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Myocarditis in the Athlete

A Focus on COVID-19 Sequelae

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KEYWORDS

• Myocarditis • Athletes • Cardiac magnetic resonance imaging • SARS-CoV-2 • COVID-19

KEY POINTS

- Myocarditis is an inflammatory disease of the myocardium, frequently caused by viral infections, with a broad spectrum of clinical presentations from mild self-resolving symptoms to fulminant heart failure, arrhythmias, and death. It is an important cause of sudden cardiac death in athletes.
- Higher than expected prevalence of myocardial injury associated with severe adverse events in hospitalized patients with COVID-19 raised concern regarding the risk of return-to-play in athletes recovered from infection. Screening strategies were established to identify evidence of cardiac injury in such athletes.
- Small, single-center reports of minimally symptomatic SARS-CoV-2–infected athletes using cardiac MRI as a screening tool reported a wide range of incidence of cardiac injury. These studies have highlighted the importance of the judicious use of advanced imaging in such evaluations.
- Large multicenter registries of athletes have demonstrated a low incidence of significant cardiac injury, which is consistent with the observed prevalence of adverse events in this population. These reassuring data have lead to revision of screening recommendations in athletes post-COVID-19, with increasing focus on only evaluating those with clinical suspicion for myocarditis.
- On-going research is required to define the long-term risk of "subclinical myocarditis," the impact of COVID-19 variants, and the optimal evaluation and treatment of post-acute sequalae of COVID-19.

INTRODUCTION

Myocarditis is an inflammatory disease of the myocardium with wide-ranging clinical presentations from mild self-limited cardiac symptoms to the presence of cardiac

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dysfunction and possible fulminant heart failure.[1] Myocarditis is frequently due to acute viral infection and has become a focus of concern during the coronavirus disease 2019 (COVID-19) pandemic.[1–3] Among competitive athletes and highly active individuals, exercise during active viral myocarditis may exacerbate myocardial inflammation with precipitation of malignant ventricular arrhythmias. Indeed, myocarditis is a leading cause of sudden cardiac death (SCD) in athletes.[4–7] In consideration of return-to-play (RTP) for competitive athletes diagnosed with myocarditis, consensus guidelines exist that emphasize temporal abstinence from exercise training coupled with complete resolution of myocardial inflammation, normalization of cardiac function, and absence of ventricular arrhythmias with exertion.[8,9]

In the general population, infection with SARS-CoV-2 may lead to severe cardiac sequalae, especially in older individuals with significant underlying comorbidities.[10–13] Recognition of the high prevalence of clinically relevant cardiac injury among hospitalized patients with COVID-19 that was documented to be associated with poor outcomes led to significant apprehension in the care of competitive athletes. Whether athletes with asymptomatic or mild-COVID-19 infection might harbor myocarditis and remain at high risk for adverse cardiac events after recovery was of particular concern.[13–15] Since the early stages of the pandemic, considerable data have been acquired to provide sports medicine practitioners with updated prevalence estimates of cardiac injury in competitive athletes convalesced from COVID-19.[16–26] In this review, the authors detail the pathophysiology and clinical evaluation of athletes diagnosed with clinical myocarditis. They also discuss key developments focused on athletes infected by COVID-19. They aim to provide an evidence-based rationale in the care of athletes and highly active individuals for sports medicine and cardiology practitioners in the context of myocarditis- and COVID-19–related cardiac injury.

PATHOPHYSIOLOGY

Viruses are the most common pathogens known to cause myocarditis. Endomyocardial biopsy samples have revealed adenovirus, enteroviruses (Coxsackie type B and cytomegalovirus), parvovirus B-19 (B19V), and human herpesvirus 6 to be most frequent, with variations in prevalence by geographic regions.[1–3] Bacterial, fungal, and protozoal infections; drug-induced hypersensitivity eosinophilic reactions; and other autoimmune conditions represent less frequent causes of myocarditis.[1–3,27] With infection, usually from the upper respiratory system or gastrointestinal tract, viral myocarditis is thought to progress over 3 phases: (1) an *acute phase* typically lasting 3 to 7 days during which the virus gains entry to myocardial and vascular endothelial cells via viral-specific mechanisms or receptors followed by viral replication and subsequent myocyte necrosis; (2) a *subacute phase* of approximately 1 to 3 months with host immune cells and cytokine activation causing further cardiac damage and potential impairments in cardiac function. Although most myocarditis cases will resolve spontaneously, a minority will progress to (3) a *chronic phase* (chronic myocarditis or chronic inflammatory cardiomyopathy) characterized by myocyte abnormalities (variations in cell diameter), focal or diffuse fibrosis, and inflammatory cell infiltrates, which seem to be mediated through autoimmune processes rather than persistent viral-mediated injury.[2,27]

Myocarditis has been implicated in 3% to 10% of cases of SCD in young athletes.[4–7] Athletes may be particularly vulnerable to myocarditis, given the repetitive physical exhaustion associated with exercise training as well as the ancillary stresses that accompany competitive sports participation.[6,28] Prolonged intense physical exertion such as marathon running and training may lead to impaired immune responses

and increased susceptibility to infection for 3 to 72 hours.[29] In addition, in murine models, forced exercise following coxsackievirus infection increases viral titers and the cytotoxic T-cell response, leading to increased myocardial necrosis and mortality.[30,31]

MYOCARDITIS CLINICAL PRESENTATION

The clinical presentation of myocarditis can be variable. Fulminant myocarditis often presents with acute, severe heart failure symptoms (dyspnea, chest pain) and potentially catastrophic malignant arrhythmias, heart block,[7] or cardiogenic shock.[32] In more typical cases of myocarditis, clinical symptoms are generally less severe but may still manifest angina, dyspnea, palpitations, or syncope. In some cases, specific complaints may be absent or attributed to the initial systemic symptoms of seasonal viral infections. Athletes may be more attuned to minor physiologic disturbances and complain of nonspecific symptoms such as fatigue, myalgias, or exercise intolerance.[28] Highlighting the variability in symptomatic myocarditis presentation, a recent analysis of 97 myocarditis-related sudden death cases in young individuals (mean age 19.3 $\pm$ 6.2 years) determined that only 47% reported symptoms before death.[7] These data should be interpreted cautiously, however, as retrospective evaluation of symptoms in autopsy-based studies may be unreliable.

MYOCARDIAL INJURY AND COVID-19

With the emergence of the COVID-19 pandemic, initial reports detailed an alarmingly high prevalence of myocardial injury in hospitalized patients.[11–15] These observational reports indicated biomarker evidence of cardiac injury was common among hospitalized patients with COVID-19 and that those with cardiac injury were at particularly high risk of mortality.[11,12] Importantly, patients included in these studies had severe illness (reason for hospitalization), were older, and displayed a high incidence of comorbid conditions.[11–15] Nevertheless, this high rate of cardiac involvement suggested a possible SARS-CoV-2 tropism for cardiac cells and raised concerns for individuals experiencing asymptomatic or mild COVID-19 infection.[33,34] Entry of the virus via the ACE-2 receptor in respiratory and cardiac tissue was purported as a potential underlying mechanism leading to the high prevalence of observed cardiac injury.[35] However, subsequent autopsy-based studies have noted absence of lymphocytic predominant myonecrosis[36,37] and classic histologic evidence of myocarditis associated with COVID-19 infection.[36] Given these data, mechanisms underlying COVID-19–related cardiac injury seem multifactorial, and caution is required in the clinical interpretation of patients diagnosed with COVID-19 myocarditis.

COVID-19 CARDIAC INJURY IN ATHLETES

Clinical diagnosis of myocarditis in athletes can be extremely challenging (**Figs. 1** and **2**).[7,28,38] As the compilation of COVID-19 data in athletes has evolved over time, differentiating clinically relevant cardiac injury and presumed myocarditis from subclinical injury of unclear clinical significance remains a critically important issue. Given early concerns taken from observational data in hospitalized patients with COVID-19,[10–15] prior expert consensus recommendations advised a postinfection screening evaluation in athletes, beginning with a focused medical history and examination, no earlier than 10 days after COVID-19 test positivity.[39] Inclusion of so-called “triad” testing (electrocardiogram [ECG], troponin, and echocardiography) was also recommended as the cornerstone of the RTP evaluation. However, as clinical outcomes of athletes

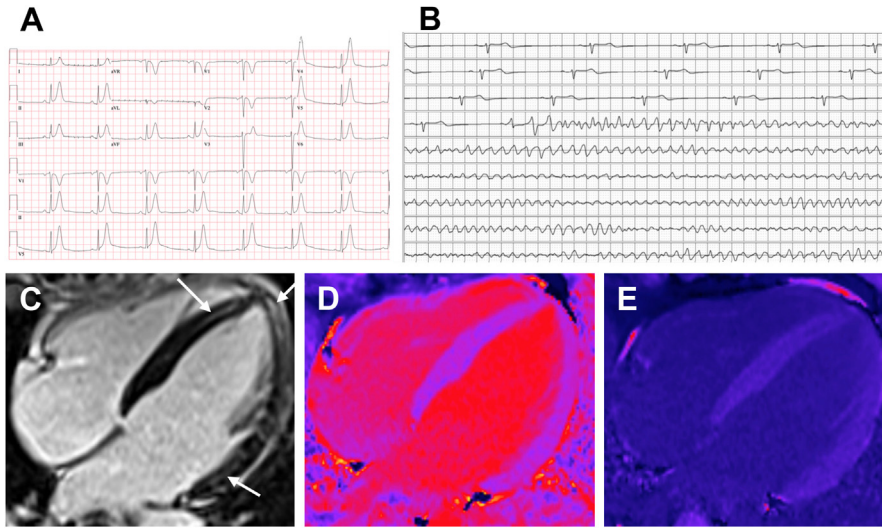

Fig. 1. Case 1. A 34-year-old former professional rugby player and recreational cyclist, presenting with cardiac arrest. Two week earlier, he suffered a witnessed spell during sleep with erratic breathing, loss of bladder continence, and transient unresponsiveness. He woke shortly before arrival of emergency responders and felt otherwise normal. Initial evaluation including 12-lead ECG (*A*), head CT and EEG, high sensitivity troponin, transthoracic echocardiography, and coronary CT angiography (not shown) were unremarkable. The patient was discharged with an event monitor and maintained his exercise routine without symptom limitation. Two days after cycling 80 miles, he suffered a ventricular fibrillation arrest captured on the event monitor (*B*); again, recognized by erratic breathing during sleep. Following successful resuscitation, he experienced transient LV dysfunction requiring circulatory support with V-A ECMO. Ventricular function normalized by hospital day 2 and the patient was weaned from cardiopulmonary support. Serial COVID-19 testing was negative. Cardiac MRI 1 week after admission revealed normal cardiac chamber dimensions, LV wall thickness, and biventricular function (EF 65%). Delayed gadolinium enhancement images (*C*) revealed a midmyocardial stripe of LGE (*arrows*) involving the mid- and distal septum and basal and apical lateral walls (quantitative scar burden 8%). Parametric mapping demonstrated diffusely elevated native T1 (*D*, *E*) and T2 values. Clinical history and MRI features were most consistent with myocarditis.

convalesced from COVID-19 and prevalence of cardiac injury in this population were reported, it became clearer that (1) most competitive athletes experienced either asymptomatic or mild COVID-19 symptoms, (2) prevalence of cardiac injury was low in this population, and (3) those diagnosed with clinical myocarditis usually report cardiopulmonary symptoms consistent with myocarditis.[40] As such, it must be emphasized that COVID-myocarditis in the athlete remains a *clinical diagnosis* associated with high pretest probability of disease.

As with other causes of myocarditis, presenting symptoms in individuals with cardiac involvement due to COVID-19 may include chest pain, dyspnea, palpitations, and syncope. For athletes who have RTP, a decline in the athlete's peak performance, prolonged dyspnea, or persistence of an elevated heart rate during recovery from exercise might herald the existence of myocardial inflammation and may require ongoing clinical investigation to exclude the presence of cardiac injury if there is sufficient clinical suspicion. The highly fit and competitive athlete may be less inclined to

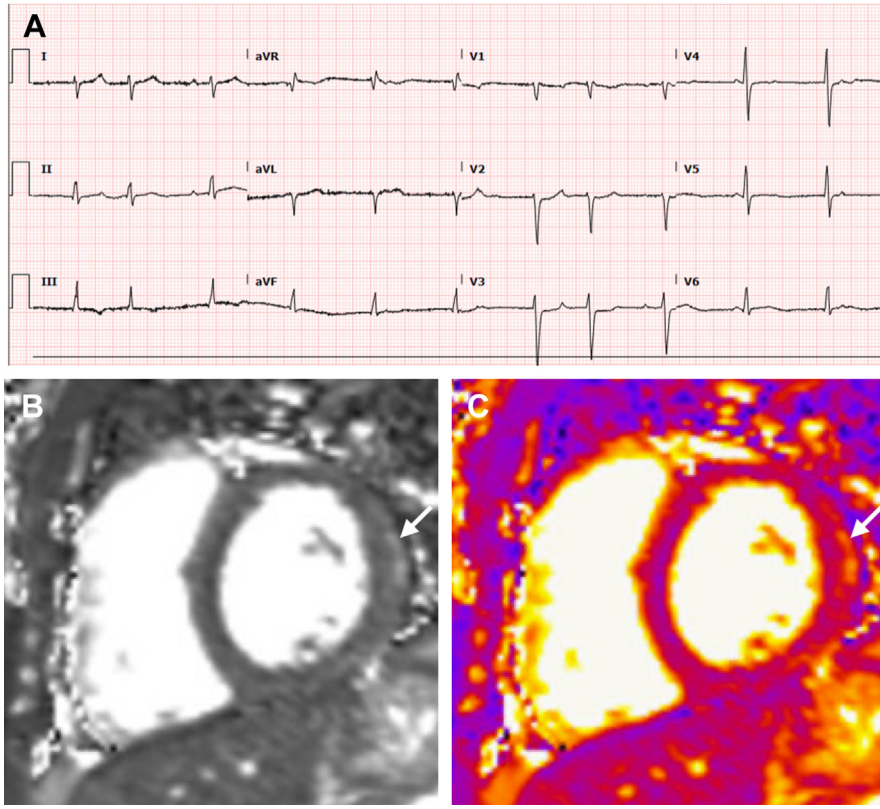

Fig. 2. Case 2. A 25-year-old highly active male presented with pharyngitis and an irregular pulse. ECG (*A*) showed a junctional rhythm with occasional atrial activity and a variable PR interval. He reported no chest discomfort or shortness of breath. High-sensitivity troponin was elevated at 5452 ng/L, and COVID-19 testing was positive. Echocardiography revealed normal left ventricular chamber and wall thickness with low to normal LV systolic function (EF 53%). No regional wall motion abnormalities were evident, and global longitudinal strain was normal at −17.3%. RV size and function were normal, and a trivial posterior pericardial effusion was noted. Troponin levels normalized within 2 weeks. Cardiac MRI performed 3 weeks after presentation revealed a mildly dilated LV chamber with normal wall thickness and an LVEF of 67%. Subepicardial LGE was present in the basal to apical inferior and apical lateral segments (*B*) with a scar size of 14%. Native T1 values were mildly elevated along the lateral segments (*C*) and normal in all other regions. T2 values were normal.

acknowledge symptoms due to concern of being withheld from training and competition or loss of team standing/position. Therefore, it is imperative for coaches, trainers, and team physicians to encourage athletes to remain attentive and be forthright with suggestive symptoms.

CLINICAL EVALUATION OF MYOCARDITIS

Electrocardiogram

The 12-lead ECG may provide invaluable clues in patients with myocarditis, although this test is limited by poor sensitivity (47%) and specificity.[41–43] Suggestive features may include subtle increases in resting heart rate, PR and QRS interval durations,

premature ventricular contraction burden, or reduction of QRS amplitude (Table 1). More striking abnormalities include new bundle branch blocks or fractionated QRS (>120 msec), sinus arrest, high-grade AV block, complex ventricular ectopy, and ST-segment changes mimicking acute myocardial infarction. The incidence of abnormal ECG findings varies by study population, severity of symptoms, and extent and distribution of myocardial inflammation. In a contemporary series of 443 mostly young (median age 34 years) and highly symptomatic patients with acute myocarditis from the Lombardy region of Italy, ST-segment elevation was the most common ECG finding (57.5%), with other ST-segment abnormalities noted in an additional 23.5%.[44] Harris and colleagues[7] suggested that among lethal cases of myocarditis, inflammatory involvement of the conduction system is relatively common (38%) and may result in sudden death from heart block.

By contrast, ECG abnormalities appear infrequently among athletes with myocarditis following COVID-19 infection. In the 2 largest series of athletes evaluated after COVID-19 infection, ECG changes were uncommon, even among those with CMRI findings of myocarditis.[23,26] The Big 10 COVID-19 Registry (N = 1597 athletes) identified 37 individuals with clinical or subclinical myocarditis using CMRI.[23] Overall, 4 of 9 athletes (44%) with clinical symptoms of myocarditis (chest pain, dyspnea, and palpitations) and just 1 of 28 (14%) without cardiac symptoms exhibited abnormal ECG findings. The Outcomes Registry for Cardiac Conditions in Athletes identified 21 cases with myocardial or pericardial involvement by CMRI from screening of 3018 post-COVID athletes with mostly mild or moderate symptoms. ECG abnormalities were rare (4/21 or 19%) with T-wave inversion in $V_{5\text{-}6}$ observed in just one case.[26] Because many athletes exhibit ST-segment or T-wave alterations, which can simulate pathologic findings, adherence to standardized interpretation guidelines for athletes and direct comparison with previously obtained ECG tracings is crucial.[45]

CLINICS CARE POINT

- Abnormal ECG findings occur infrequently among athletes following COVID-19 infection, even when MRI features that suggest acute myocarditis are present.

Cardiac Biomarkers

In the clinical assessment of myocarditis, high-sensitivity troponin is the preferred biomarker (alternatively early generation troponin or creatine kinase-myocardial band assays) to assess myocyte necrosis along with C-reactive protein.[41,44] The differential complete blood count may show eosinophilia in the presence of eosinophilic myocarditis.[46] Peripheral blood serologic and virologic tests are frequently unrevealing, except with suspected Lyme disease or human immunodeficiency virus.[41] Antinuclear antibody testing may be appropriate in patients with known or suspected history of autoimmune disorders.[47] When considering biomarker interpretation in athletes diagnosed with COVID-19, it is important to consider the training history, as recent physical activity may precipitate troponin release (see Table 1).[48] It has been recommended that high-sensitivity troponin assessment not be performed within ~24 to 48 hours of exercise.[40]

Recently, a novel circulating micro-RNA produced by cardiac myosin–specific type 17 helper lymphocytes has been identified in mice and humans with myocarditis. The human homologue, designated hsa-miR-Chr8:96, may have the potential to differentiate patients with myocarditis from those with acute coronary syndromes. Although

Table 1
Comparison of typical training effects on the heart versus "red flag" findings raising suspicion for acute viral-related cardiac injury/myocarditis

	Athletic Remodeling/Training Effects	"Red Flags" Suggesting Disease
Symptoms	• None	• Chest pain, abnormal shortness of breath beyond normal exercise-induced symptoms, palpitations, presyncope or syncope, decrement in performance
ECG	• Changes related to high vagal tone (such as bradycardia, early repolarization, first degree heart block, or Mobitz type I AV block) or athletic remodeling (LVH, atrial enlargement)	• Any pathologic changes compared with prior study • Frequent or multiform premature ventricular beats or arrhythmias • ST and T-wave changes • Left bundle branch block • Advanced AV block
Biomarkers	• Troponin and BNP/NT-Pro BNP may be mildly elevated immediately after strenuous exercise but return to normal quickly (<48 h)	• Persistent (>48 h) or more than mild elevation in cardiac biomarkers • Elevation in C-reactive protein, erythrocyte sedimentation rate, and leukocytosis
Echocardiography	• Symmetric dilation of all 4 cardiac chambers without regional wall motion abnormalities • Symmetric eccentric LV hypertrophy • Normal or low-normal EF with normal diastolic function • Normal augmentation of biventricular function with exercise ($\geq$10% with exercise) • Normal/low-normal global longitudinal strain, better than $-$16%. • Prominent LV apical trabeculations with normal LVEF and wall thickness	• Disproportionate LV or RV enlargement • Asymmetric wall thickening (>2 mm between contiguous segments) • Any segmental wall motion abnormalities • Abnormal EF (<50% LVEF, <44% RVEF) particularly if associated with low tissue Doppler/abnormal diastolic function • Failure to augment biventricular function with exercise • Abnormal global longitudinal strain, worse than $-$16% • >Trivial pericardial effusion
Cardiac MRI	• Morpho-functional changes outlined in the earlier echocardiographic section • LGE is absent with possible exception of right ventricular insertion point LGE • Parametric maps are normal	• Morpho-functional changes outlined in the earlier echocardiographic section. • LGE in a mid- or subepicardial distribution • >Trivial pericardial effusion with prominent pericardial enhancement • Abnormal T1 or T2 mapping

Abbrevations: BNP, B-type natriuretic peptide; EF, ejection fraction; LGE, late gadolinium enhancement; LV, left ventricle; LVH, left ventricle hypertrophy; RVEF, right ventricular ejection fraction.

promising, further studies are necessary (including patients with dilated cardiomyopathy) in order to validate the suitability of this novel biomarker in clinical practice.[49]

CLINICS CARE POINT

- Intense physical activity may precipitate cardiac biomarker release, high-sensitivity troponin testing in athletes recovered from COVID-19 should generally not be performed within ~24 to 48 hours of exercise.

Echocardiography

Echocardiography remains an integral part of the evaluation of athletes with suspected myocarditis.[2,28,38] Early on, although left ventricular ejection fraction (LVEF) typically remains normal, findings such as increased LV wall thickness and enhanced myocardial echogenicity, mild regional hypokinesis (particularly in the inferior and inferolateral segments), and abnormalities of tissue-Doppler and regional strain imaging may be recognized.[2,50,51] Right ventricular (RV) dysfunction may also be evident, especially in those with severe pulmonary injury.[28] Pericardial effusions have been observed with varying frequencies. In the early phases of myocarditis, LV dimensions are generally normal, even when the EF is reduced. LV dilation often implies chronicity, with the caveat that the athlete's type of exercise training (particularly endurance modalities) and corollary cardiovascular adaptations may affect chamber dimensions (see **Table 1**). Recognition of LV dysfunction should also continue to prompt the clinician to consider potential effects of performance enhancing (anabolic steroid, amphetamines) and recreational drugs (cocaine). Finally, prominent LV apical trabeculations are increasingly recognized as nonpathologic findings in athletes and are likely to be encountered with broader application of post-COVID-19 cardiovascular imaging.[52]

Endomyocardial Biopsy

Endomyocardial biopsy (EMB) remains the "gold standard" for a confirmatory diagnosis of myocarditis.[1,2,41,53] However, given the invasive nature and risk of complications, EMB is generally reserved for defining treatment in severely affected individuals. In experienced hands, the risk of complications (perforation, tamponade, severe dysrhythmias) is acceptably low (~1%–2%).[54] An additional shortcoming of EMB is potential sampling error, as myocardial inflammation may be patchy or confined to regions inaccessible by RV sampling (ie, lateral LV wall). The timing of sampling relative to phase of illness may also affect the diagnostic yield of EMB.[53]

Cardiac MRI

CMRI has evolved into the most sensitive and comprehensive noninvasive diagnostic tool for assessment of myocardial tissue characterization, including recognition and quantitation of inflammation and replacement fibrosis resulting from acute myocarditis.[55] CMRI also serves as the reference standard for quantitation of cardiac mass, cardiac chamber dimensions, and EF assessment. CMRI is recommended (class I) for patients with *clinically* suspected acute myocarditis or in patients with chest pain, normal coronary arteries, and elevated troponin (myocardial infarction with non-obstructive coronary arteries).[56] CMRI is not only a powerful diagnostic tool but also provides important information regarding risk stratification during recovery from acute myocarditis. The absence of late gadolinium enhancement (LGE) post-

myocarditis portends an excellent prognosis, whereas multiple trials have shown that the presence of LGE is associated with an increased risk of major adverse cardiac events.[57–59] Whether the presence of LGE in athletes post-COVID-19 proves to be a substrate of ventricular arrhythmias is unknown.

CMRI should ideally be performed within 2 to 3 weeks from onset of symptoms and/or detection of biomarker abnormalities, as diagnostic accuracy may be reduced during the first days of illness or beyond this temporal window. In the context of recent controversies surrounding the utility of CMRI screening for athletes post-COVID-19 infection and because of the exquisite high sensitivity for detection of subtle abnormalities of myocardial tissue characterization, there remains uncertainty regarding the clinical relevance of subtle abnormal CMRI findings in asymptomatic patients or those without ECG, biomarker, or echocardiographic abnormalities.

The original Lake Louise Criteria, published in 2009, designated 3 key elements of myocardial inflammation detected by CMRI: (1) *hyperemia*—identified by intense signal on early gadolinium enhancement images; (2) *edema*—indicated by increased myocardial T2 relaxation time or increased signal intensity on T2-weighted images; and (3) *necrosis/fibrosis*—as exhibited on LGE images.[60] In this first iteration, abnormal findings in 2 of the 3 elements diagnosed acute myocarditis with a 74% sensitivity and 86% specificity.[61] The addition of novel parametric (T1 and T2) mapping techniques has been shown to improve the diagnostic accuracy of CMRI for acute myocarditis. The 2018 Updated Lake Louise Criteria include T2-mapping for edema and native T1 mapping and extracellular volume (ECV) for inflammatory injury.[55] One study examining the updated criteria reported enhanced sensitivity (87.5%) while preserving high specificity (96.2%) for diagnosis of acute myocarditis.[62]

At present, there have been 11 separate reports, primarily small observational case series, detailing CMRI findings in athletes following COVID-19 infection (**Table 2**). These studies vary in terms of subject age, sex, race, ethnicity, geographic distribution, sporting discipline, and symptomatology, and detailed correlations of ECG, biomarker, and echocardiographic findings have been inconsistent. Indications for CMRI, either clinically directed or universally mandated, and timing relative to symptom onset or COVID-19 positivity have also been nonuniform. Further, scanner type (1.5 vs 3 T), imaging protocols/sequences, and the experience of the interpreter have not been standardized. Finally, although prior studies incorporated the updated Lake Louise criteria, absence of case-control comparative groups of noninfected athletes and nonathletes represent a critical omission in most of these studies. Additional limitations are present in careful review of these studies. First, there is stark discrepancy in the observed frequency of CMRI-defined myocarditis with rates ranging between 0% and 17%.[16–26] In the Big Ten COVID-19 Registry (N = 1597 athletes), among the 13 participating institutions, incidence rates for myocarditis varied by site from 0% to 7.6%.[23] A second limitation of CMRI studies in athletes has been the lack of standardized CMRI interpretation by a core laboratory to validate abnormal findings. As such, given the expertise required for CMRI interpretation, interpreter bias is a clear, critical limitation. For example, although Brito and colleagues[21] observed a high prevalence of pericardial enhancement and associated effusions in 39.5% (N = 19) of a cohort of convalesced COVID-19 athletes (N = 48), in no other CMR-based athletic study has this degree of presumed pericarditis been replicated.

Fibrosis confirmed by LGE is often observed in myocarditis (see **Table 2**). Yet, whether LGE reported in prior COVID-19 convalesced athlete case series data represents recent COVID-19 injury is unknown in the absence of comparative baseline CMRI data. Prior investigators appropriately excluded focal septal RV insertion site fibrosis as an indicator of COVID-19 injury, given the increasing recognition of this

Table 2
MRI studies in athletes diagnosed with COVID-19

Reference	Site	Cohort	Timing of MRI after Diagnosis and Symptom Frequency	MRI Parameters	Frequency of Abnormal MRI Findings	Additional Observations
Rajpal et al. *JAMA Card* (Published Online Sept 11, 2020)	Ohio State University	26 collegiate athletes Mean age: 19.5 y Female: 42.3%	(11–53 d) Mild: 12 (46%) None: 14 (54%)	Cine, T1/T2, ECV, & LGE (1.5 T)	Myocarditis: 4/26 (15%); pericardial effusion: 2	No ↑ troponin, LGE in 12 (46%): 4 with & 8 without ↑ T2
Brito et al. *JACC CV Imag* (Published Online Nov 4, 2020)	W. Virginia University	54 collegiate athletes Mean age: 19 y; female: 15%	Symptoms: None: 16 (30%) Mild: 36 (66%) Moderate: 2 (4%)	Serial MRI in 48 (89%)	Abnormal: 27 (56.3%) Pericardial effusion or LGE: 19 (39.5%)	6 (12.5%) ↓ GLS and/or ↑ native T1; LGE in 1, ↓EF w/s ↑ T1; normal T2 in all, ↑ Troponin 1 (3%)
Vago et al. *JACC CV Imag* (Published Online Dec 16, 2020)	Hungary	12 pro athletes Median age: 23 y Female: 83.3% [15 athletic & 15 healthy controls]	(Median: 67 d [female], 90 d [male]) Symptoms: None: 2 (17%) Mild to mod: 10 (83%)	Cine, T1 &T2, (1.5 T)	No myocarditis/LGE, normal T1 and T2	—
Clark et al. *Circulation* (Published Online Dec 17, 2020)	Vanderbilt University	59 collegiate athletes; 60 athletic controls; 27 healthy controls	(10–162 d; median 21.5 d)	Cine, T1/T2 mapping, & ECV (1.5 T)	Myocarditis: 2 (3%) but no symptoms, 1 late ↓ EF (45%)	Focal infero-septal LGE in 22% COVID (+) vs 24% athletic controls
Starekova et al. *JAMA Card* (Published Online Jan 14, 2021)	Univ. of Wisconsin	145 collegiate & high school athletes Female: 25.5%	(11–194; median 15 d) Symptoms: None: 24 (16.6%) Mild: 71 (49%); Moderate: 40 (27.6%)	(1.5 or 3 T)	Myocarditis: 2 (1.4%) 1 with extensive LGE, ↑T2, & (+) troponin; 1 with mild LGE & (−) troponin	—

Malek et al. *J Mag Res Imag* (Jan 20, 2021)	Warsaw, Poland	26 Olympic & pro athletes Mean age: 24 y Female: 81%	(1–2 mo)	Cine, T1/T2, dark blood T2, LGE (1.5 T)	Abnormal: 19% (5/26), No myocarditis by MRI	4 with borderline myocardial edema, 1 with LGE and pleural-pericardial effusion
Martinez et al. *JAMA Card* (Online Mar 4, 2021)	US	789 pro athletes [MLS, MLB, NHL, NFL, WNBA] Male: 98.5% MRI in 27	(3–156 d)	NS*	Abnormal MRI in 5 (0.6%): myocarditis 3 (0.4%) pericarditis 2 (0.3%)	
Hendrickson et al. *Circulation* (May 11, 2021)	Univ. of Tennessee	137 D-I, II, III (age 18-27) Male: 68% MRI in 5	(Median: 16 d) 87% mild or moderate symptoms	Cine, T2, LGE	No (0/5) abnormal MRI	Trace of small effusions in 4 athletes T1/T2 mapping & ECV not on all
Daniels et al. *JAMA Card* (Online May 27, 2021)	13 Big Ten Universities	1597 collegiate athletes male: 60.3%	(10-77 days)	Cine, T1 & T2	37 (2.3%) Clinical myocarditis: 9 Subclinical:28 31 Fulfilled LL Criteria	MRI yield 7.4x > f/u MRI in 27: Resolution ↑T2 in all & LGE in 11
Hwang et al. *Clin J Sport Med* (Published Online June 24, 2021)	Stanford University	55 collegiate athletes MRI in 8 for abnormal screening	NS	NS*	Myocarditis: (1) Pericarditis: (1) + CP	
Moulson et al. *Circulation* (July 27, 2021)	US (ORCCA Registry)	3,018 COVID (+) collegiate athletes - 42 US schools CI-MRI: (119) 1°-MRI: (198)	(18-63 days; Median 33 days)	NS*	Definite, possible, or probable cardiac involvement in 21/3018 (0.7%)	CI: -15/2820 (0.5%) Dx yield 4.2x higher when MRI CI: -15/119 (12.6%) CI -6/198 (3%) in 1° screening MRI

finding as a likely benign marker in athletes, particularly masters-level endurance athletes.[63,64] A recent report demonstrated focal nonischemic fibrosis in 17% of asymptomatic triathletes, which seemed to correlate with exercise-induced hypertension and competition history.[63] Another study identified focal LGE in 37.6% of healthy endurance athletes versus 2.8% in healthy control subjects ($P < 0.001$), with a typical pattern in the RV insertion points.[64] In each of these studies, athletes with LGE also tended to exhibit higher ECV in remote, nonfibrotic myocardium assessed with T1 mapping.

The significance of "subclinical" myocarditis detailed with CMR-based screening remains uncertain. Present short-term cardiac outcomes are reassuring after RTP in competitive athletes, and to-date, no sports-related cardiac events clearly linked to COVID-19 have been confirmed in any athlete included in published registry data.[23,26] Another reassuring observation from the Big-10 Registry was derived from a subset of 27 athletes who underwent follow-up CMRI and demonstrated normalization of T2 elevation in all subjects with resolution of LGE in 11 (40.7%).[23] In addition to evidence suggesting CMRI-based screening does not improve athlete health outcomes, we must also acknowledge the legitimate concerns of costs in implementing widespread CMRI screening, limited scanner availability, and inappropriate health care resource allocation as separate reasons why CMRI screening for all athletes convalesced from COVID-19 is not practical. Future unfortunate and tragic athlete SCD cases will undoubtedly still occur, just as before the COVID-19 pandemic; this emphasizes the importance of careful adjudication of follow-up data from US and multinational registries, avoidance of overreaching correlation with potential prior COVID-19 infection, and continued vigilance with emergency preparedness to prevent such tragic events.

CLINICS CARE POINT

- Cardiac MRI is recommended for athletes with *clinically* suspected acute myocarditis, including those with chest pain, elevated high-sensitivity troponin levels, and abnormal ECG changes in the absence of obstructive or anomalous coronary arteries. Imaging should typically be performed within 2 to 3 weeks of symptom onset and/or abnormal biomarker or ECG findings with interpretation by experienced imaging specialists.

ACTIVITY RESTRICTION AND RETURN-TO-PLAY

As exercise may augment pathogen virulence in other acute viral infections, it is prudent to assume this may also be the case with SARS-CoV2.[29–31] Although RTP algorithms for athletes diagnosed with COVID-19 are continually evolving, most expert opinions have recommended athletes refrain from vigorous exercise, especially while symptomatic.[39,40,65,66] Early recommendations prescribed a period of rest for all athletes diagnosed with COVID-19 as well as further cardiac workup in those with any symptoms.[39,65] Subsequent recommendations have refined RTP strategies to be tailored to symptom severity, with more severe symptoms warranting a longer period of rest and more extensive cardiac risk stratification.[40,66]

An important unaddressed clinical issue is whether athletes with a remote history of COVID-19 and have fully recovered should undergo cardiovascular risk assessment; this also applies to those found to have a positive COVID-19 antibody test without any history of prior clinical symptoms. Currently, definitive outcomes data to address this issue are lacking. However, there are currently no data to suggest that athletes with

prior COVID-19 infection are suffering from increased rates of SCD or incident heart failure.[16–26] Future recommendations based on athlete registry data[23,26] will be forthcoming and may offer further guidance on which athletes warrant activity restriction and advanced evaluation.

Athletes diagnosed with clinical myocarditis, whether due to COVID-19 or other causes, should generally follow current American College of Cardiology/American Heart Association sports eligibility guidelines for myocarditis.[8] These athletes should be restricted from physical training for at least 3 to 6 months following resolution of initial symptoms. After this period of convalescence, cardiac enzyme and ventricular systolic function should be reevaluated and ambulatory rhythm monitoring and exercise testing should be performed. If these tests reveal no biomarker evidence of ongoing cardiac injury/inflammation, normalization of LV function, and no significant rhythm disturbances, athletes can gradually return to training.[8] The use of CMRI for follow-up imaging of athletes diagnosed with myocarditis, based on previous abnormal CMRI findings, may be preferred. Although persistent LGE following clinical recovery still has unclear clinical implications, improvement of inflammatory findings on CMRI after 3 to 6 months of exercise abstinence is a reassuring finding and therefore reasonable to proceed with RTP after careful shared risk and decision-making between practitioner, athlete, and other key stakeholders.

MYOCARDITIS TREATMENT

A severe clinical presentation of myocarditis, or fulminant myocarditis, includes the presence of cardiogenic shock or unstable arrythmias and warrants emergent transfer for intensive cardiac care at an experienced medical center. Clinical management may include initiation of mechanical circulatory support, extracorporeal membrane oxygenation, parenteral inotropic therapy, and EMB.[2,32] The empirical use of corticosteroids may be considered, although clear outcomes data are lacking on the effectiveness of steroid or immunotherapy in nonspecific cases of myocarditis. For specific autoimmune conditions such as giant-cell or sarcoid myocarditis, corticosteroids and advanced immunosuppressive regimens are indicated and recommended by most experts.[65,66] If clinical myocarditis as a consequence of an active viral infection is suspected, specific antiviral therapy may be considered, although evidence-based treatment courses are not well established.[3] For all patients presenting with acute myocarditis and reduced EF, regardless of cause, medical management for heart failure is the cornerstone of treatment. Consultation with a cardiology or heart failure specialist is recommended, and medications should be initiated in accordance with contemporary heart failure guidelines, including β-blocker, angiotensin receptor and neprilysin inhibitor, mineralocorticoid antagonist, sodium-glucose cotransporter-2 inhibitor, and diuretics as indicated.[67]

FUTURE RESEARCH DIRECTIONS

Numerous clinical uncertainties relevant to athletes convalesced from COVID-19 infection persist. First, although LGE is an established risk factor in patients with cardiomyopathy, the natural history and predictive value of nonspecific LGE observed in athletes is unclear. Second, in the context of subclinical myocarditis detected by CMRI, ongoing follow-up of long-term clinical outcomes of athletes convalesced from COVID-19 remains imperative. Although cardiac outcomes to date are reassuring, unknown long-term outcomes concomitant with emerging COVID-19 variants necessitate ongoing scientific vigilance and maintenance of current registry data. Finally, the emergence of postacute sequalae of COVID-19 (PASC), or “long-haul”

COVID-19, represents a critical challenge in sports medicine and cardiology. Ruling out myocarditis as a cause of persistent symptoms is a key first step; however, delineating underlying mechanisms and best practices for clinical management of athletes suffering from PASC is a pressing challenge in the care of recovered athletes post-COVID-19.

CONCLUSIONS

Concern for acute myocarditis warrants thorough investigations and thoughtful clinical judgment for athletes in consideration of RTP. Advanced cardiac imaging, although increasing test sensitivity for myocarditis, has also introduced a new element of clinical uncertainty in the evaluation of athletes convalesced from COVID-19. Athletes diagnosed with COVID-19 should undergo cardiac testing based on clinical presentation, with specific attention paid to the presence of cardiopulmonary symptoms. Athletes with higher pretest probability for myocarditis should undergo appropriate cardiac testing, including selective consideration for CMRI before RTP versus a universal screening approach. Emerging conundrums in the care of athletes throughout the COVID-19 pandemic include the challenges presented by PASC, which requires continued follow-up in large athletic registry cohorts, and the concern for new COVID-19 variants, which requires ongoing vigilance in assessing potential untoward cardiac outcomes in recovered athletes after COVID-19 infection.

DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Fung G, Luo H, Qiu Y, et al. Myocarditis. Circ Res 2016;118:496–514.
2. Ammirati E, Frigerio M, Adler E, et al. Management of acute myocarditis and chronic inflammatory cardiomyopathy. Circ Heart Fail 2020;13e:007405.
3. Law Y, Lai A, Chen S, et al. Diagnosis and management of myocarditis in children. a scientific statement from the American Heart Association. Circulation 2021;144:e123–35.
4. Harmon KG, Asif IM, Maleszewski JJ, et al. Incidence, cause, and comparative frequency of sudden cardiac death in national collegiate athletic association athletes. Circulation 2015;132:10–9.
5. Peterson DF, Kucera K, Thomas LC, et al. Aetiology and incidence of sudden cardiac arrest and death in young competitive athletes in the USA: a 4-year prospective study. Br J Sports Med 2021;55:1196–203.
6. Maron BJ, Doerer JJ, Haas TS, et al. Sudden deaths in young competitive athletes. Circulation 2009;119:1085–92.
7. Harris K, Mackey-Bojack S, Bennett, et al. Sudden unexpected death due to myocarditis in young people, including athletes. Am J Cardiol 2021;143:131–4.
8. Maron BJ, Udelson JE, Bonow RO, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 3: hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and other cardiomyopathies, and myocarditis. Circulation 2015;132:e273–80.
9. Pelliccia A, Solberg EE, Papadakis M, et al. Recommendations for participation in competitive and leisure time sport in athletes with cardiomyopathies, myocarditis,

and pericarditis: position statement of the sport cardiology section of the European Association of Preventive Cardiology (EAPC). Eur Heart J 2019;40:19–33.
10. Clerkin KJ, Fried JA, Raikhelkar J, et al. COVID-19 and cardiovascular disease. Circulation 2020;141:1648–55.
11. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020;5:802–10.
12. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:811–8.
13. Pinney S, Giustino G, Halperin J, et al. Coronavirus historical perspective, disease mechanisms, and clinical outcomes. J Am Coll Cardiol 2020;76:1999–2010.
14. Puntman V, Carerj M, Wieters I, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:1265–73.
15. Huang L, Zhao P, Tang D, et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. JACC Cardiovasc Imaging 2020;13:2330–9.
16. Rajpal S, Tong MS, Borchers J, et al. Cardiovascular magnetic resonance findings in competitive athletes recovering from COVID-19 infection. JAMA Cardiol 2021;6:116–8.
17. Starekova J, Bluemke DA, Bradham WS, et al. Evaluation for myocarditis in competitive student athletes recovering from coronavirus disease 2019 with cardiac magnetic resonance imaging. JAMA Cardiol 2021;6:945–50.
18. Małek ŁA, Marczak M, Miłosz-Wieczorek B, et al. Cardiac involvement in consecutive elite athletes recovered from Covid-19: a magnetic resonance study. J Magn Reson Imaging 2021;53:1723–9.
19. Clark DE, Parikh A, Dendy JM, et al. COVID-10 myocardial pathology evaluation in athletes with cardiac magnetic resonance (COMPETE CMR). Circulation 2021; 143:609–12.
20. Martinez MW, Tucker AM, Bloom OJ, et al. Prevalence of inflammatory heart disease among professional athletes with prior COVID-19 infection who received systematic return-to-play cardiac screening. JAMA Cardiol 2021;4:E1–8. Published online March.
21. Brito D, Meester S, Yanamala N, et al. High prevalence of pericardial involvement in college student athletes recovering from COVID-19. JACC Cardiovasc Imaging 2021;14:541–55.
22. Hendrickson BS, Stephens RE, Chang JV, et al. Cardiovascular evaluation after COVID-19 in 137 collegiate athletes. Results of an algorithm-guided screening. Circulation 2021;143:1926–8.
23. Daniels CJ, Rajpal S, Greenshields JT, et al. Prevalence of clinical and subclinical myocarditis in competitive athletes with recent SARS-CoV-2 infection: results from the big ten COVID-19 cardiac registry. JAMA Cardiol 2021;27:E1–10. Published online May.
24. Vago H, Szabo L, Dohy Z, et al. Cardiac magnetic resonance findings in patients recovered from COVID-19. Initial experience in elite athletes. JACC Cardiovasc Imaging 2021;14:1279–81.
25. Hwang CE, Kussman A, Christle JW, et al. Findings form cardiovascular evaluation of national collegiate athletic association division I collegiate student-athletes after asymptomatic or mildly symptomatic SARS-CoV-2 infection. Clin J Sport Med 2022;(32):103–7.

26. Moulson N, Petek BJ, Drezner JA, et al. Outcomes registry for cardiac conditions in athletes investigators. SARS-CoV-2 cardiac involvement in young competitive athletes. Circulation 2021;144:256–66.
27. Kindermann I, Barth C, Mahfoud F, et al. Update on myocarditis. J Am Coll Cardiol 2012;59:779–92.
28. Halle M, Binzenhöfer L, Mahrholdt H, et al. Myocarditis in athletes: a clinical perspective. Eur J Prev Cardiol 2020;3. Published online March.
29. Nieman DC. Marathon training and immune function. Sports Med 2007;37:412–5.
30. Kiel R, Smith F, Chason J, et al. Coxsackie-virus B3 myocarditis in C3H/HeJ mice: description of an inbred model and the effect of exercise on virulence. Eur J Epidemiol 1989;5:348–50.
31. Gatmaitan B, Chason J, Lerner A. Augmentation of the virulence of murine coxsackie-virus B-3 myocardiomyopathy by exercise. J Exp Med 1970;131:1121–36.
32. Kociol RD, Cooper LT, Fang JC, et al. Recognition and initial management of fulminant myocarditis. Circulation 2020;141:e69–92.
33. Madjid M, Safavi-Naeini P, Solomon SD, et al. Potential effects of coronaviruses on the cardiovascular system: a review. JAMA Cardiol 2020;5:831–40.
34. Yancy CW, Fonarow GC. Coronavirus Disease 2019 (COVID-19) and the heart-is heart failure the next chapter? JAMA Cardiol 2020;5:1216–7.
35. Vaduganathan M, Vardeny O, Michel T, et al. Renin-angiotensin-aldosterone system inhibitors in patients with Covid-19. N Engl J Med 2020;382:1653–9.
36. Kawakami R, Sakamoto A, Kawai K, et al. Pathological evidence for SARS-CoV-2 as a cause of myocarditis: JACC review topic of the week. J Am Coll Cardiol 2021;77:314–25.
37. Basso C, Leone O, Rizzo S, et al. Pathological features of COVID-19-associated myocardial injury: a multicentre cardiovascular pathology study. Eur Heart J 2020;41:3827–35.
38. Eichhorn C, Bière L, Schnell F, et al. Myocarditis in athletes is a challenge. JACC Cardiovasc Imaging 2020;13:494–507.
39. Phelan D, Kim JH, Chung EH. A game plan for the resumption of sport and exercise after coronavirus disease 2019 (COVID-19) Infection. JAMA Cardiol 2020;5:1085–6.
40. Phelan D, Kim J, Elliott M, et al. Screening of potential cardiac involvement in competitive athletes recovering from COVID-19. An expert consensus statement. JACC Cardiovasc Imaging 2020;13:2635–52.
41. Carforio A, Pankuweit S, Arbustini E, et al. Current state of knowledge on etiology, diagnosis, management, and therapy of myocarditis: A position statement of the european society of cardiology working group on myocardial and pericardial disease. Eur Heart J 2013;34:2636–2648a.
42. Ukena C, Mahfoud F, Kindermann I, et al. Prognositic electrocardiographic parameters in patients with suspected myocarditis. Eur J Heart Fail 2011;13:398–405.
43. Mogera T, Di Lenarda A, Dreas L, et al. Electrocardiography of myocarditis revisited: Clinical and prognostic ssignificance of electrocardiographic changes. Am Heart J 1992;124:455–67.
44. Ammirati E, Cipriani M, Moro C, et al. Clinical presentation and outcome in a contemporary cohort of patients with acute myocarditis: multicenter lombardy fegistry. Circulation 2018;138:1088–99.
45. Sharma S, Drezner J, Baggish A, et al. International recommendations for electrocardiographic interpretation in athletes. J Am Coll Cardiol 2017;69:1057–75.

46. Brambatti M, Matassini MV, Adler ED, et al. Eosinophic myocarditis: characteristics, treatment, and outcomes. J Am Coll Cardiol 2017;70:2363–75.
47. Carforio A, Marcolongo R, Jahns R, et al. Immune-mediated and autoimmune myocarditis: clinical presentation, diagnosis, and management. Heart Fail Rev 2013;18:715–32.
48. Shave R, Baggish A, George K, et al. Exercise-induced cardiac troponin elevation. Evidence, mechanisms, and implications. J Am Coll Cardiol 2010;56: 169–76.
49. Blanco-Dominguez R, Sanchez-Diaz R, de la Fuente H, et al. A novel circulating microRNA for the detection of acute myocarditis. N Engl J Med 2021;384: 2014–27.
50. Ammirati E, Veronese G, Brambatti M, et al. Fulminant versus acute nonfulminant myocarditis in patients with left ventricular systolic dysfunction. J Am Coll Cardiol 2019;74:299–311.
51. Hsiao J, Koshino Y, Bonnichsen C, et al. Speckle tracking echocardiography in acute myocarditis. Int J Cardiovasc Imaging 2013;29:275–84.
52. Caselli S, Ferreira D, Kanawati E, et al. Prominent left ventricular trabeculations in competitive athletes: A proposal for risk stratification and management. Int J Cardiol 2016;223:590–5.
53. Cooper L, Baughman K, Feldman A, et al. The role of endomyocardial biopsy in the management of cardiovascular disease: a scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology: endorsed by the Heart Failure Society of America and the Heart Failure Association of the European Society of Cardiology. J Am Coll Cardiol 2007;50:1914–31.
54. Yilmaz A, Kindermann I, Kindermann M, et al. Comparative evaluation of left and right ventricular endomyocardial biopsy: differences in complication rate and diagnostic performance. Circulation 2010;122:900–9.
55. Ferreira V, Schulz-Menger J, Holmvang G, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. J Am Coll Cardiol 2018;72:3158–76.
56. Pasupathy S, Air T, Dreyer R, et al. Systematic review of patients presenting with suspected myocardial infarction and non-obstructive coronary arteries. Circulation 2015;131:861–70.
57. Grani C, Eichhorn C, Biere L, et al. Prognostic value of cardiac magnetic resonance tissue characterization in risk stratifying patients with suspected myocarditis. J Am Coll Cardiol 2017;70:1964–76.
58. Aquaro G, Perfetti M, Camastra G, et al. Cardiac magnetic resonance working group of the Italian Society of Cardiology. Cardiac MR with late gadolinium enhancement in acute myocarditis with preserved systolic function: ITAMY study. J Am Coll Cardiol 2017;70:1977–87.
59. Di Marco A, Anguera I, Schmitt M, et al. Late gadolinium enhancement and the risk for ventricular arrhythmias or sudden death in dilated cardiomyopathy: systematic review and meta-analysis. JACC Heart Fail 2017;5:28–38.
60. Frierich M, Sechtem U, Schulz-Menger, et al. Cardiovascular magnetic resonance in myocarditis: a JACC white paper. J Am Coll Cardiol 2009;53:1475–87.
61. Pan JA, Lee YJ, Salerno M. Diagnostic performance of extracellular volume, native T1, and T2 mapping versus Lake Louise criteria by cardiac magnetic resonance for detection of acute myocarditis: a meta-analysis. Circ Cardiovasc Imaging 2018;11:e007598. Published online July 16.

62. Luetkens JA, Faron A, Isaak A, et al. Comparison of the original and the 2018 Lake Louise criteria for diagnosis of acute myocarditis: results of a validation cohort. Radiol Cardiothorac Imaging 2019;1:e190010. Published online July 25.
63. Tahir E, Starekova J, Muellerleile K, et al. Myocardial fibrosis in competitive triathletes detected by contrast-enhanced CMR correlates with exercise-induced hypertension and competition history. JACC Cardiovasc Imaging 2018;11:1260–70.
64. Domenech-Ximenos B, Sanz-de la Garza M, Prat-Gonzalez S, et al. Prevalence and pattern of cardiovascular magnetic resonance late gadolinium enhancement in highly trained endurance athletes. J Cardiovasc Magn Reson 2020;22:62.
65. Kandolin R, Lehtonen J, Salmenkivi K, et al. Diagnosis, treatment, and outcome of giant-cell myocarditis in the era of combined immunosuppression. Circ Heart Fail 2013;6:15–22.
66. Fussner L, Karlstedt E, Hodge D, et al. Management and outcomes of cardiac sarcoidosis: a 20-year experience in two tertiary care centres. Eur J Heart Fail 2018;20:1713–20.
67. Writing Committee, Maddox TM, Januzzi JL Jr, Allen LA, et al. 2021 Update to the 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology solution set oversight committee. J Am Coll Cardiol 2021;77:772–810.