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ORIGINAL ARTICLE

Cardiac involvement in coronavirus disease 2019 assessed by cardiac magnetic resonance imaging: a meta-analysis

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Abstract

In this systematic review and meta-analysis, we sought to evaluate the prevalence of cardiac involvement in patients with COVID-19 using cardiac magnetic resonance imaging. A literature review was performed to investigate the left ventricular (LV) and right ventricular (RV) ejection fraction (EF), the prevalence of LV late gadolinium enhancement (LGE), pericardial enhancement, abnormality on T1 mapping, and T2 mapping/T2-weighted imaging (T2WI), and myocarditis (defined by modified Lake Louis criteria). Pooled mean differences (MD) between COVID-19 patients and controls for LVEF and RVEF were estimated using random-effects models. We included data from 10.462 patients with COVID-19, comprising 1.010 non-athletes and 9.452 athletes from 29 eligible studies. The meta-analysis showed a significant difference between COVID-19 patients and controls in terms of LVEF [MD = − 2.84, 95% confidence interval (CI) − 5.11 to − 0.56, $p < 0.001$] and RVEF (MD = − 2.69%, 95% CI − 4.41 to − 1.27, $p < 0.001$). However, in athletes, no significant difference was identified in LVEF (MD = − 0.74%, 95% CI − 2.41 to − 0.93, $p = 0.39$) or RVEF (MD = − 1.88%, 95% CI − 5.21 to 1.46, $p = 0.27$). In non-athletes, the prevalence of LV LGE abnormalities, pericardial enhancement, T1 mapping, T2 mapping/T2WI, myocarditis were 27.5% (95%CI 17.4–37.6%), 11.9% (95%CI 4.1–19.6%), 39.5% (95%CI 16.2–62.8%), 38.1% (95%CI 19.0–57.1%) and 17.6% (95%CI 6.3–28.9%), respectively. In athletes, these values were 10.8% (95%CI 2.3–19.4%), 35.4% (95%CI − 3.2 to 73.9%), 5.7% (95%CI − 2.9 to 14.2%), 1.9% (95%CI 1.1–2.7%), 0.9% (0.3–1.6%), respectively. Both LVEF and RVEF were significantly impaired in COVID-19 patients compared to controls, but not in athletes. In addition, the prevalence of myocardial involvement is not negligible in patients with COVID-19.

Keywords COVID-19 · Cardiac involvement · Meta-analysis

Abbreviations

ACE 2	Angiotensin converting enzyme 2
COVID-19	Coronavirus disease 2019
CI	Confidence interval
CK-MB	Creatinine kinase myocardial band
CMR	Cardiac magnetic resonance
SARS-CoV-2	Severe acute respiratory syndrome-coronavirus-2
LGE	Late gadolinium enhancement
LV	Left ventricular
MD	Mean difference
MRI	Magnetic resonance imaging
RV	Right ventricular
T2WI	T2 weighted image

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Introduction

Coronavirus disease-2019 (COVID-19), caused by the novel severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), has become a global pandemic [1]. Cardiac involvement is a serious complication in patients with COVID-19 and elevated serum troponin levels are observed in 17–36% of the COVID-19 patients [2]. Cardiac involvement includes a variety of clinical manifestations, such as acute myocardial injury, heart failure, pulmonary embolism, myocarditis/pericarditis, and ventricular arrhythmias [3]. The mechanism of cardiac involvement is uncertain, but it may be related to endothelial dysfunction, systemic cytokine-mediated injury, or stress-related cardiomyopathy [4, 5]. Importantly, COVID-19 patients with cardiac involvement have worse clinical outcomes than those without cardiac involvement [6]. Therefore, elucidation of the imaging characteristics indicative of cardiac involvement may contribute to effective risk stratification for patients with COVID-19.

Cardiac magnetic resonance (CMR) imaging has emerged as a non-invasive imaging modality to accurately assess ventricular function, myocardial edema, and myocardial injury. Recently, several studies have demonstrated the utility of CMR imaging in detecting cardiac involvement in COVID-19 [7–11]. However, heterogeneity of data exists among these studies regarding the severity and prevalence of cardiac involvement detected by CMR imaging. Therefore, this study aimed to determine the prevalence of cardiac abnormalities detected by CMR imaging in patients with COVID-19.

Materials and methods

Literature search

The electronic database search formulas for PubMed, Web of Science Core Collection, Cochrane Advanced Search, and EMBASE are listed in the appendix (Supplemental material). Databases from the end of 2021 were searched on January 20, 2022. In addition, two review authors (SK and MA) independently performed additional manual searches. Potential research articles were screened and subjected to full-test scrutiny (KS, MA). When two authors could not resolve a disagreement, a third author participated in the discussion. The protocol for this systematic review, which complies with the Meta-analyses of Observational Studies in Epidemiology guidelines, has been registered on the website of the University Medical Informatics Network (UMIN000044237UMIN).

Eligibility criteria and outcomes

Publications including the CMR data of patients recovered from COVID-19 were screened. All study design types were used, including prospective studies, retrospective studies, and case series. However, we did not include case reports or case series with fewer than five cases because they are not suitable for estimating the frequency of adverse events. Eligible papers were written in English and both full articles and conference abstracts were accepted. Key study characteristics, such as author name, publication year, country of origin, and the number of COVID-19 patients, were extracted by two review authors (SK, MA). In addition, the outcome data were read by the authors. The main outcomes were mean averages of LVEF and RVEF, the prevalence of LV LGE, pericardial enhancement, abnormal T1 (native T1 time) mapping, abnormal T2 mapping/ T2 weighted image (T2WI), and myocarditis (defined by the modified Lake Louise criteria) [12]. LVEF and RVEF were compared between COVID-19 patients and controls. If one study had two cohorts (e.g., symptomatic vs. asymptomatic; LGE (+) vs. LGE (-)), we used patient data with abnormal findings and compared them to those of the controls (e.g., Brito 2021 symptomatic; Altay 2021 LGE (+); Chen 2021 troponin (+)). As the prevalence of cardiac involvement may differ between non-athletes and athletes, we analyzed these populations separately. In addition, the multisystem inflammatory syndrome is a different pathophysiologic response to SARS-CoV-2 exposure and is different (with a much different time course) from the convalescent phase post-acute COVID-19. We did not include multisystem inflammatory syndromes in our analysis [13].

Statistical analysis

The frequency of each cardiac abnormality was pooled using a random-model meta-analysis using the generic inverse variance method (RevMan ver 5.4. Cochrane Collaboration, London, UK). The standard error was calculated using the Agrestia method [14]. Random model meta-analysis was performed using RevMan 5.41 (Cochrane Collaboration, London, UK). LVEF and RVEF were expressed as median (range) in both COVID-19 patients and controls. Heterogeneity was indicated by I^2, with 0% indicating no heterogeneity and 100% indicating the strongest heterogeneity.

Results

Study characteristics

Of the 738 candidate studies, we finally selected 29 eligible reports [7–11, 15–38] (Fig. 1). Four of the studies presented two cohorts [8, 10, 21, 31]; therefore, we included a total of 33 independent cohorts. Among the 29 included studies, nine were from the USA [8, 15, 20, 22, 24, 32, 36–38], six were from China [10, 11, 16, 18, 21, 30], three each from the UK [19, 22, 26] and Germany [7, 23, 28, 35], two each from Italy [9, 27] and Turkey [29, 31], and one each from Poland [17], Norway [34], Hungary [33] and Spain [25]. The publication year was 2020 or 2021 (**Table 1**). Ten studies enrolled athletes recovered from COVID-19 [8, 15, 17, 20, 24, 32, 33, 36–38] and one study enrolled suspected myocarditis with COVID-19 [9]. Finally, 10.462 patients with COVID-19, including 1010 non-athletes and 9.452 athletes, and 746 controls were included in our analysis. A 1.5 T MR scanner was used in 15 studies [8, 9, 11, 15, 17, 22–26, 28, 29, 33–35] and a 3.0 T MR scanner was used in six studies [7, 10, 16, 18, 21, 30], Both 1.5 T and 3.0 T scanners were used in one study [20] and data regarding MR scanners were not provided in seven studies [19, 27, 31, 32, 36–38]. As the myocardial native T1 time substantially differs between different magnetic field strengths and sequences [39], we investigated the number patients with abnormal T1 time, rather than those with absolute value of native T1 time, among the nine studies presenting the prevalence of patients with abnormal native T1 times [7–9, 11, 17, 22, 26, 27, 32].

Meta-analysis of CMR imaging findings in patients with COVID-19

LVEF and RVEF were measured in 27 cohorts of 1414 COVID-19 patients. In COVID-19 patients, the median LVEF was 60.3% (range: 50.3–67.1%), and the median RVEF was 54.3% (range: 36.5–61.1%). In non-athlete, the median LVEF was 60.8% (range: 50.3–67.0%), and the median RVEF was 54.7% (range: 36.5–61.1%). In athlete, the median LVEF was 60.0% (range: 57.0–60.3%), and the median RVEF was 54.6% (range: 53.0–56.0%). In the controls, the median LVEF and RVEF were 61.3% (range: 57.0–67.0%) and 57.7% (range: 45.0–64.0%), respectively. The meta-analysis showed a significant difference between COVID-19 patients and controls in terms of LVEF [mean difference (MD) = − 2.84, 95% confidence interval (CI) − 5.11 to − 0.56, $p < 0.001$] and RVEF (MD = − 2.69%, 95% CI − 4.41, − 1.27, $p < 0.001$) (Fig. 2). However, in athletes, no significant differences were identified in LVEF (MD = − 0.74%, 95% CI − 2.41 to − 0.93, $p = 0.39$) and RVEF (MD = − 1.88%, 95% CI − 5.21 to 1.46, $p = 0.27$) (Fig. 3). Figure 4 illustrates the results of the meta-analysis of LGE of LV myocardium, pericardial enhancement, abnormal T1 mapping, and T2 mapping/T2WI in non-athletes.

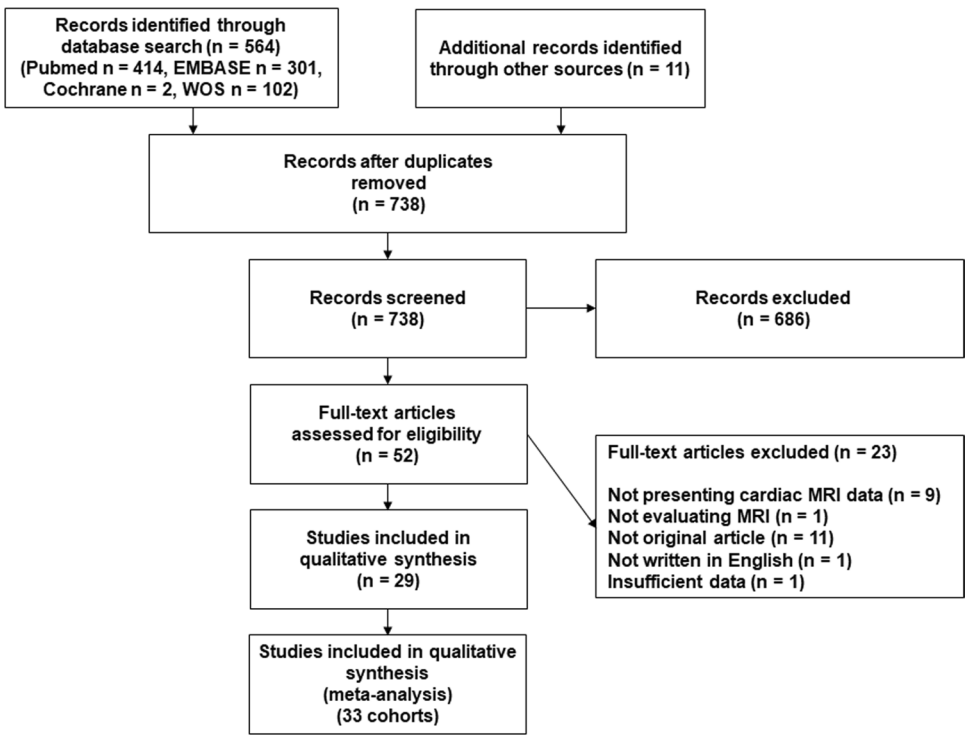

Fig. 1 PRISMA flow diagram

Table 1 Characteristics of 29 eligible studies

Cohort	Country	MRI machine	Number of patients	Patient characteristics	Time from diagnosis (symptom) to MRI	LVEF, %	RVEF, %	LGE of LV, *N* (%)	Abnormal T1 map, *N* (%)	Abnormal T2 map/T2WI, *N* (%)	Pericardial enhancement, *N* (%)	Myocarditis, *N* (%)
Brito 2021	USA	1.5 T	37 asymptomatic; 11 symptomatic	Student athlete recovered from COVID-19	27 days	59.09 (54.79–61.64) % in asymptomatic; 60.32 (56.66–63.33) % in symptomatic	54.60% (47.55–59.77) in asymptomatic; 51.32% (50.82–57.22) in symptomatic	0 (0%) in asymptomatic; 1 (3%) in symptomatic	1 (9%) in asymptomatic; 8 (22%) in symptomatic	0 (0%) in asymptomatic; 0 (0%) in symptomatic	9 (82%) in asymptomatic; 10 (27%) in symptomatic	0 (0%)
Clark 2021	USA	1.5 T	59	COVID-19–positive athletes	21.5 days	60 (56–63) %	53 (50–56) %	1 (2%)	N/A	N/A	1 (2%)	4 (15%)
Huang 2020	China	3.0 T	26 CMR abnormal; 11 CMR normal	Patients recovered from COVID-19 (abnormal findings on CMR)	48 days in CMR abnormal; 50 days in CMR normal	60.7 ± 6.4% in CMR abnormal; 64.3 ± 5.8% in CMR normal	36. 5 ± 6.1% in CMR abnormal; 41.1 ± 8.6% in CMR normal	8 (26%) in CMR abnormal; N/A in CMR normal	N/A	N/A	N/A	N/A
Li 2021	China	3.0 T	40	Patients recovered from COVID-19	158 days	62.6 ± 5.2%	54.7 ± 5.8%	1 (3%)	N/A	N/A	N/A	N/A
Pan 2021	China	3.0 T	21	Patients recovered from COVID-19	N/A	61.6 ± 6.5%	54.7 ± 7.1%	N/A	N/A	N/A	N/A	N/A
Puntmann 2020	Germany	3.0 T	100	Patients recovered from COVID-19	71 days	57 ± 6%	54 ± 7%	32 (32%)	73 (73%)	60 (60%)	22 (22%)	N/A
Raisi-Estabragh 2021	UK	N/A	70	UK Biobank participants with positive COVID-19 PCR	N/A	59.6 ± 6.5%	61.1 ± 6.2%	N/A	N/A	N/A	N/A	N/A
Wang 2021	China	3.0 T	44	Patients recovered from COVID-19	100.8 days in LGE positive; 103.3 days in LGE negative	64.3 ± 5.9% in LGE positive; 62.2 ± 4.4% in LGE negative	59.5 ± 8.6% in LGE positive; 56.6 ± 8.3% in LGE negative	13 (29.5%)	N/A	N/A	N/A	N/A
Esposito 2020	Italy	1.5 T	10	COVID-19 patients suspected for myocarditis	N/A	N/A	N/A	3 (30%)	8 (100%)	8 (100%)	N/A	8 (80%)
Malek 2021	Poland	1.5 T	26	Elite athletes positive for COVID-19 PCR	32 days	61 (60–62) %	59 (57–60) %	1 (4%)	0 (0%)	4 (15%)[a]	N/A	0 (0%)
Ng 2020	China	1.5 T	16	Patients recovered from COVID-19	56 days	59 (56–65) %	53 (48–57) %	3 (19%)	4 (25%)	1 (5%)	N/A	N/A

Table 1 (continued)

Cohort	Country	MRI machine	Number of patients	Patient characteristics	Time from diagnosis (symptom) to MRI	LVEF, %	RVEF, %	LGE of LV, *N* (%)	Abnormal T1 map, *N* (%)	Abnormal T2 map/T2WI, *N* (%)	Pericardial enhancement, *N* (%)	Myocarditis, *N* (%)
Starekova 2021	USA	1.5 T or 3.0 T	145	Competitive student athletes recovered from COVID-19	16 days	58 ± 5%	54 ± 6%	42 (29%)	N/A	N/A	N/A	2 (1.4%)
Altay 2021	Turkey	N/A	15	Symptomatic patients with COVID-19	81 days	51 ± 16%	45 ± 12%	7 (46%)	N/A	N/A	N/A	N/A
Breitbart 2021	Germany	1.5 T	56	Post COVID-19 patients without previous heart diseases	71 days	62.3 ± 5.0%	N/A	7 (12.5%)	N/A	N/A	N/A	1 (2%)
Çakmak 2021	Turkey	1.5 T	64	Patients with cardiac symptoms after recovering from COVID-19	71 days	67 (58–76) % in cardiac involvement (-); 62 (30–72) % in cardiac involvement (+)	N/A	46 (69%)	N/A	N/A	11 (17%)	0 (0%)
Chen 2021	China	3.0 T	25	Confirmed COVID-19 and at least one marker of cardiac involvement	6.7 ± 5.7 days	64.6 ± 4.6%	N/A	N/A	N/A	N/A	N/A	N/A
Daniels 2021	USA	N/A	1597	Athletes with COVID-19	N/A	N/A	N/A	36 (2.3%)	5 (0.3%)	N/A	N/A	37 (2.3%)
Galea 2021	Italy	N/A	27	Active COVID-19 and suspected cardiac involvement	20 (13.5–31.5) days	50.3 ± 7.2%	48.8 ± 8.2%	12 (44.4%)	11 (40.7%)	14 (51.9%)	2 (7.4%)	9 (33%)
Joy 2021	UK, USA	1.5 T	149	Patients from COVID consortium	N/A	67.1 ± 4.9%	N/A	13 (8.7%)	6 (4%)	9 (6%)	N/A	N/A
Kotecha 2021	UK	1.5 T	148	All patients admitted with a diagnosis of COVID-19	68 (39–103) days	67 ± 11%	61 ± 9%	70 (47.3%)	19 (12.8%)	4 (2.7%)	N/A	40 (27%)
Kravchenko 2021	Germany	1.5 T	41	SARS-CoV-2 infection who had persistent CCS symptoms	103 (88–158) days	62 ± 5%	N/A	3 (7.3%)	N/A	N/A	N/A	0 (0%)

Table 1 (continued)

Cohort	Country	MRI machine	Number of patients	Patient characteristics	Time from diagnosis (symptom) to MRI	LVEF, %	RVEF, %	LGE of LV, *N* (%)	Abnormal T1 map, *N* (%)	Abnormal T2 map/T2WI, *N* (%)	Pericardial enhancement, *N* (%)	Myocarditis, *N* (%)
Myhre 2021	Norway	1.5 T	58	Survivors from the prospective COVID MECH study	175 (105–217) days	58.7 ± 7.4%	57.3 ± 6.3%	N/A	N/A	N/A	N/A	N/A
Rajpal 2021	USA	1.5 T	26	Competitive athletes referred to the sports medicine clinic after testing positive for COVID-19	11–53 days	N/A	N/A	12 (46.2%)	N/A	N/A	N/A	4 (15%)
Szabó 2021	Hungary	1.5 T	147	Athletes after SARS-CoV-2 infection	Median of 32 days	57 (54–60)%	56 (53–59)%	N/A	N/A	N/A	N/A	1 (0.6%)
Tanacli 2021	Germany	1.5 T	32	Persistent cardiac symptoms after a COVID-19 infection	95 ± 59 days	62 ± 10%	54 ± 8%	6 (18.8%)	N/A	N/A	3 (9.4%)	3 (9%)
Urmeneta 2021	Spain	1.5 T	57	Post-COVID-19 patients	81 ± 27 days,	61 ± 10%	60 ± 9%	13 (22.8%)	N/A	N/A	2 (3.5%)	N/A
Martinez 2021	USA	N/A	789 (30 MRI performed)	Professional athletes	N/A	N/A	N/A	N/A	N/A	N/A	N/A	5 (0.6%)
Moulson 2021	USA	N/A	3018 (317 MRI performed)	Collegiate athletes	N/A	N/A	N/A	N/A	N/A	N/A	N/A	21 (0.7%)
Petek 2021	USA	N/A	3597 (44 MRI performed)	Young competitive athletes	N/A	N/A	N/A	N/A	N/A	N/A	N/A	5 (0.1%)

LVEF and RVEF were presented as mean ± standard deviation or median (interquartile range). Myocarditis was diagnosed by modified Lake Louise Criteria

COVID-19 coronavirus diease-2019, *CMR* cardiac magnetic resonance, *IQR* interquartile range, *LGE* late gadolinium enhancement, *LVEF* left ventricular ejection fraction, *MRI* magnetic resonance imaging, *RVEF* right ventricular ejection fraction, *T2WI* T2 weighted image

[a]Three patients had abnormality in T2WI and one patient had abnormality in T2 mapping

The prevalence of abnormalities of LV LGE, pericardial enhancement, T1 mapping, T2 mapping/T2WI were 27.5% (95%CI 17.4–37.6%), 11.9% (95%CI 4.1–19.6%), 39.5% (95%CI 16.2–62.8%), 38.1% (95%CI 19.0–57.1%), respectively (Fig. 4). In athletes, these values were 10.8% (95%CI 2.3–19.4%), 35.4% (95%CI − 3.2 to 73.9%), 5.7% (95%CI − 2.9 to 14.2%), 1.9% (95%CI 1.1–2.7%), respectively (Fig. 5). Figure 6 illustrates the prevalence of myocarditis, as defined by the modified Lake Louise criteria. The prevalence was 17.6% (95%CI 6.3–28.9%) for non-athletes and 0.9% (0.3–1.6%) for athletes.

Discussion

The main findings of this study are as follows: both LVEF and RVEF were significantly reduced in non-athlete patients with COVID-19 compared with controls, whereas both parameters were not significantly reduced in athletes with COVID-19. There was a moderate prevalence of LV LGE, pericardial enhancement, abnormal T1 mapping, T2 mapping/T2WI, and myocarditis (defined by modified Lake Louise criteria) in patients with COVID-19. The prevalence of cardiac involvement was substantially higher in non-athletes than in athletes. These results indicate that cardiac involvement is not negligible in patients with COVID-19, and CMR imaging is useful for the non-invasive detection of cardiac abnormalities in patients with COVID-19.

The incidence of myocardial injury assessed by serum troponin was reported as 17–36% and is associated with poor clinical outcomes in patients with COVID-19 [6, 40–43]. For example, a report from New York including 2736 COVID-19 patients demonstrated that 36% of patients showed elevation of serum troponin T (defined as > 0.03 ng/dL), and even slight elevation of troponin I (> 0.03–0.09 ng/dL) was a significant predictor of mortality in COVID-19 patients [42]. A report from Wuhan revealed that serum creatinine kinase myocardial band (CK-MB), myoglobin, troponin I, and NT-proBNP were significantly elevated in deceased COVID-19 patients compared with survivors of COVID-19 [6]. In addition, higher CK-MB, myoglobin, and troponin I levels were associated with higher mortality, especially in older patients [6]. Therefore, an accurate assessment of cardiac involvement is crucial in patients with COVID-19.

Several echocardiographic studies have described the characteristics of cardiac abnormalities in patients with COVID-19. Szekely et al. investigated the echocardiographic spectrum of cardiac disease in hospitalized patients with COVID-19 and reported that the prevalence of RV dilatation/dysfunction was 39%, LV systolic dysfunction was 10%, and LV diastolic dysfunction was 16% [44]. Another echocardiographic study showed that the prevalence of right ventricular dilatation (basal diastolic RV diameter > 41 mm) was 31% and a significant predictive factor for worse clinical outcomes in COVID-19 patients [45]. Giustino et al. reported that the prevalence of RV dysfunction, LV wall motion abnormality, LV diastolic dysfunction, and LV global dysfunction were 26.3%, 23.7%, 13.2%, and 18.4%, respectively [5]. As shown in these studies, RV dysfunction is prevalent and clinically important in patients with COVID-19; however, an important limitation of echocardiographic assessment of RV function is that the accuracy is substantially dependent on the operator's skill. Furthermore, the reproducibility of measurement of RV function is limited owing to the complexity of the anatomy of the RV.

CMR imaging is an accurate and highly reproducible technique for assessing RV function [46]. Previous studies have demonstrated the clinical relevance of CMR-derived RV function. A study including 250 patients with dilated cardiomyopathy showed that impaired RVEF (defined as RVEF ≤ 45%) is a significant predictor of transplant-free survival and adverse heart failure outcomes [47]. RV volume by cine CMR imaging after correction for age, sex, and body surface area strongly predicted mortality in patients with idiopathic pulmonary hypertension [48]. CMR-derived RVEF is a powerful prognostic marker, even in patients with non-cardiac diseases, such as interstitial lung disease [49]. In our study, RVEF by cine MRI was significantly lower in patients with COVID-19 than in controls, suggesting that RV dysfunction is an important spectrum of cardiac disease in patients with COVID-19 (Fig. 2).

In our analysis, several pathological changes in the LV which cannot be evaluated using echocardiology were observed, such as decreased LVEF, LGE, abnormal native T1 time, and T2 time/T2WI. These findings may be related to myocardial edema, necrosis, and fibrosis caused by SARS-CoV-2 infection [2]. Recently, an update of the CMR imaging diagnostic criteria for myocardial inflammation in patients with suspected acute myocardial inflammation has been published (modified Lake Louise criteria) [12]. These criteria include T2-based criteria (global or regional increase in myocardial T2 relaxation time or an increased signal intensity in T2WI) and T1-based criteria (increased myocardial T1, extracellular volume, or LGE), and maybe useful for evaluating myocarditis caused by COVID-19. Furthermore, the presence of LGE is associated with poor clinical outcomes in patients with acute myocarditis [50], indicating that the presence of LV LGE has the potential to effectively risk-stratify patients with COVID-19 suspected myocarditis. Further studies are necessary to clarify whether this is the case.

The precise mechanisms underlying cardiac disease in COVID-19 patients remain unclear. Direct viral infection, oxygen supply–demand imbalance (type 2 myocardial infarction), inflammation-related injury, coronary plaque rupture (type 1 myocardial infarction), microvascular

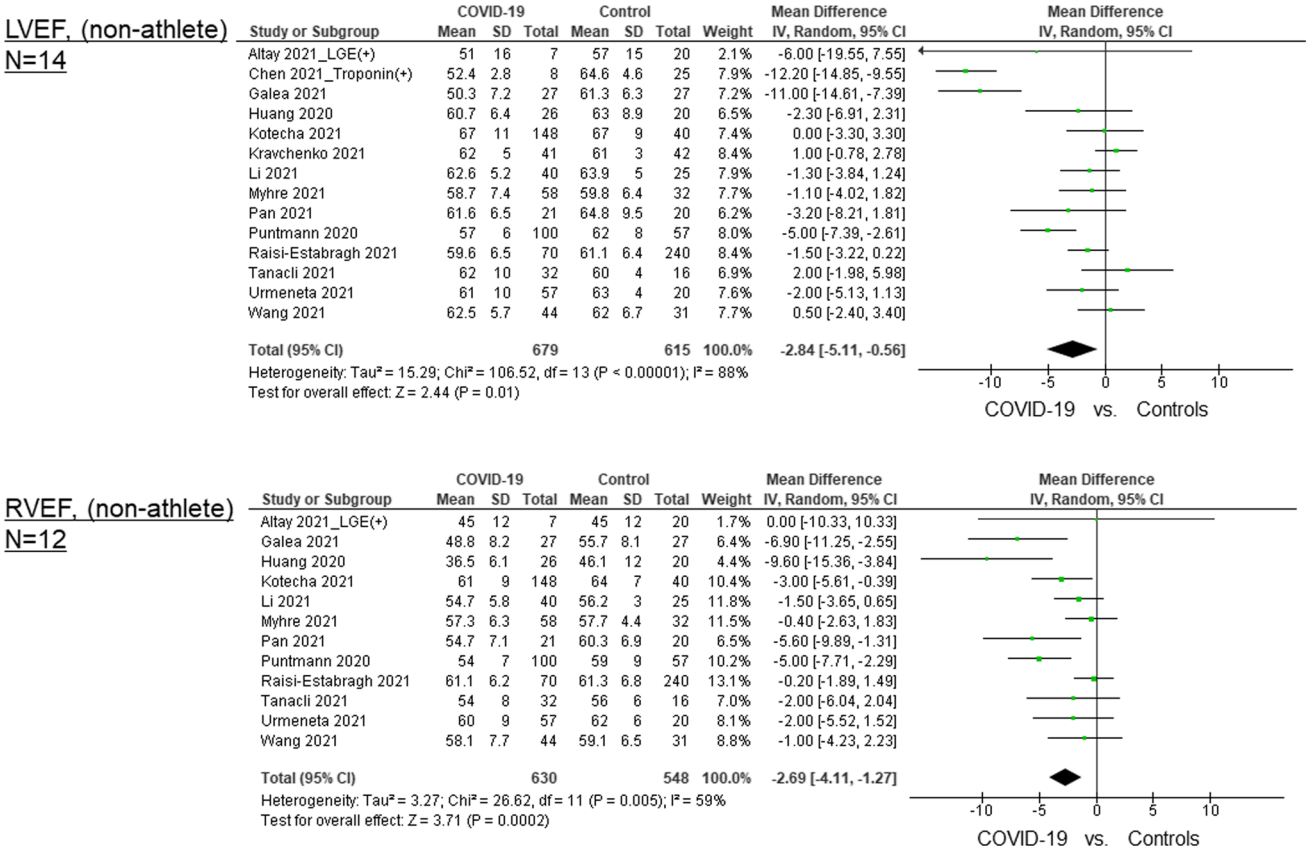

Fig. 2 Forest plot of comparison of LVEF and RVEF between non-athletes with COVID-19 and controls. The meta-analysis showed a significant difference between COVID-19 patients and controls in terms of LVEF (MD = − 2.84, 95%CI − 5.11 to − 0.56, $p < 0.001$) and RVEF (MD = − 2.69%, 95% CI − 4.41 to − 1.27, $p < 0.001$). *CI* confidence interval; *CMR* cardiac magnetic resonance; *COVID-19* coronavirus disease-2019, *LVEF* left ventricular ejection fraction; *MD* mean difference; *RVEF* right ventricular ejection fraction

dysfunction/thrombosis, and stress cardiomyopathy are possible pathophysiologies [2]. The angiotensin-converting enzyme 2 (ACE2) receptor may play an important role in COVID-19. SARS-CoV-2 is a single-stranded ribonucleic acid virus whose outer membrane spike protein binds with high affinity to the ACE2 receptor. Because ACE2 is primarily related to the conversion of angiotensin II to angiotensin 1–7, decreased ACE2 receptor density and impairment of ACE2 activity leads to an accumulation of angiotensin II, which results in vasoconstriction, inflammation, and fibrosis [2]. In another study, endothelial cell infection and endotheliitis of the kidney, small bowel, and lung tissue were demonstrated histopathologically [4]. For RV dysfunction, increased afterload following lung injury or hypoxemia, and RV ischemia due to hypoperfusion may be important pathophysiologies [51]. Further studies are required to confirm these points.

This meta-analysis had some limitations. First, the number of studies analyzed was small, and a multicenter study has not been published in this field. Second, we could not compare absolute T1 and T2 times between COVID-19 patients and controls, as these values substantially differ between different magnetic field strengths and sequences. Third, the inclusion criteria of each study were substantially variable; therefore, selection bias was not negligible. A large-scale prospective multicenter study will be required to address these limitations. Fourth, it should be noted that RVEF assessment is often less robust even with CMR imaging and more subjective with LVEF assessment due to problems with delineation of RV contours.

In conclusion, the meta-analysis showed that both LVEF and RVEF were significantly reduced in non-athletic patients with COVID-19 compared with the controls; however, these parameters were not significantly reduced in athletes with COVID-19. Furthermore, various abnormalities, such as LV LGE, pericardial enhancement, and abnormalities in T1 mapping and T2 mapping/T2WI were prevalent, and the occurrence of myocarditis was substantially higher in non-athletes than in athletes.

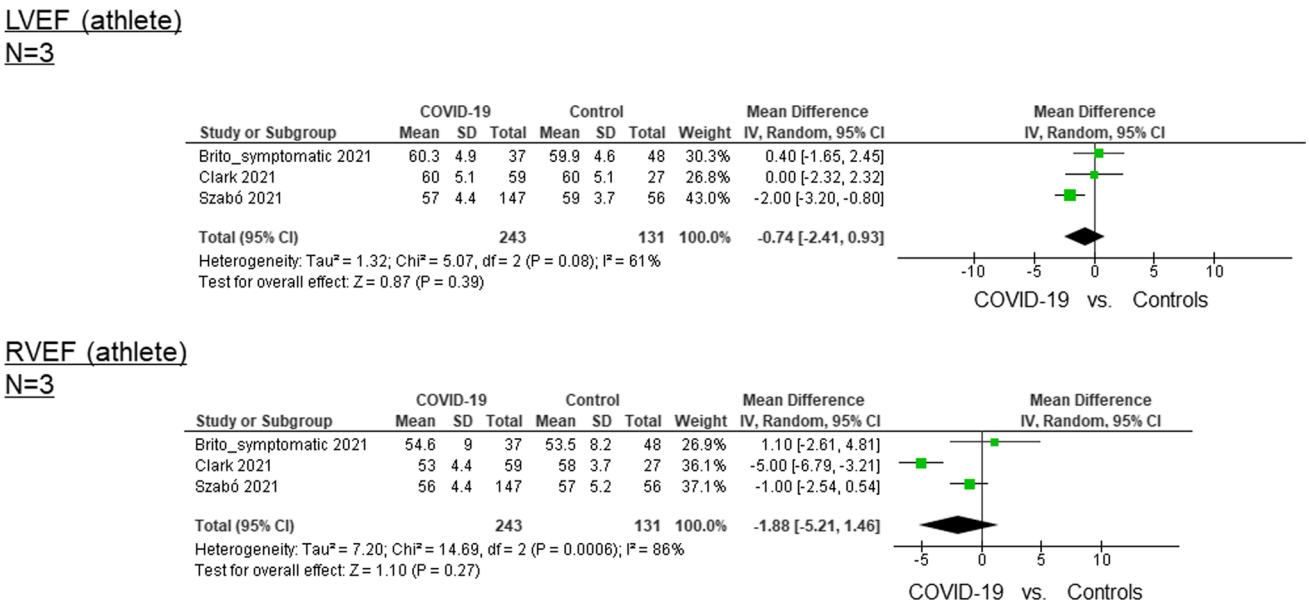

Fig. 3 Forest plot of comparison of LVEF and RVEF between athletes with COVID-19 and controls. No significant difference was identified in LVEF (MD = − 0.74%, 95% CI − 2.41 to − 0.93, $p = 0.39$) and RVEF (MD = − 1.88%, 95% CI − 5.21 to 1.46, $p = 0.27$). *CI* confidence interval; *COVID-19* coronavirus disease-2019, *LVEF* left ventricular ejection fraction; *MD* mean difference; *RVEF* right ventricular ejection fraction

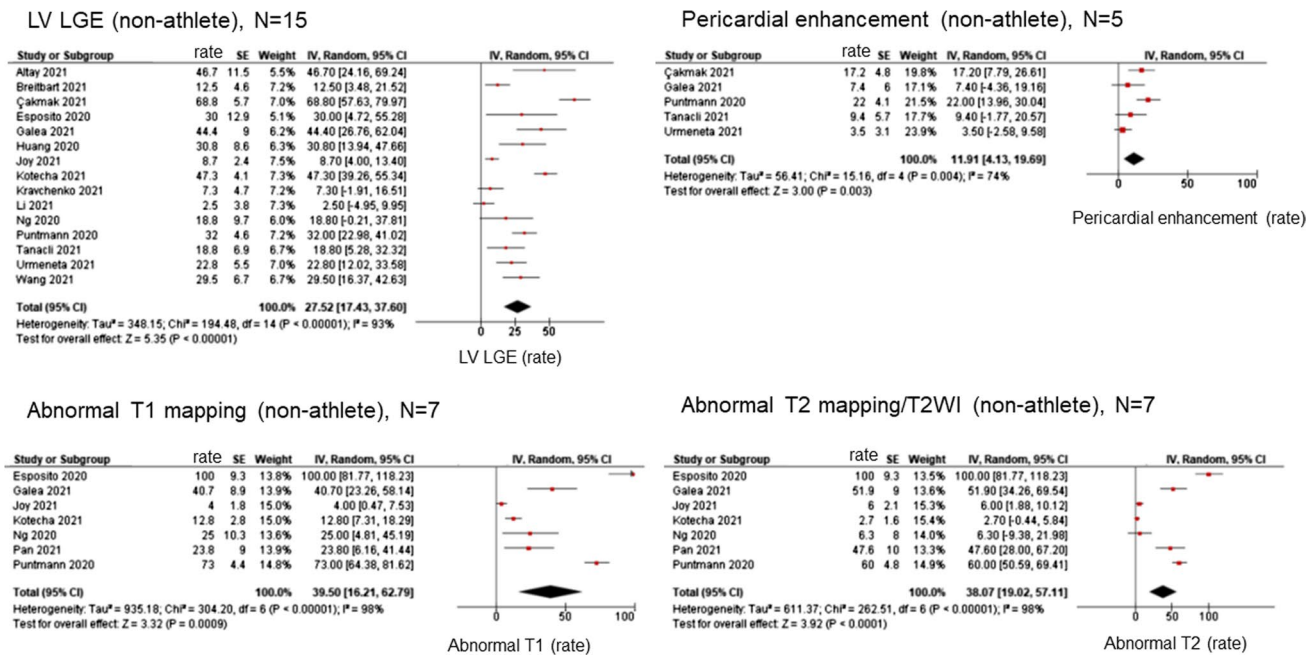

Fig. 4 Prevalence of cardiac abnormalities on CMR imaging in non-athletes with COVID-19. The prevalence of abnormalities such as LV LGE, pericardial enhancement, T1 mapping, T2 mapping/T2WI, and myocarditis were 27.5% (95%CI 17.4–37.6%), 11.9% (95%CI 4.1–19.6%), 39.5% (95%CI 16.2–62.8%), 38.1% (95%CI 19.0–57.1%). *CI* confidence interval; *CMR* cardiac magnetic resonance; *COVID-19* coronavirus disease-2019, *LGE* late gadolinium enhancement; *LV* left ventricle

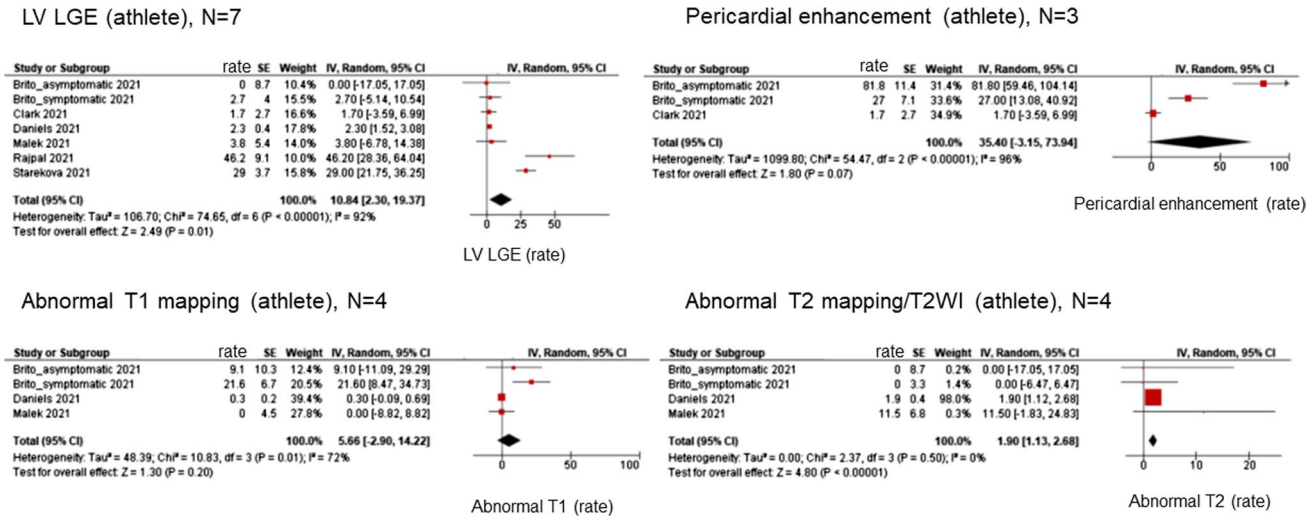

Fig. 5 Prevalence of cardiac abnormalities on CMR imaging in athlete COVID-19. The prevalence of abnormalities of LV LGE, pericardial enhancement, T1 mapping, and T2 mapping/T2WI were 10.8% (95%CI 2.3–19.4%), 35.4% (95%CI − 3.2 to 73.9%), 5.7% (95%CI − 2.9 to 14.2%), 1.9% (95%CI 1.1–2.7%). *CI* confidence interval; *CMR* cardiac magnetic resonance; *COVID-19* coronavirus disease-2019, *LGE* late gadolinium enhancement; *LV* left ventricle

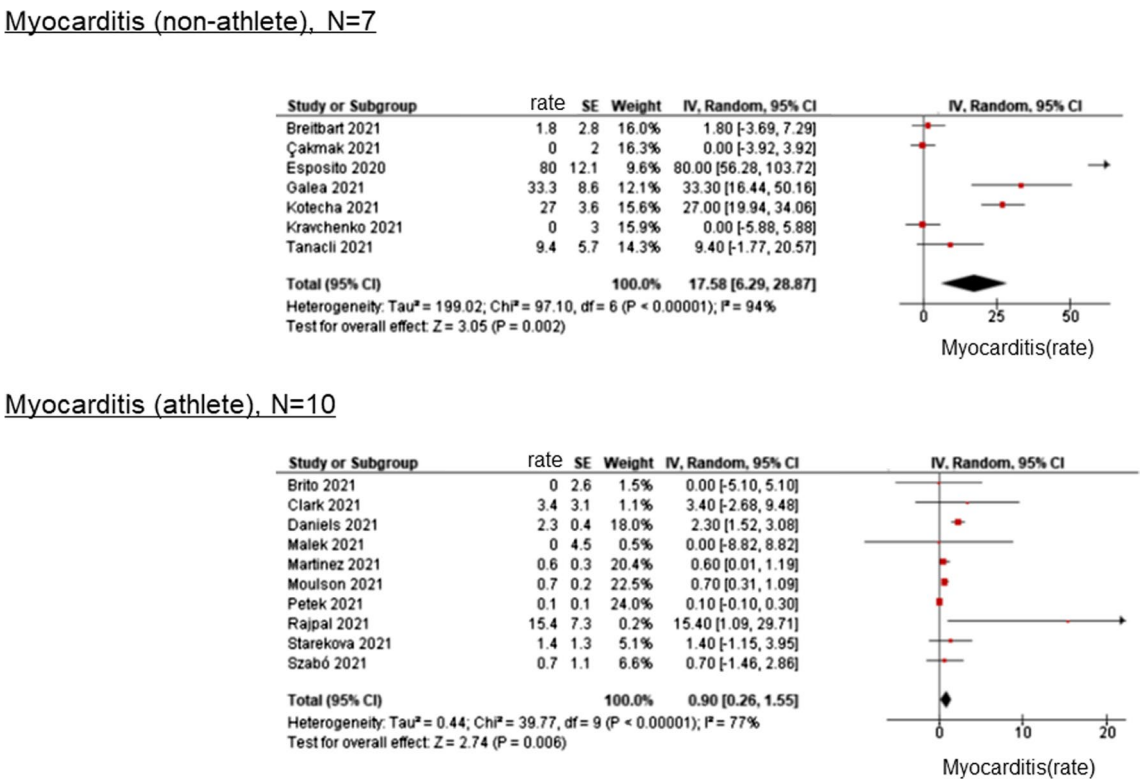

Fig. 6 Prevalence of myocarditis diagnosed by the modified Lake Louise criteria. The prevalence of myocarditis was 17.6% (95%CI 6.3–28.9%) for non-athletes and 0.9% (0.3–1.6%) for athletes

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Declarations

Conflict of interest Nothing to declare.

Ethical approval The present study is a meta-analysis of published articles. Accordingly, there is no need for IRB approval to conduct this study.

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