Journal of Heart

Clinical Research | Vol 3 Iss 1

Comparison of Cardiac Magnetic Resonance Imaging Findings in COVID-19 Associated Myocarditis and Nonspecific Viral Myocarditis

Sedat Altay*, Kazım Ayberk Sinci, Ezgi Suat Bayraktar, Emre Özdemir, and Cesur Gümüş

Department of Radiology İzmir Katip Çelebi University Ataturk Research and Training Hospital, Basın Sitesi, Turkey

Correspondence should be addressed to Sedat Altay, Department of Radiology İzmir Katip Çelebi University Ataturk Research and Training Hospital, Basın Sitesi, 35360 Izmir, Turkey

Received Date: September 30, 2022; **Accepted Date:** October 10, 2022; **Published Date:** October 17, 2022

ABSTRACT

BACKGROUND

This study aimed to compare laboratory, echocardiography, and cardiac magnetic resonance imaging (CMR) findings in patients with coronavirus disease-2019 (COVID-19) associated myocarditis and nonspecific viral myocarditis (NSVM).

METHODS

We retrospectively evaluated 25 patients who were considered to have COVID-19-associated myocarditis according to the Lake-Louise criteria and clinical findings. We retrospectively evaluated 41 patients who were accepted as NSVM according to the Lake Louse criteria between January 2016 and March 2020. Late gadolinium enhancement (LGE), ejection fraction, stroke volume, peak ejection rate, and cardiac index data were analyzed for two groups. Echocardiography findings and clinical data were evaluated. Comparisons were made one-way analysis of variance and Student's t-test.

RESULTS

LGE was detected in 25 (30%) patients with COVID-19 through CMR examination. LGE was detected most frequently in the inferior segments (mean 2.8 segments) in the patients. Pericardial thickening was observed in 8 (32%) patients. In the NSVM patients, LGE was observed only in the inferior segments in 25 patients, in the lateral - inferior segments in 10 patients, and in the septal-inferior segments in 6 patients (mean of 2.4 segments). Pericardial thickening was present in 14 (34%) patients. T2 hyperintensity was not observed. Echocardiography findings were within normal limits in myocarditis groups. There was no statistically significant difference between myocarditis groups' CMR functional data ($p = 0.027$).

CONCLUSION

Functional heart parameters and laboratory findings were similar and within normal limits, and no significant difference was observed in imaging features and functional data between NSVM and COVID-19-associated myocarditis.

Citation: Sedat Altay, Comparison of Cardiac Magnetic Resonance Imaging Findings in COVID-19 Associated Myocarditis and Nonspecific Viral Myocarditis. J Heart 3(1): 5-13.

KEYWORDS

Myxoma; Cardiac malignancy; Surgical procedure

INTRODUCTION

Nonspecific viral myocarditis (NSVM) is inflammation of the myocardium secondary to viral infection. The clinical presentation of viral myocarditis is very heterogeneous and can range from subclinical nonspecific symptoms of malaise and fatigue to a more severe presentation such as acute cardiogenic shock and, in severe cases, sudden cardiac death [1-3]. In the early days of viral myocarditis, there is edema, necrosis, and myocyte damage due to direct viral spread. The myocardium is usually cleared of the virus within 5 days. Complete tissue and functional recovery usually occur within 3 weeks to 4 weeks. Necrosis and fibrosis occur in severe myocarditis [3]. Endomyocardial biopsy is an invasive procedure and is the gold standard test to confirm viral myocarditis. However, the sensitivity is low when myocardial involvement is focal. Cardiac imaging hence plays an essential role in the non-invasive evaluation of viral myocarditis [4].

Coronavirus disease-2019 (COVID-19) has been a global epidemic since March 2020. COVID-19 disease due to severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection has spread to more than 200 countries. The coronavirus attacks tissue through Angiotensin-converting enzyme 2 (ACE2). The lungs and cardiovascular structures are therefore the main organs affected by COVID-19 [4-8]. Myocarditis-related problems are an important clinical problem in patients with COVID-19. In the literature, it has been reported that highly sensitive cardiac troponin I (Hs-cTnI), which indicates myocardial damage, is elevated in 12%-15% of patients, and cardiac involvement reaches up to 31% in patients with severe COVID-19 [9-11]. Clinical information, endomyocardial biopsy (EMB), and cardiac magnetic resonance imaging (CMR) are used in the diagnosis of COVID-19 myocarditis [4,7].

This study aimed to compare the laboratory, echocardiography, and CMR imaging features and clinical findings in patients with COVID-19-associated myocarditis and NSVM, and to determine the similarities and differences between the features.

METHODS

Overview

The local ethics committee approved this retrospective study and waived the need for informed consent because of the retrospective evaluation of anonymized medical data. All CMR studies were analyzed by a board-certified radiologist with extensive CMR experience (>9 years).

In the NSVM group, clinical, laboratory, and CMR characteristics of 97 patients who were found to have NSVM in routine CMR examination between January 2016 and January 2020 were analyzed retrospectively. Patients were evaluated using CMR, echocardiography, laboratory, and clinical findings.

Eighty-three patients with COVID-19 confirmed by polymerase chain reaction (PCR) test who underwent CMR between June 2020 and March 2022 were retrospectively analyzed. The patients were evaluated based on clinical findings, laboratory values, echocardiography, and CMR imaging features. To calculate the range of contact and CMR, we assumed the date of admission to the hospital as the first day of probable COVID-19 diagnosis. Baseline characteristics and hospital treatment details were obtained from patients' medical records

CMR Protocols

All examinations are planned with standardized image interpretation and post-processing in CMR 2020 update [12]. CMR studies were performed on a 1.5 Tesla scanner (Aera®, Siemens Healthineers, Erlangen, Germany). Patients were scanned with the electrocardiogram (ECG)- triggered using a 16-channel surface phased array of body coils. After standard localizer scan images, breath-hold cine images were acquired in the 2-chamber and 4-chamber views for ventriculus. We administered a 0.2 mmol/kg intravenous injection of contrast agents Dotarem (Gadoterate meglumine; Guerbet LLC, Villepinte, France).

CMR Imaging Analysis

CMR images were acquired from our picture archive system. CMR examinations were evaluated by a radiologist who has a cardiac imaging certificate with extensive CMR experience (>9 years). Left ventriculi (LV) ejection fraction (EF), stroke volume (SV), mass, and cardiac output (CO) were calculated automatically over functional sequences in multi-sectional 2 and 4 chamber images. Contrast enhancement in late gadolinium enhancement (LGE) images were marked with the AHA 17 segment model. The presence of myocardial fibrosis was analyzed as present or absent regardless of segment size. Myocardial edema was evaluated on short tau inversion recovery (STIR) and T2 weighted image (WI) images. A comparison was made with the muscle tissue included in the section for the presence of myocardial edema. STIR and T2WI signals increased 2 times more than muscle tissue was considered myocardial edema. Current Lake Louise criteria were used for the diagnosis of myocarditis [13]. T1 and T2 mapping images were not included in the study because they were not available in all patients.

Laboratory Analysis

We obtained laboratory data from the patient information system of our hospital database. We evaluated High-sensitivity cardiac troponin I (Hs-cTnI), and C-reactive protein (CRP). Hs-cTnI levels greater than 3 pg/ml were considered significant.

Statistical Analysis

All statistical analysis was performed using SPSS version 23.0 (IBM statistics, Armonk, New York). Categorical variables were expressed as counts (percentage), and continuous variables as mean ± SD. Qualitative values were reported as percentages. For normally distributed data, the unpaired T-test was used under the non-equal variances condition, and the Wilcoxon test otherwise. Comparison between the 2 groups was performed using an unpaired Student's t-test (for normal distribution) or Mann-Whitney U test (for non-normal distribution). For all tests, significance was set to $p < 0.05$.

RESULTS

A total of 97 patients with nonspecific viral myocarditis (NSVM) according to the Lake Louise criteria were included in the study. Fifty-Six of these patients with hypertension (31), diabetes mellitus (12), a history of coronary artery disease (10), and inadequate CMR images (3) were excluded from the study. As a result, 41 NSVM patients were included in the study, their mean age was 43 years (24 years-66 years), and 26 of them were women. The reasons for admission were fatigue (35), palpitation (22), rhythm disturbance (12), dyspnea (7), and syncope (3). The time between contact and CMR could not be evaluated because the acute infections of the patients were usually unclear. In the pericardial examination, pericardial thickness increased by an average of 3.4 mm (3 mm - 5 mm) in 14 (36%) patients. In NSVM cases, ECG examinations showed bundle branch block in 2 (4%) patients and T inversion in 8 (19%) patients. echocardiography

examination revealed minimal hypokinesia in 3 (7%) patients and a diffuse increase in myocardial echogenicity in 2 (4%) patients. Laboratory values were within normal limits.

Gender	Age (year)	LV EF (%)	LV SV (ml)	LV CO (L/min)	LV mass (gr)	Number of LGE segments	The time between PCR and CMR (day)
Male	56	54	78	7	163	1	250
Woman	45	56	86	5,5	123	2	140
Woman	55	49	52	3,8	90	2	210
Woman	45	59	71	5,8	94	2	362
Male	26	49	85	6,3	122	3	260
Male	66	43	87	6,3	155	3	170
Woman	55	38	56	3,7	69	5	180
Male	26	62	106	6,2	144	1	254
Male	45	57	88	5,3	161	2	145
Male	32	59	102	6,6	120	1	124
Male	25	50	87	6,5	131	3	156
Woman	30	55	65	7	96	3	189
Male	61	55	65	4	124	3	231
Male	25	54	101	6,6	156	3	256
Male	32	40	54	3,6	124	5	195
Woman	22	63	63	5	89	1	257
Male	36	52	84	5,8	116	5	167
Male	35	53	99	8,3	163	4	201
Male	56	36	56	3,2	127	2	94
Woman	24	55	68	5,4	102	2	157
Male	54	41	75	7,5	188	3	144
Male	59	35	42	2,7	63	4	282
Male	49	50	80	5,3	137	2	104
Male	22	46	65	6,1	163	3	301
Male	17	58	94	6,1	140	6	45
MEAN	39,92	50,76	76,36	5,584	126,4	2,84	194,96

Table 1: The CMR characteristics of patients with COVID-19 myocarditis and the time between PCR and CMR are shown in the table.

Note: Left ventriculi (LV); ejection fraction (EF); stroke volume (SV); cardiac output (CO); polymerase chain reaction (PCR); Cardiac magnetic resonance imaging (CMR)

In the CMR examination of 83 patients diagnosed with COVID-19 by PCR, 25 (30%) patients were accepted as probable myocarditis according to the Lake Louise criteria and included in the study. 58 patients' CMR had no LGE, and other findings are not according to myocarditis. The mean age of the patient was 40.88 years (22 years - 61 years), and seven patients were female (Table 1). Fifteen patients were treated as inpatients in the hospital. In 13 (52%) hospitalized patients, Hs-cTnI was higher at 18 pg/ml (8-34) on average and CRP at 25 mg/L (8-65) during the acute infection period. Oxygen therapy with a mask was required for an average of 40 hours (10 hours - 45 hours) in 4 patients. All patients were considered moderately infected with COVID-19, as respiratory and life support were not needed. Remdesivir was used in 22 patients and remdesivir with hydroxychloroquine in 18 patients. Antiviral treatment was not applied to three patients. The reasons for admission after recovery were chest pain (17), palpitation (12), dyspnea (9), and rhythm disturbance (5). The mean time between contact and CMR was 192,88 days (45 days - 362 days). Concurrent laboratory data with CMR examination were normal in patients. A mean increase of 4.1 mm (3.2 mm - 7 mm) was detected in 8 (32%) patients in the pericardium examination in COVID-19 cases. ECG examinations performed simultaneously with CMR revealed ST depression in seven patients and T inversion in two patients. The mean time between contact and echocardiography examination was 175, 4 days (35 days - 310 days). Echocardiography examinations and myocardial echoes were normal. No significant pathology was detected in the functional data.

On CMR examination on day 45 after diagnosis of COVID-19, an increase in signal consistent with myocarditis was observed in the STIR sequence (Figure 1). In PSIR sequences taken in the late phase, an average of 2.8 LGE for COVID-19 myocarditis was observed (in 1-6 segments) (Figure 2 and 3) and an average of 2.4 (1-7 segments) LGE

for NSVM (Figure 4). Involvement of myocardial inferior and septal segments was common in both groups of myocarditis patients. No contraction pathology was observed in the cine images. Heart functional data were similar in both groups compared to the normal group. No statistically significant difference was observed. Constrictive pericarditis was not observed in patients with pericarditis sequela imaging findings.

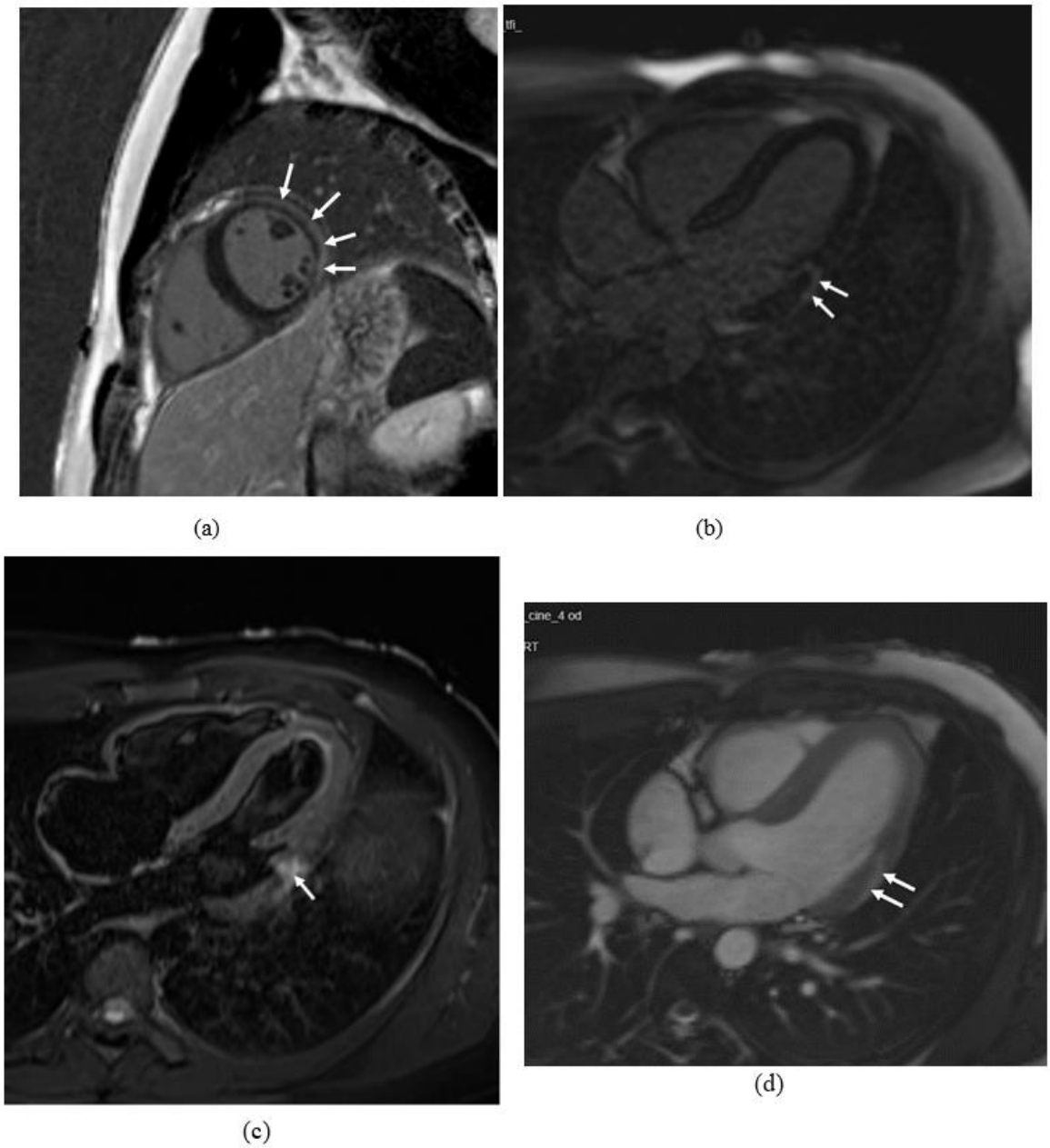

Figure 1: 25-years-old male post-COVID-19 patient with myocarditis. on the 45th day after PCR positivity, myocarditis is showing on the left ventricular lateral wall in 2 chamber 2D-phase-sensitive-inversion-recovery (2D-PSIR) (a), and 4 chamber PSIR (b) images in the CMR examination. (arrows). 4 chamber Short-tau-inversion-recovery (STIR) (c) and 4 chambers Steady-state free precession (SSFP) (d) images show regional myocardial edema (arrows).

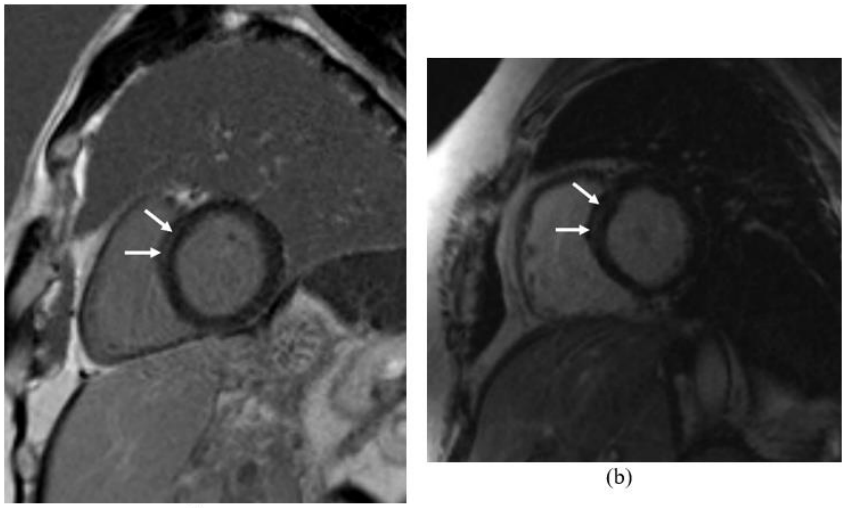

Figure 2: 2-chamber PSIR images show mid myocardial late gadolinium contrast (LGE) in the interventricular septum (A) in a 52-years-old man (a) and a 60-year-old woman (b) with COVID-19-associated myocarditis (arrows).

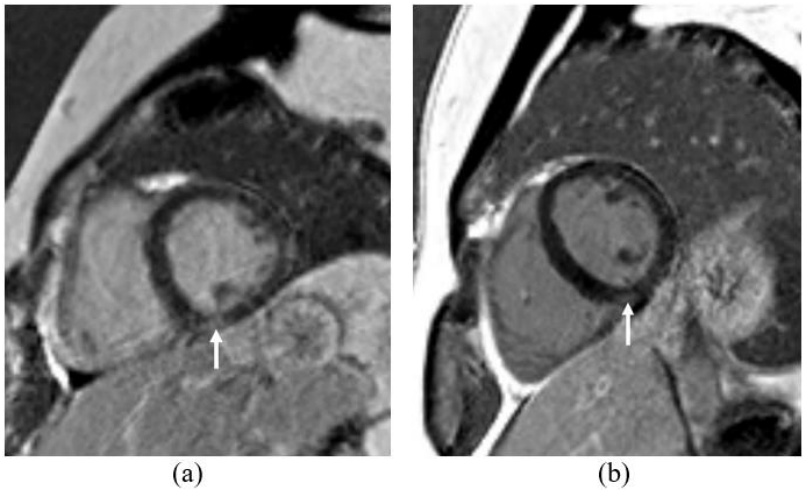

Figure 3: Focal late gadolinium potentiation (LGE) was observed in 2-chamber PSIR images in cases of a 43-years-old female (a) and a 30-years-old male (b) with COVID-19-associated myocarditis (arrows).

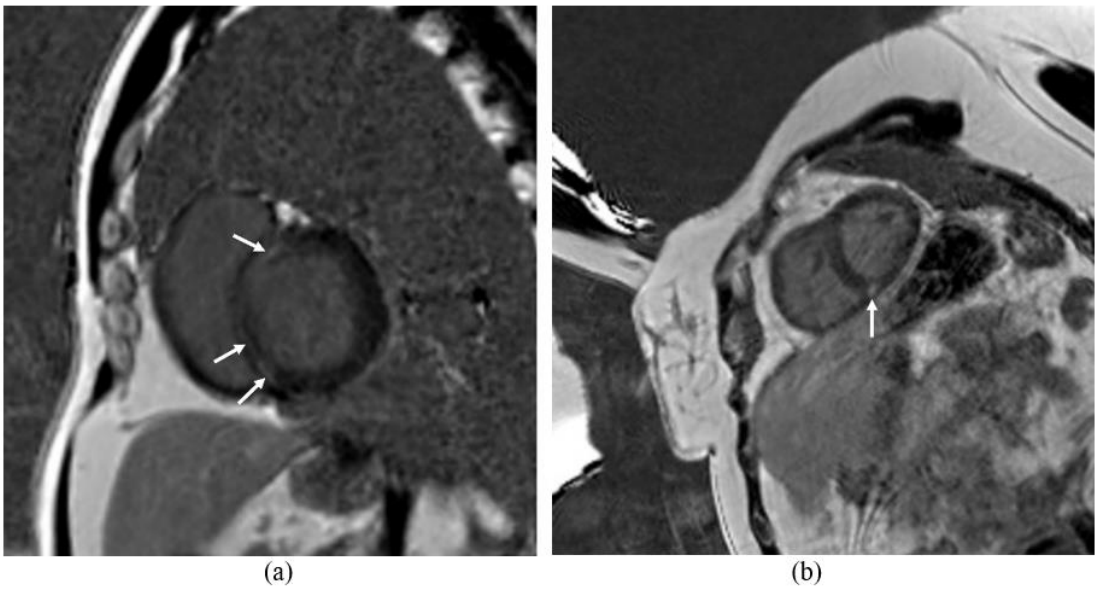

Figure 4: 2-chamber PSIR sequences of a 43-years-old female (a) and a 30-years-old man (b) NSVM patients show focal late gadolinium potentiation (LGE) in the septum which is a non-ischemic myocardial injury (arrows).

There was no statistical difference between laboratory and CMR data between NSVM and COVID-19 myocarditis patients (p = 0.002). LGE-detected segments were similar in both groups. When the functional data of both groups were compared no statistically significant difference was observed (p = 0.062). Myocarditis cases were compared in terms of cardiac functions, and no change was observed in functional data. Myocarditis did not cause a statistically significant deterioration in cardiac functions.

DISCUSSION

In this study, cases of COVID-19-associated myocarditis and nonspecific viral myocarditis (NSVM) were evaluated in comparison with clinical, laboratory, and imaging findings. In our study, the frequency of myocarditis (25%) in cardiac symptomatic patients with COVID-19 was found to be like that in the literature. When the patients were evaluated together with their CMR, echocardiography, laboratory, and clinical data, no significant difference was observed between the NSVM and COVID-19 myocarditis groups. The segments involved in myocarditis patients were similar. We did not observe a statistically significant difference between the myocarditis groups due to cardiac functional values and preserved systolic functions. Cardiac functional values were within normal limits. Our study showed that COVID-19 myocarditis and NSVM imaging and laboratory data were similar; in addition, they did not cause deterioration in cardiac functional values.

Huang et al. also found in their study that ventricular functions were preserved in patients with myocarditis [9,14]. Fulminant myocarditis secondary to acute COVID-19 shows severe functional deterioration, and left ventricular functions are within normal limits in many studies after recovery [9]. Our study showed the importance of PCR positivity in the diagnosis of COVID-19 since there was no difference between imaging and laboratory data between COVID-19 myocarditis and NSVM. In the differential diagnosis of COVID-19 myocarditis, a PCR test and infection history are required.

Caforio et al. defined our current knowledge on the diagnosis and treatment of myocarditis using endomyocardial biopsy (EMB) [15-17]. The success of myocarditis treatment depends on the etiologic diagnosis to distinguish between infectious and immune-mediated disease [15,16]. Early intervention with intravenous immunoglobulins has been the most effective treatment for inflammatory viral myocarditis. With the COVID-19 pandemic, the coronavirus is an important factor in the etiology of myocarditis. Our study is useful in detecting the etiology of NSVM in CMR examinations. Dilated cardiomyopathy, another possible outcome of myocarditis, also requires an etiologic diagnosis [18].

This study had some limitations. First, the sample size was small. Second, the included patients had moderate COVID-19; therefore, this study does not include severe and critical COVID-19 patients. Possible myocarditis was included in our study because there was no pathological evaluation. One of our clinical limitations was the lack of CMR examination and long-term clinical follow-ups in the acute infection period. Another limitation is the lack of early pandemic hospital cardiac biomarker data in 12 (55%) patients. In addition, patient selection was not unbiased, as all CMR studies were obtained retrospectively and performed with clinical indications. A major limitation was that the CMR examination was performed by a single radiologist.

Therefore, the inter and intra-observer reliability could not be evaluated.

As seen in the results of our study, COVID-19 myocarditis and NSVM have similar imaging and laboratory data. Cardiac functions were preserved in myocarditis cases and were like the normal group. This study should be extended prospectively with EMB data and a larger patient group.

CONFLICT OF INTERESTS

All authors declare no conflict of interest.

Financial Support

The authors have no relevant financial information to disclose.

Authors' Contributions

Initials of the contributing authors were listed in brackets after the relevant parts of the research: Literature search (SA, KAS, ESB), study design (SA, KAS, ESB), legislative applications (SA), data collection (SA, EÖ) supervision and quality control (CG), statistical advice (SA, KAS, ESB), statistical data analysis (SA), data interpretation (SA, EÖ, CG), drafting the manuscript (SA). All authors were involved in the writing and critical revision of the manuscript and approved the final version.

SA took responsibility for the paper as a whole.

REFERENCES

1. Leone O, Pieroni M, Rapezzi C, et al. (2019) The spectrum of myocarditis: From pathology to the clinics. Virchows Archiv : An International Journal of Pathology 475(3): 279-301.
2. Ammirati E, Veronese G, Bottiroli M, et al. (2021) Update on acute myocarditis. Trends in Cardiovascular Medicine 31(6): 370-379.
3. Olejniczak M, Schwartz M, Webber E, et al. (2020) Viral myocarditis-incidence, diagnosis and management. Journal of Cardiothoracic and Vascular Anesthesia 34(6): 1591-1601.
4. Friedrich MG, Marcotte F (2013) Cardiac magnetic resonance assessment of myocarditis. Circulation: Cardiovascular Imaging 6(5): 833-839.
5. Tanacli R, Doeblin P, Götze C, et al. (2021) COVID-19 *vs.* classical myocarditis associated myocardial injury evaluated by cardiac magnetic resonance and endomyocardial biopsy. Frontiers in Cardiovascular Medicine 8: 737257.
6. Giustino G, Croft LB, Stefanini GG, et al. (2020) Characterization of myocardial injury in patients with COVID-19. Journal of the American College of Cardiology 76(18): 2043-2055.
7. Adeboye A, Alkhatib D, Butt A, et al. (2022) A review of the role of imaging modalities in the evaluation of viral myocarditis with a special focus on COVID-19 related myocarditis. Diagnostics (Basel) 12(2): 549.
8. Huang L, Zhao P, Tang D, et al. (2020) Cardiac Involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. Journal of the American College of Cardiology Cardiovascular Imaging 13(11): 2330-2339.
9. Urmeneta Ulloa J, Martínez de Vega V, Salvador Montañés O, et al. (2021) Cardiac magnetic resonance in recovering COVID-19 patients. Feature tracking and mapping analysis to detect persistent myocardial involvement. International Journal of Cardiology. Heart & Vasculature 36: 100854.
10. Chapman AR, Bularga A, Mills NL (2020) High-sensitivity cardiac troponin can be an ally in the fight against COVID-19. Circulation 141(22).

11. Wu Z, McGoogan JM (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA 323(13): 1239-1242.
12. Kramer CM, Barkhausen J, Bucciarelli-Ducci C, et al. (2020) Standardized cardiovascular magnetic resonance imaging (CMR) protocols: 2020 update. Journal of Cardiovascular Magnetic Resonance 22: 17.
13. Ferreira VM, Schulz-Menger J, Holmvang G, et al. (2018) Cardiovascular magnetic resonance in non-ischemic myocardial inflammation: Expert recommendations. The Journal of American College of Cardiology 72(24): 3158-3176.
14. Huang C, Wang Y, Li X, et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan China. The Lancet 395: 497-506
15. Rose NR (2016) Viral myocarditis. Current Opinion of Rheumatology 28(4): 383-389.
16. Reinthaler M, Empen K, Herda LR, et al. (2015) The effect of a repeated immunoadsorption in patients with dilated cardiomyopathy after recurrence of severe heart failure symptoms. Journal of Clinical Apheresis 30(4): 217-223.
17. Kindermann I, Barth C, Mahfoud F, et al. (2012) Update on myocarditis. Journal of the American College of Cardiology 59(9): 779-792.
18. Pankuweit S, Lüers C, Richter A, et al. (2015) Influence of different aetiologies on clinical course and outcome in patients with dilated cardiomyopathy. European Journal of Clinical Investigation 45(9): 906-917.