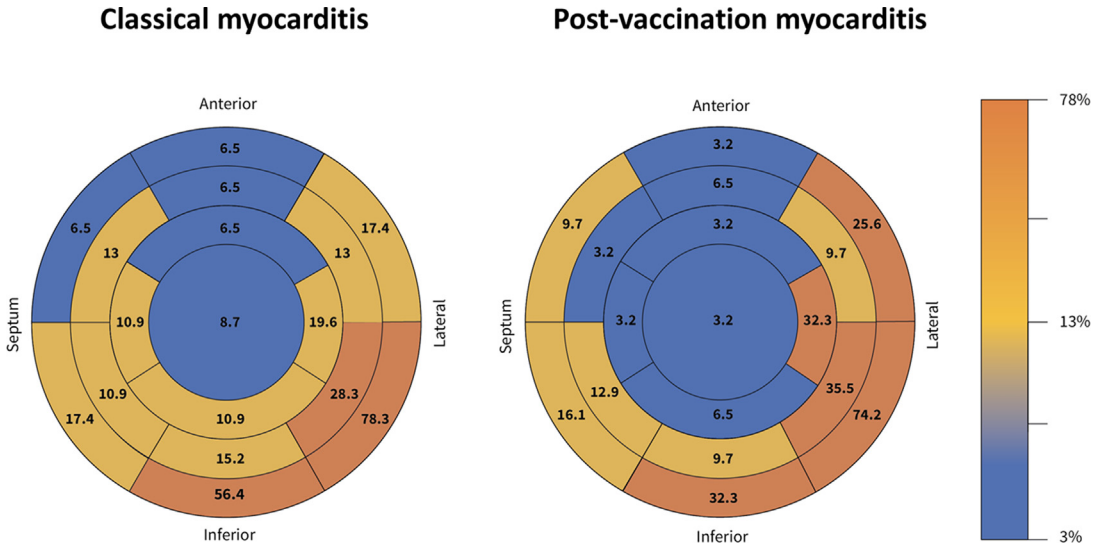


Percentage of patients with abnormal global T1 relaxation time values (≥1,060 ms), abnormal extracellular volume (ECV) (≥28%) and abnormal global T2 relaxation time values (≥57 ms) in classical myocarditis and post-vaccination myocarditis. Global T1 and T2 relaxation times were significantly lower in PVM vs CM, while ECV showed borderline significance. CM = classical myocarditis; PVM = postvaccination myocarditis.

However, shorter T1 relaxation times, more frequent pericardial involvement and a mid-wall LGE patterns were more frequently observed in PVM compared with CM. CM more commonly had a subepicardial LGE pattern. Similar clinical presentation and similar favorable short-term clinical outcomes were seen in both forms of myocarditis.

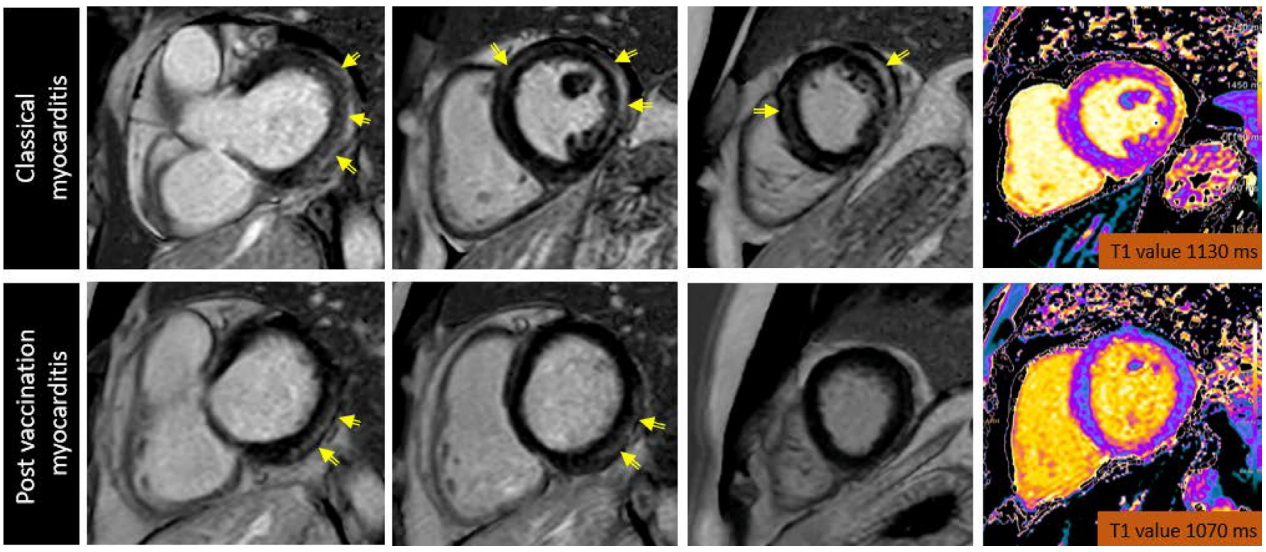
To the best of our knowledge, this is the largest report to date including a comprehensive clinical evaluation and in-depth CMR imaging evaluation of

FIGURE 3 LGE Segmental Distribution in Postvaccination Myocarditis and Classical Myocarditis



Segmental distribution of late gadolinium enhancement (LGE) in post-vaccination myocarditis (right) and classical myocarditis (left) according to a standardized 17-segment model. Segments are color coded according to percentage of patients with segment involvement. Orange = very often involved (>25%); yellow = often involved (10%-25%); blue = seldom involved (<10%). Both groups showed similar distribution, with predilection to inferolateral segments.

FIGURE 4 Representative Cases Images



Representative CMR images of classical myocarditis (top) and post-vaccination myocarditis (bottom). Please note the lower T1 time in post-vaccination myocarditis. CMR = cardiac magnetic resonance.

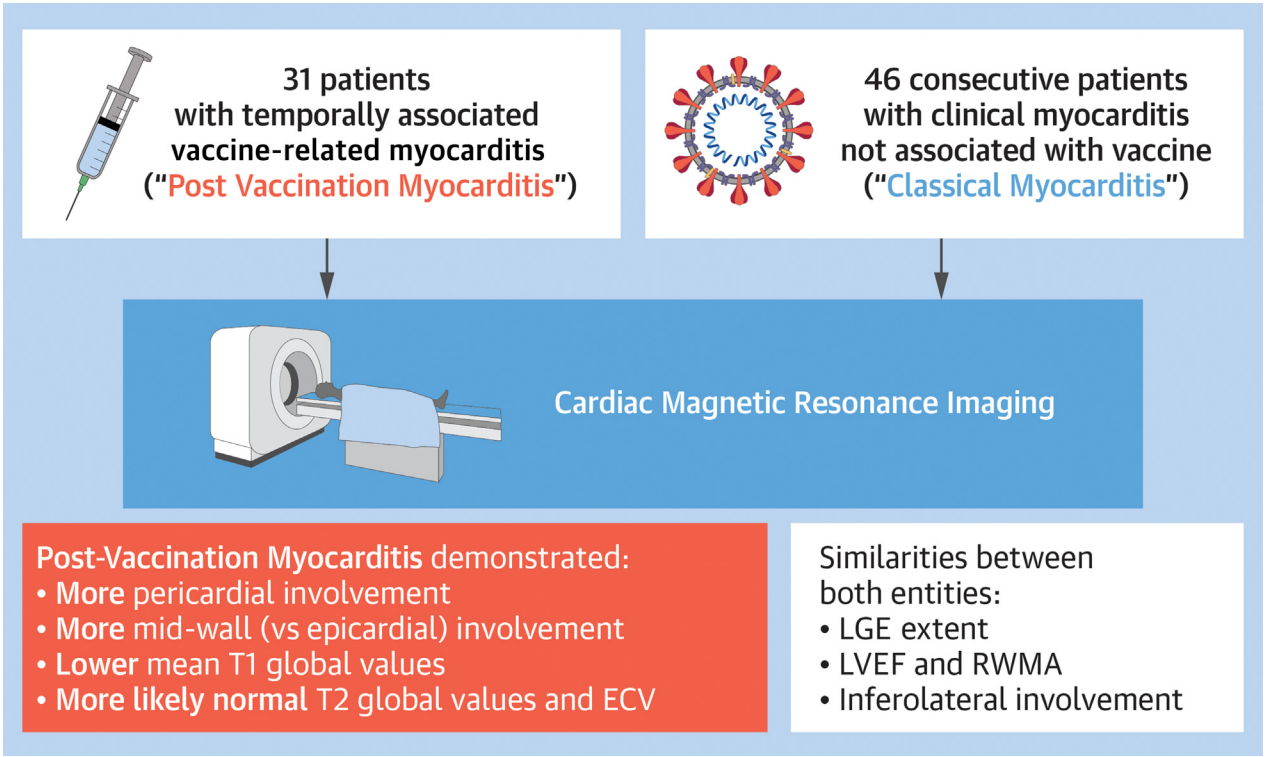
mRNA-based COVID-19 vaccine-associated myocarditis in comparison with CM. Nearly all patients were scanned on the same CMR scanner using the same comprehensive CMR protocol, allowing better comparison of CMR imaging parameters. During the short time since the first reports of COVID-19 mRNA vaccine-associated myocarditis, various reports have described a mild clinical presentation, mild CMR imaging abnormalities, and no serious adverse events over short-term follow-up.[4,13] The results of this current study highlight these findings and are in close agreement with those of a recently published systemic review and meta-analysis of 468 patients with PVM from 102 studies,[14] in which most patients presented with an inferolateral LGE pattern and normal LVEF. Furthermore, an inferolateral LGE pattern in myocarditis has previously been shown to be associated with a favorable clinical outcome.[15]

A recent study comparing 21 patients with PVM, post-COVID-19 myocarditis, and CM demonstrated similar pattern of myocardial injury in vaccine-associated myocarditis compared with other causes, although abnormalities were less severe, including lower native T1 values and fewer wall motion abnormalities.[16] Similar to that study, the current study demonstrates similar extent of LGE involvement and distribution in both PVM and CM; however, more frequent mid-wall LGE pattern and higher rates of pericardial involvement in PVM compared with CM. In contrast, our study included ECV in the analysis and excluded patients with post-COVID-19 myocarditis allowing us to directly compare PVM with CM.

Despite the clinical similarities, PVM appears to have milder CMR imaging findings—with significantly lower global T1 values than CM, while the extent of LGE was similar in both groups. This parameter, associated with interstitial tissue fibrosis and edema, might possibly be more closely associated with prognosis than LVEF, similar to LGE%.[15,17] Similarly, global T2 value was also more likely to be normal (eg, <57 ms) in PVM compared with CM. Abnormal T2, representing ongoing inflammation and edema, has previously been associated with worse outcomes.[18,19] To summarize, global T1 and T2 values are quantitative tissue characteristics that provide complementary information, particularly in the setting of myocardial inflammation and may possibly be associated with prognosis.[16]

Among CM patients, abnormal ECV (eg, >28%), also corresponding with tissue infiltration and fibrosis, was borderline significantly more common in CM than in PVM. Higher ECV values have also previously been shown to be associated with worse prognosis.[20]

CENTRAL ILLUSTRATION **CMR Imaging Findings in COVID-19 Vaccine-Associated Myocarditis Compared With Classical Myocarditis**



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CMR = cardiac magnetic resonance; ECV = extracellular volume; LGE = late gadolinium enhancement; LVEF = left ventricular ejection fraction; RWMA = regional wall motion abnormality.

CMR can also be useful in the long-term follow-up examination of patients with myocarditis to detect disease activity and progression. A recent follow-up study from our group revealed that in 7 patients with PVM, both LVEF and LGE% significantly improved in a second CMR scan performed 5.3 months after the first CMR scan.[21] This is hypothesis generating, as PVM could not only present with milder imaging findings compared with CM, but could also improve over time. These parameters are of clinical significance to the individual risk stratification and patient management during follow-up.[22] A comparison between follow-up scans of both PVM and CM is therefore needed to determine whether these differences are maintained during a longer follow-up.

Our study demonstrated that similar to CM, PVM has an excellent short-term prognosis, with no HF hospitalizations or mortality in either group during a short-term follow-up.

STUDY LIMITATIONS. First, endomyocardial biopsy, the gold standard for the definitive diagnosis of myocarditis, was not performed. Instead, a diagnosis based on clinical and laboratory criteria was used in this study. Second, due to CMR performed mostly during convalescence and not acutely following clinical diagnosis in both groups, CMR imaging findings are not consistent with the updated Lake Louise criteria for the early diagnosis of myocarditis[23] in the majority of patients included. Third, the retrospective nature of the study is a limitation in itself Fourth, referral to CMR as an inclusion criterion might be a cause for some selection bias.

CONCLUSIONS

Our study demonstrated relatively similar CMR imaging findings, clinical presentation, and short-term outcomes in this series of patients with PVM and CM. However, PVM was associated with less severe

myocardial abnormalities and more frequent pericardial involvement, as presented in the **Central Illustration**. The overall limited CMR abnormalities and good clinical outcomes are reassuring and may be helpful for clinicians counseling patients. Further studies are needed to examine the long-term effects of mRNA-based COVID-19 vaccine-associated myocarditis in comparison with CM.

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ADDRESS FOR CORRESPONDENCE: Dr Yaron Aviv, Cardiology department, Rabin Medical Center, 39 Jabotinski Street, 4941492 Petah Tikva, Israel. E-mail: yaron.aviv@gmail.com.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: CMR findings in patients with COVID-19 mRNA vaccine-associated myocarditis are similar to patients with sporadic ("classical" and presumed viral) myocarditis. However, global T1 relaxation times were lower in vaccine-associated myocarditis. Vaccine-associated disease was also more likely to include features of pericardial involvement (effusion and enhancement) and mid-wall involvement. Clinical outcomes were similarly good in both groups. Data showing that vaccine-associated disease has a benign clinical course and slightly milder imaging findings may be helpful for clinicians counseling patients.

TRANSLATIONAL OUTLOOK: Further studies are needed to examine the long-term effects (both clinical and imaging findings) of mRNA-based COVID-19 vaccine-associated myocarditis in comparison with classical myocarditis.

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KEY WORDS COVID-19 vaccination, MRI, myocarditis

APPENDIX For a supplemental table, please see the online version of this paper.