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STATE-OF-THE-ART PAPERS

The Role of Cardiovascular Magnetic Resonance Imaging in the Assessment of Highly Trained Athletes

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ABSTRACT

Exercise-associated benefits on the cardiovascular systems are well established. Although exercise-associated sudden cardiac death is rare, most deaths in young athletes are due to hereditary or congenital cardiac diseases. Athletic adaptation itself is associated with several structural changes that overlap those observed in individuals with cardiomyopathies, often leading to dilemmas for the clinician regarding life-changing decisions including advice against competitive sports participation. Cardiac magnetic resonance plays an increasingly important role in helping to establish an accurate diagnosis in these individuals. This review highlights the role of cardiac magnetic resonance in differentiating physiological adaptation in athletes from pathology. (J Am Coll Cardiol Img 2018;11:247-59) Crown Copyright © 2018 Published by Elsevier on behalf of the American College of Cardiology Foundation. All rights reserved.

The benefits of exercise on the cardiovascular system are well established (1). Exercise curbs several risk factors for atherosclerosis and reduces the risk of an adverse event from coronary artery disease by 50% in the fifth and sixth decades of life. In this regard, young athletes symbolize the essence of good health. These individuals impress with their extraordinary physical skills and stamina. However, occasionally a young athlete may die suddenly during training or competition. Such events are catastrophic, not only because of the number of life years lost in an apparently healthy individual, but also because they frequently occur in the public domain.

Exercise-associated sudden cardiac death (SCD) in the young is rare, affecting 1 in 50,000 athletes. The mean age of the athletes affected in Europe is 23 years old. Male athletes are more vulnerable than female athletes are with a 9:1 ratio and black athletes are more susceptible than white athletes with an 8:1 ratio (2). Almost 80% of athletes are asymptomatic prior to death. Most deaths occur during or just after exercise, suggesting that the multiple stresses of exercise including dehydration, electrolyte imbalance, adrenergic surge, and acid base disturbance may act as a trigger for arrhythmia in these predisposed athletes. The majority of deaths are due to electrical and structural diseases, which can be diagnosed during life and for which there are several interventions to modify the natural history of diseases, including prevention of sudden death.

Based on the aforementioned considerations, there are several initiatives to identify young athletes at risk. These range from mandatory cardiovascular screening in the highest echelons of sport, charitable organizations offering subsidized screening programs, or investigation of a young person with symptoms suggestive of cardiovascular disease or a family history of inherited cardiovascular disease. However athletic adaptation itself is associated with a

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ABBREVIATIONS AND ACRONYMS

ARVC = arrhythmogenic right ventricular cardiomyopathy

CMR = cardiac magnetic resonance

DCM = dilated cardiomyopathy

ECG = electrocardiography

ECV = extracellular volume

EF = ejection fraction

HCM = hypertrophic cardiomyopathy

LGE = late gadolinium enhancement

LV = left ventricle

LVEDD = left ventricular end-diastolic dimension

LVH = left ventricular hypertrophy

LVNC = left ventricular noncompaction

RV = right ventricle

SCD = sudden cardiac death

number of electrical and structural changes that overlap with commonly recognized features of several cardiomyopathies. Such issues usually affect athletes with a left ventricular wall thickness >12 mm or athletes with large left or right ventricular cavities and reduced ejection fraction. Athletes of African or Afro-Caribbean origin (black) engaged in explosive sprint sports with a start-stop nature, such as soccer, and endurance athletes provide challenging clinical scenarios where an inaccurate diagnosis may result in unnecessary disqualification or potentially jeopardize a young life. Cardiac magnetic resonance (CMR) is an essential tool for facilitating an accurate diagnosis in these athletes, and this review will address the role of CMR in differentiating athlete's heart from structural heart disease.

ROLE OF CMR

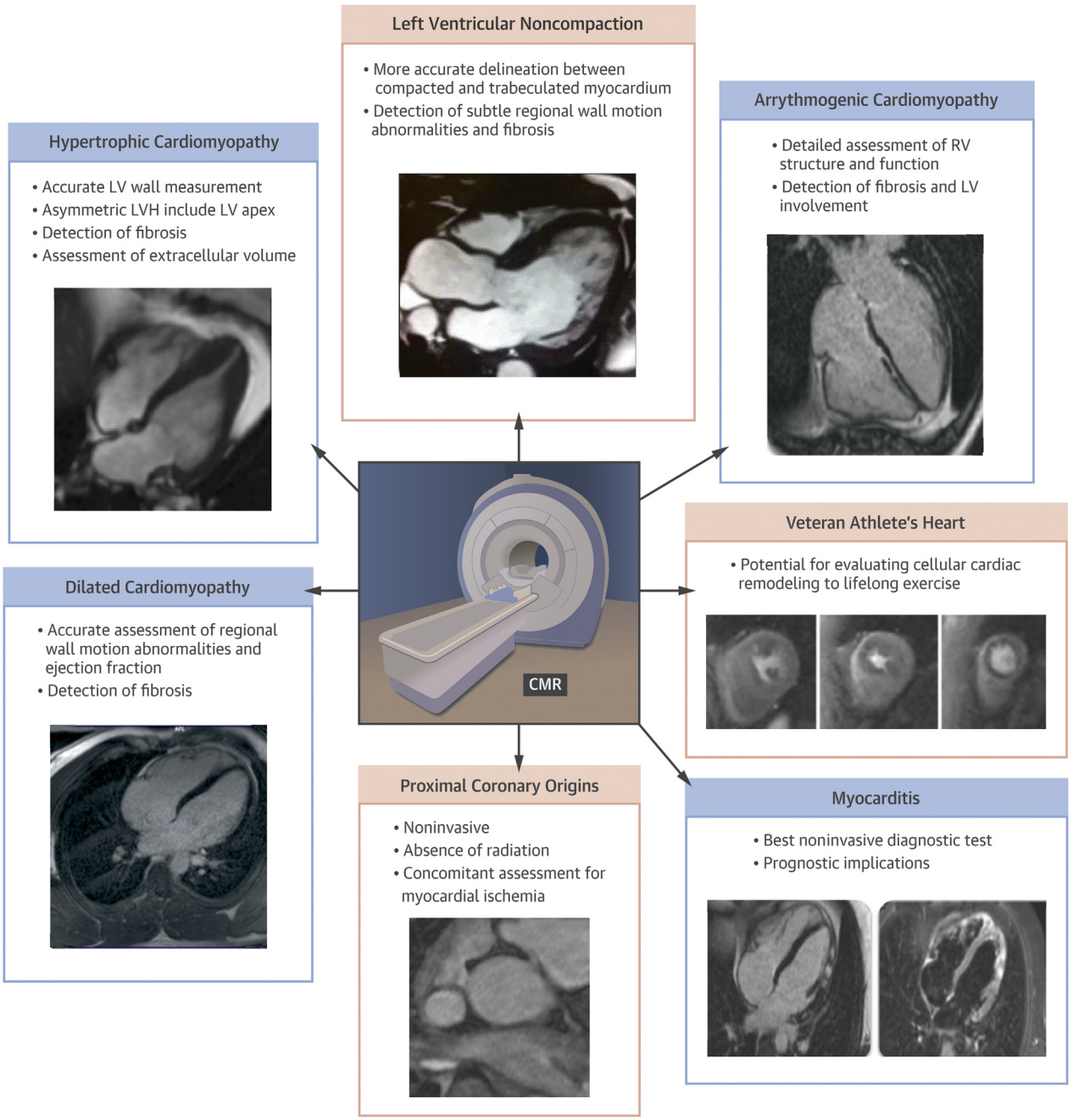
CMR has an important role in providing detailed characterization of the myocardium with high temporal and spatial resolution. Functional cine CMR sequences (i.e., steady-state free precession) allow delineation of the epicardial and endocardial borders of the ventricles, accurate measurement of ventricular wall thickness, regional hypertrophy, and wall motion abnormalities. CMR also provides full ventricular coverage with no interslice gap for accurate assessment of ejection fraction, the ability to image in any plane, and permits analysis of coronary origins. CMR also has the unique capability of detecting myocardial fibrosis with late gadolinium imaging, which often provides clarification of a disease process in athletes with structural features overlapping with cardiomyopathy ("the gray zone"), (**Central Illustration**). Other CMR sequences of value include stress perfusion for ischemia assessment, T_2 short tau inversion recovery (or T2 mapping) for myocardial edema in acute myocarditis, and T_1 mapping/extracellular volume assessment for interstitial fibrosis.

DIFFERENTIATING ATHLETE'S HEART FROM HCM

Approximately 2% of white athletes and up to 13% of black athletes have a left ventricular (LV) wall thickness of 13 to 16 mm, which may be consistent with morphological mild hypertrophic cardiomyopathy (HCM). The differentiation between HCM and physiological left ventricular hypertrophy (LVH) is among the commonest scenarios encountered in sports cardiology. Although there are echocardiography-based algorithms to help differentiate physiological LVH from HCM, the data available make comparisons between sedentary individuals with HCM and athletes with physiological LVH (3,4). In general, HCM is characterized by LVH with a nondilated LV and abnormal diastolic function in 80% (5). Until recently the cardiovascular adaptation in athletes with HCM was unknown. In 2015, Sheikh et al. (6) reported electrical and structural cardiac manifestations in 102 athletes diagnosed with HCM during pre-participation screening or family screening. The athletes were asymptomatic and competed in regular sports at regional, national, or international levels at the time of diagnosis. The study showed that most athletes with HCM have relatively mild LVH (15 to 16 mm), a larger LV cavity and normal indices of diastolic function compared with sedentary HCM patients. Among athletes with HCM, 85% showed an asymmetric pattern of LVH, which was confined to the LV apex in 36% of cases. Only a very small proportion of athletes fulfilled the conventional gray zone, that is, concentric LVH with maximum LV wall thickness ranging between 13 and 15 mm. In these individuals, an important minority (13%) had an LV cavity size of ≥54 mm, and almost 100% had normal indices of diastolic function measured by continuous wave Doppler and tissue Doppler imaging. Another important point emphasized by this study was that almost all athletes (98%) showed lateral T-wave inversion on the electrocardiogram. If current echocardiographic criteria were applied to competitive athletes with HCM, then a significant proportion with apical HCM, those with a large LV cavity and those with entirely normal diastolic function, may not be detected. In this regard, the 12-lead electrocardiography (ECG) may be the "tell-tale" feature and for this reason all athletes with deep T-wave inversion (other than T-wave in leads V_1 to V_4 in black athletes) should be investigated with CMR (**Figure 1**) (7). In a recent study, Schnell et al. (8) assessed 155 athletes with deep T-wave inversion, of which 80% was confined to the lateral leads. Almost 40% of the athletes were subsequently diagnosed with cardiomyopathy. Echocardiography was diagnostic in 24% of athletes. CMR confirmed all of the echocardiographic diagnoses and revealed additional cases of cardiomyopathy or healed myocarditis in a further 24 athletes, demonstrating that CMR significantly increases the diagnostic yield of cardiomyopathy in athletes with marked repolarization changes and a normal echocardiogram.

CMR with its high spatial resolution can better define wall thickness where echocardiographic

CENTRAL ILLUSTRATION **The Role of CMR in the Assessment of Cardiovascular Diseases in Athletes**



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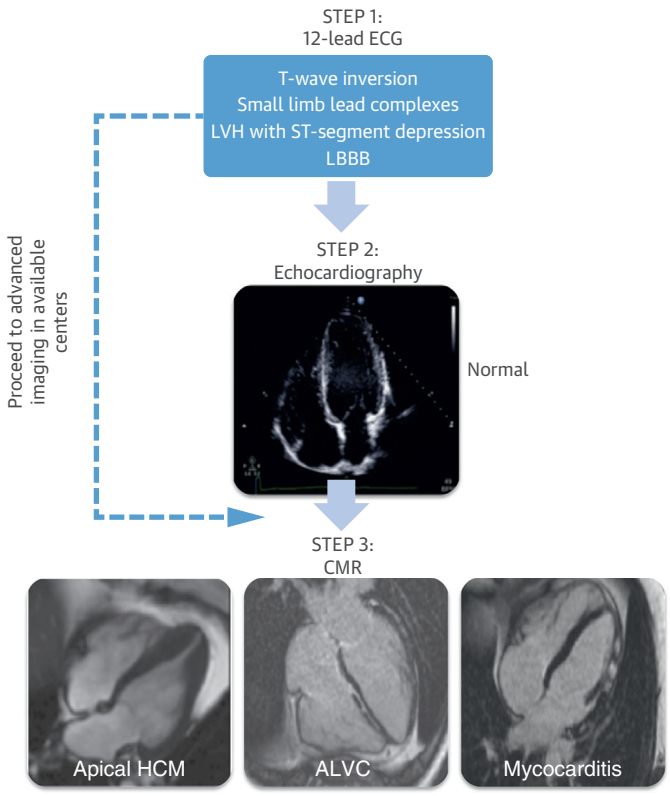
The role of CMR in assessing various cardiovascular diseases was explored. The cardiovascular diseases include hypertrophic cardiomyopathy LV noncompaction, arrhythmogenic cardiomyopathy, dilated cardiomyopathy, proximal coronary origins, veteran athlete's heart, and myocarditis. RV = right ventricle; other abbreviations as in Figures 1 and 3.

FIGURE 1 Step-Wise Approach to Cardiovascular Assessment of Athletes



Step 1: 12-lead electrocardiography (ECG) is used to assess any training unrelated electrocardiographic changes. Step 2: Echocardiography is used to assess biventricular size, regional wall motion, function, and valves. Step 3: Cardiac magnetic resonance (CMR) is performed either in the presence of normal echocardiographic findings or for prognostic value. In centers where advanced imaging is available, the clinician may proceed directly to CMR following identification of abnormalities on the 12-lead ECG. ALVC = arrhythmogenic right ventricular cardiomyopathy; HCM = hypertrophic cardiomyopathy; LBBB = left bundle branch block; LVH = left ventricular hypertrophy.

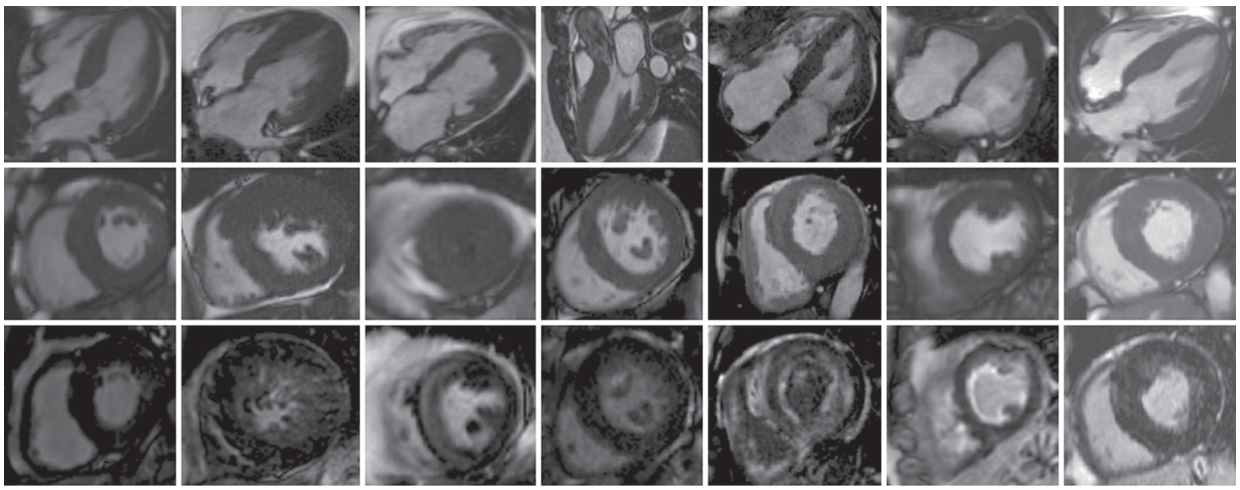
images are ambiguous. In addition, CMR can define regions of subtle localized patterns of hypertrophy not clearly visualized on echocardiography, including apical and lateral wall hypertrophy (**Figure 2**). Tissue characterization using late gadolinium enhancement (LGE) allows identification of macroscopic replacement fibrosis. In HCM, myocardial fibrosis is usually patchy, occurring within maximally hypertrophied segments. In the presence of LVH, the existence of fibrosis greatly helps to clarify the diagnosis of HCM. One study has shown that quantification of fibrosis may be relevant to arrhythmic risk and prognosis (9); however, other studies have only been able to show an association between LGE in subsequent development of heart failure rather than SCD (10,11). Macroscopic myocardial fibrosis is detected in just over 50% of HCM patients; therefore, the absence of LGE cannot be used to exclude HCM (9). In such cases, the novel technique of T_1 mapping and extracellular volume (ECV) assessment, which is still a research tool, mighty provide quantitative assessment of myocardial composition (i.e., total extent of expanded extracellular space) for athletes with a wall thickness between 12 and 15 mm.

Swoboda et al. (12) assessed 40 highly trained athletes with physiological LVH with CMR and T_1 mapping and demonstrated an inverse relationship between ECV and LV wall thickness. These findings suggest that physiological LVH is due to myocyte enlargement rather than increased extracellular matrix. In contrast, the pathological LVH of HCM correlated directly with ECV, indicating that a significant proportion of the LV mass is due to an increase in extracellular matrix. Among athletes with an LV wall thickness of 12 to 15 mm, an ECV >22.5% showed sensitivity of 100% and specificity of 90% for diagnosing HCM. McDiarmid et al. (13) compared the ECV in 30 endurance athletes and 15 healthy control subjects. They found that athletes with very high peak Vo_2 (>60 mls/kg/min) had the largest compartmentalized mass i.e. mass constituted by myocyte enlargement, compared with untrained athletes and individuals with a peak Vo_2 <60 ml/kg/min. Despite its potential in differentiating between physiological LVH and HCM, T_1 mapping requires validation in a much larger cohort of athletes, particularly those with HCM.

DIFFERENTIATING ATHLETE'S HEART FROM ARVC

The distinction between physiological right ventricular (RV) enlargement and arrhythmogenic right ventricular cardiomyopathy (ARVC), a genetic disease associated with fibro-fatty infiltration of the RV myocardium is increasingly important. ARVC accounts for 4% to 22% of SCD in athletes (14). CMR is superior to echocardiography in providing detailed characterization of the RV volume and function and regional wall motion abnormalities, given its high spatial resolution. It is well recognized that up to 14% of endurance athletes exhibit anterior T-wave inversion in V_1 to V_2/V_3 (15) and up to 40% of endurance athletes show RV outflow dimensions within the range that would be consistent with a diagnosis of ARVC (16). Furthermore, a significant proportion of endurance athletes reveal a borderline low RV fractional area change (17) and 2.5% of athletes have ventricular extrasystoles arising from the RV outflow tract, which are the commonest type of ventricular extrasystoles identified in patients with ARVC. The

FIGURE 2 **CMR Demonstrating Examples of LVH and Patterns of Fibrosis in Different Clinical Conditions**



(Top and middle) Long- and short-axis of cardiac structure on cine still images demonstrating pattern of LVH. **(Lower)** Myocardial fibrosis pattern on late gadolinium enhancement imaging. **(A, B)** HCM; **(C)** apical HCM; **(D)** subaortic membrane; **(E)** amyloid; **(F)** endomyocardial fibrosis; **(G)** hypertensive heart disease. Abbreviations as in Figure 1.

current imaging task force criteria for ARVC include RV dysfunction and RV akinesia before a diagnosis of ARVC can be considered. Echocardiography may fail to identify subtle RV wall motion abnormalities. Conversely, usual wall motion anomalies adjacent to the insertion of the moderator band may be potentially misinterpreted as pathology.

Zaidi et al. (16) assessed the accuracy of the diagnostic criteria for ARVC when applied to athletes with T-wave inversion and attempted to identify discriminators between physiological adaptation and pathology. The investigators comprehensively assessed 45 athletes with T-wave inversion, 35 athletes without T-wave inversion, and 35 young patients with ARVC using 12-lead ECG, echocardiography, CMR, exercise treadmill test, 24-h Holter ECG, and signal-averaged ECG. The main findings were that balanced biventricular dilatation was likely to represent a benign manifestation of training in asymptomatic athletes without a relevant family history of cardiomyopathy or SCD. In contrast, a RV ejection fraction <45% on CMR, RV end-diastolic volume/LV end-diastolic volume >1.3:1, regional wall motion abnormalities in RV and presence of LGE were highly indicative of ARVC.

The thin-walled RV poses challenges in the assessment of global RV LGE in ARVC; however, recent advances in 3-dimensional LGE allow improved visualization of fibrosis and should be considered when there is suspicion of subtle fibrosis (Figure 3). Furthermore, RV insertion point fibrosis appears to be common in athletes and may be observed in up to 40% of athletes. It is considered a benign feature from the mechanical pull of the thinned-wall RV during exercise on the RV/LV septal insertion hinge point (18).

Advances in the molecular genetics of ARVC and pathology studies have revealed that the disease process may also affect the LV and occasionally be confined solely to the LV (19–21). In the latter case, the presence of a nonischemic pattern of LGE affecting an athlete with a high ventricular ectopic burden but otherwise preserved and synchronous ventricular contraction may signal a potentially serious cardiomyopathy that will not be detected with echocardiography (22). Indeed, all athletes with a high ectopic burden with normal cardiac structure and function on echocardiography should be referred for CMR (Figure 1).

DIFFERENTIATING ATHLETE'S HEART AND DCM

Dilated cardiomyopathy (DCM) is defined as a dilated LV with reduced ejection fraction (EF) in the absence of significant ischemic heart disease, hypertension, or valvular disease and is a rare but recognized cause of SCD in athletes (23). In the majority of athletes with

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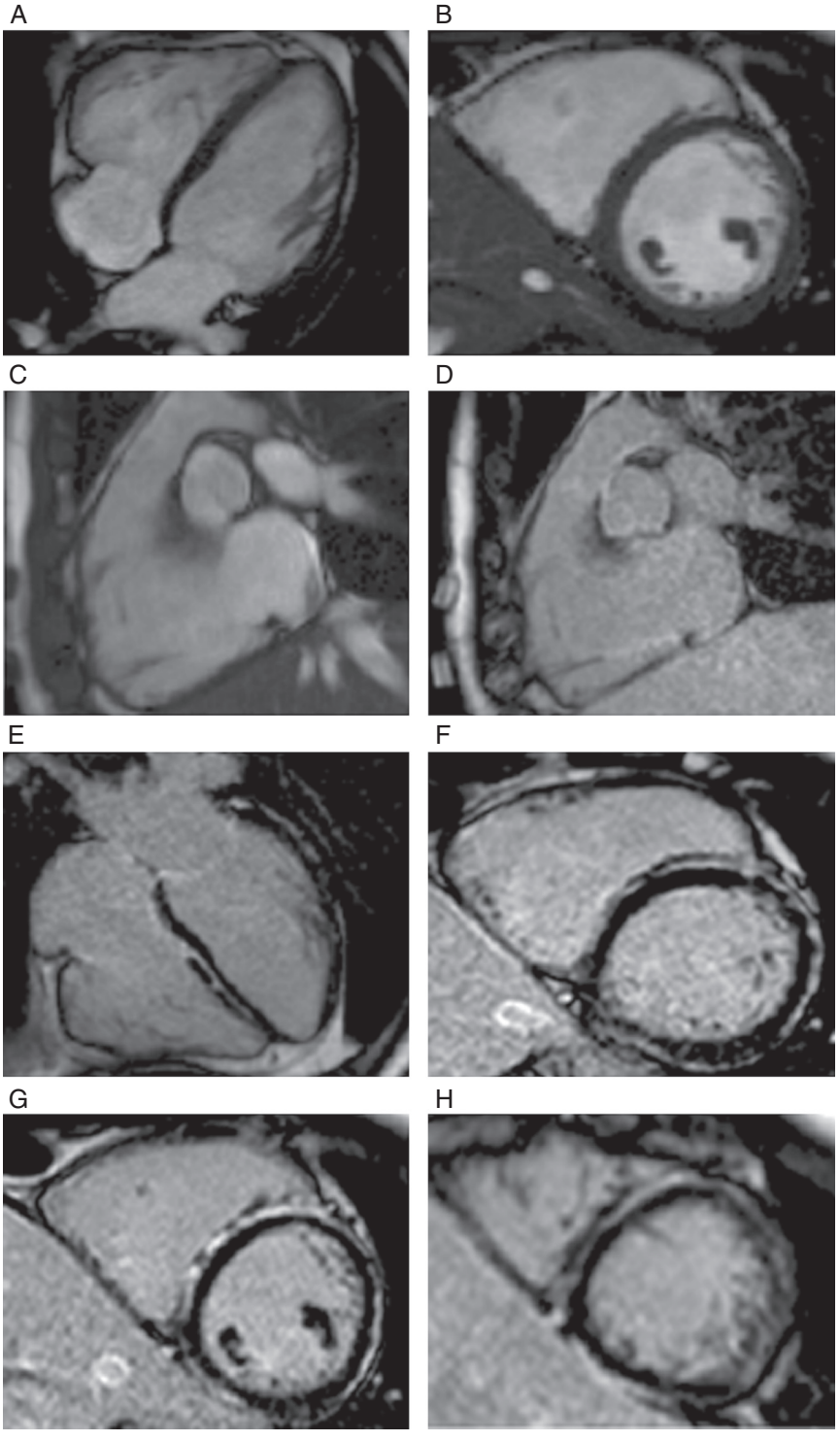
FIGURE 3 Example of an Athlete With Arrhythmogenic Cardiomyopathy of the LV



The images exhibit left and right chambers **(A to C)** and extensive subepicardial and mid-myocardial fibrosis **(D to H)** within the left ventricle (LV) in an athlete with arrhythmogenic cardiomyopathy.

DCM, the inability to generate a satisfactory cardiac output during exercise selects them out for competitive sport (24).

Endurance athletes such as long-distance runners, swimmers, rowers, and cyclists may develop significant chamber dilatation due to long-term volume and pressure overload, which overlaps with DCM. Pelliccia et al. (25) assessed 1,309 elite athletes and observed that the left ventricular end-diastolic dimension (LVEDD) exceeded the normal limits of >54 mm in 584 athletes (45%) and 14% had an end-diastolic dimension >60 mm. Similarly, an echocardiographic study by Abergel et al. (26) of 286 elite professional cyclists competing in the Tour de France showed that 214 athletes (75%) had an LVEDD outside the normal range (cutoff of 57.4 mm as the upper limit of normal), with 147 athletes (51%) having an LVEDD >60 mm and 4 (1.4%) athletes with LVEDD >70 mm.

Although there are echocardiographic values from many thousands of athletes of differing demographics and sporting practices, normal CMR values in athletes have been reported by few centers and from a less diverse sporting population. Prakken et al. (27,28) provide the largest CMR data describing the normal range of cardiac morphology and function. They compared biventricular volumes, masses, and dimensions in 222 endurance athletes (79 elite and 143 recreational; 42% female) with 114 age- and sex-matched nonathletes. Indexed LV end-diastolic volume and wall mass were higher in regular and elite athletes than in nonathletes. Male sex, body surface area, and training hours per week were associated with larger ventricular volumes and greater mass. Approximately 50% of elite male athletes revealed a short-axis LV diameter >60 mm and a RV diameter exceeding 50 mm. Of elite female athletes, 16% showed a LV diameter >60 mm or a RV diameter >50 mm.

A common misconception among physicians is that the resting LVEF should be normal in athletes. In reality, athletes with large LV volumes do not require a high EF to deliver a cardiac output of 5 l/min at rest. Indeed, endurance athletes may show a low LVEF. Among Tour de France cyclists, 37% had LVEF ≤60%, 15% had an EF of 52% to 56%, and 11% had an EF <52% but not <45% (26). Similarly, CMR also underestimates overall cardiac function at rest. Prakken et al. (27) assessed the resting EF in 79 elite athletes and revealed a mean LVEF of 55 ± 5.5% and mean RVEF of 50 ± 4.4%. Interestingly, in their cohort, 22 athletes (28%) had a resting LVEF of 45% to 50% and 19 athletes (24%) had a lower EF of 40% to 45%. These observations have the potential of an erroneous diagnosis of DCM in an athlete. In such cases, the detection of LGE in the mid wall of the LV is almost pathognomonic of an underlying cardiomyopathy in a patient with an increased LV volume and reduced EF, but the absence of LGE does not necessarily exclude a DCM (29).

Perhaps differentiating physiological LV/RV enlargement from DCM requires a technique to enable comprehensive assessment of biventricular filling and emptying during exercise. Exercise echocardiography can be helpful in cases where athletes exhibit a combination of LV dilatation and suppressed or low-normal resting EF. Abernethy et al. (30) demonstrated normalization of LV function with exercise in all their athletes with reduced resting systolic function. In contrast, patients with DCM rarely demonstrate the ability to augment cardiac output in response to increased metabolic demands (31). Simultaneous measurement of gas exchange during a cardiopulmonary exercise testing may also prove useful in the diagnosis of DCM (32) although an exercise CMR-based study comparing athletes with physiological LV enlargement and athletes with DCM showed that the peak V_{O_2} consumption values between the groups were not discriminative (33).

La Gerche et al. (34) described a novel technique of real-time-ungated CMR measuring biventricular volumes during high-intensity exercise. Electrocardiographic and respiratory movements were retrospectively synchronized, enabling compensation for the cardiac cycle and respiratory phase. The real-time-ungated sequence was compared with standard exercise CMR with ECG gating and furthermore, the accuracy of this new sequence was substantiated with invasive direct Fick method of cardiac output assessment. The investigators tested 34 active subjects of whom 4 were competitive athletes. A separate cohort of 19 subjects participated in the validation and reproducibility phase of the study. The technique was deemed feasible, reproducible, and accurate in their cohort of subjects. The same investigators subsequently developed an in-scanner real-time CMR protocol to assess dynamic increases in ventricular function with exercise (18). More recently, Le et al. (35) also described an in-scanner exercise real-time CMR protocol that was tested in 11 athletes and 11 nonathletes and showed that the technique was highly reproducible. Such techniques have the potential of facilitating the differentiation between physiology and pathology in athletes with large ventricular volumes and mildly low EF.

Although still research tools, T_1 mapping and ECV might provide quantitative assessment of myocardial composition in athletes within the gray zone. In a recent study by Mordi et al. (36), T_1 and T_2 mapping

were assessed in 16 patients with nonischemic DCM with an EF between 45% and 55%, 21 healthy control subjects, and 21 male subjects with a history of aerobic exercise for at least 6 h per week and an EF between 45% and 55%. The investigators reported higher native T_1, ECV, and T_2 relaxation times in patients with DCM than in control subjects and athletes. In their study, native T_1 provided the best method of differentiation between individuals who exercised and patients with DCM. Importantly, a quarter of the patients with DCM had mid-wall fibrosis with the potential of falsely raising the native T_1 value. Further studies in larger cohorts are necessary to establish the role of T_1 mapping in differentiating physiological cardiac adaptation from DCM.

LEFT VENTRICULAR NONCOMPACTION IN ATHLETES

Left ventricular noncompaction (LVNC) is characterized by a double-layered LV myocardial wall architecture comprising a thin compacted epicardial layer and a trabeculated inner endocardial layer. It is well recognized that a high proportion of athletes (8%) fulfill current echocardiographic criteria for LVNC criteria (**Figure 4**) (37). It is unlikely that such a high proportion of individuals have genuine cardiomyopathy (38). Data from patients with chronic anemia and pregnant women suggest that increased LV trabeculations may occur due to a chronic increase in preload (38,39). CMR with its superior spatial resolution provides a detailed assessment of the thin epicardial layer and can differentiate endocardial trabeculations from apical HCM and crypts within the epicardium, which are rarely detectable with echocardiography. Furthermore, CMR is more specific for regional wall motion abnormalities and quantifying impaired LV function as well as confirming pathology in the presence of fibrosis. There are currently several CMR criteria proposed for the diagnosis of LVNC. The first from Petersen et al. (40) in 2005 proposed a ratio of >2.3 in diastole as a differentiating factor for LVNC. MESA (Multi-Ethnic Study of Atherosclerosis) demonstrated that the Petersen criteria had low specificity for excluding people without LVNC (41). Furthermore, the measurements in the long-axis views are variable due to difficulty excluding papillary muscle structure. Jacquier et al. (42) proposed a slightly different approach to the diagnosis of LVNC by calculating the LV trabecular mass and showing that a trabecular mass >20% of the total LV mass was predictive of LVNC. Subsequent evaluation of the Jacquier criteria by others has demonstrated a poor interobserver variability (43). Captur et al. (44) summarized global LV trabecular complexity as a continuous variable termed fractal dimension. A fractal dimension cutoff ≥1.3 provided the optimal prediction for patients with LVNC. The fractal approach was reproducible compared with LVNC analysis techniques proposed by Petersen and Jacquier. However, specific software is required and large-scale trials are necessary to validate this technique. Furthermore, a diagnosis of LVNC should not solely rely on imaging alone and should take into account the clinical presentation, family history, 12-lead ECG, and cardiac function to increase sensitivity of diagnosis.

MYOCARDITIS IN ATHLETES

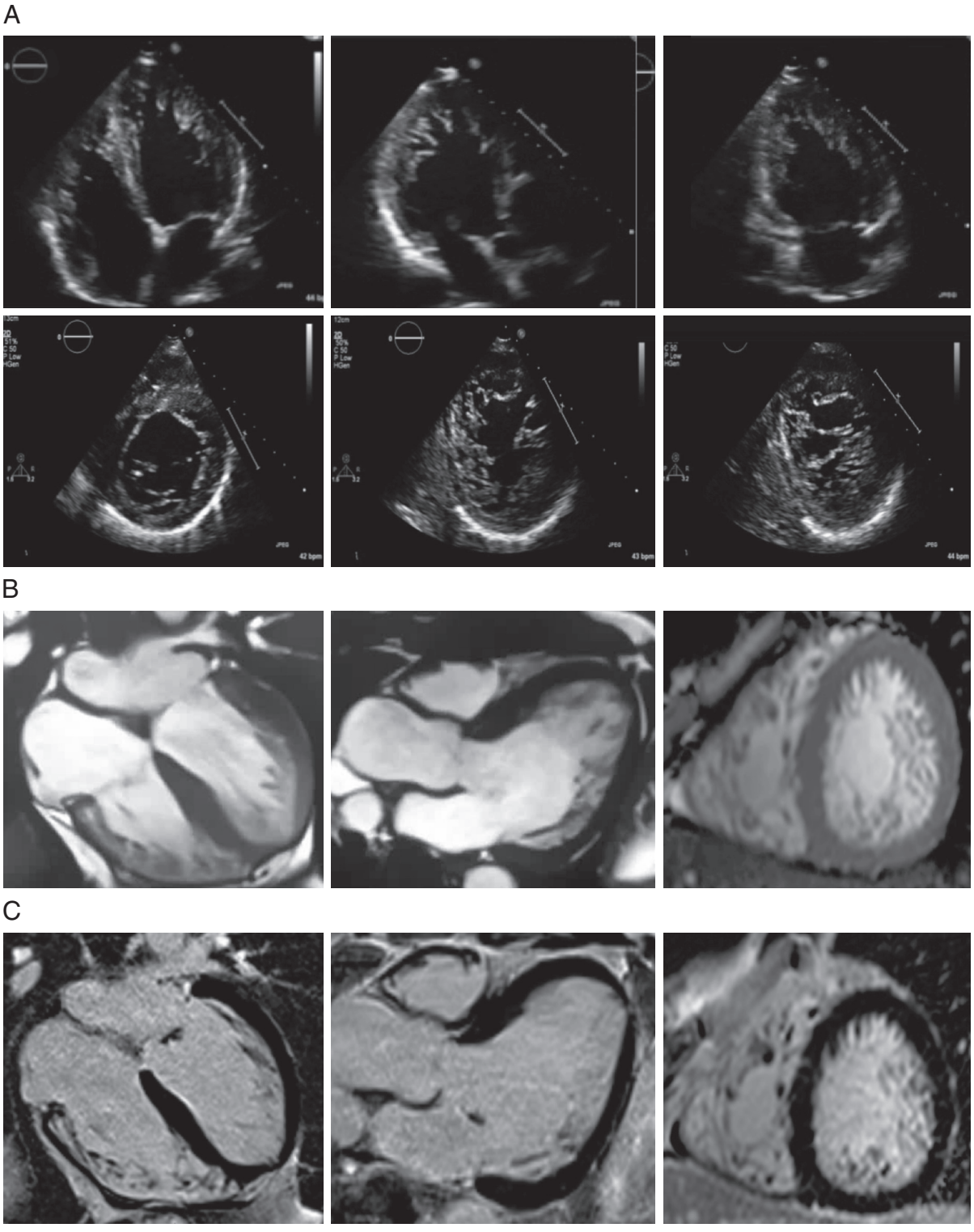
Myocarditis is an important cause of arrhythmogenic SCD in young athletes. It is recommended that all athletes in whom myocarditis is suspected should be investigated with CMR. Grun et al. (45) investigated 203 biopsy-proven viral myocarditis patients and showed that LGE was the best predictor of mortality (hazard ratio: 12.8) that was independent of symptoms, EF and LV end-diastolic volume. More recently, Gräni et al. (46) assessed 670 patients suspected of myocarditis with CMR and demonstrated that LGE was a major predictor of mortality with septal and mid-wall pattern showing a strong association with major adverse cardiac events. A normal CMR study corresponded to a low annual major adverse event rate of 0.8% and a death rate of 0.3%.

Whereas asymptomatic athletes with myocarditis may return to sports if they have a normal echocardiogram, exercise capacity, and no arrhythmias, the current European sports cardiology consensus is that the precise timing for return may be guided by the presence of LGE (**Figure 5**). Athletes with LGE should be advised to refrain for competition for 6 months. Formal prospective studies are required to determine whether LGE provides prognostic information about the management of athletes with myocarditis.

CONGENITAL CORONARY ARTERY ANOMALY IN ATHLETES

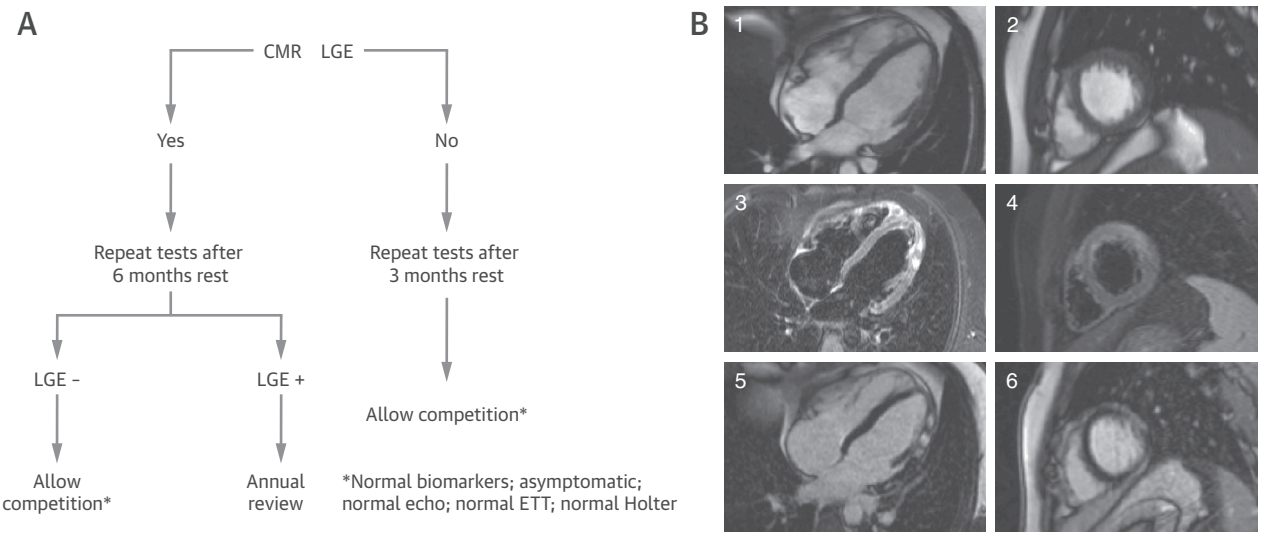
Congenital coronary artery anomalies may cause SCD in young athletes particularly if a coronary artery originates from the opposite sinus of Valsalva and has an interarterial course between the aorta and the pulmonary artery. The risk is greater if the left coronary artery originates from the right sinus of Valsalva (47). The prevalence of anomalous coronary origins is ≤0.45% (47). Anomalous coronary artery origin should be considered in any athlete presenting with unexplained chest pain or syncope. Identifying the

FIGURE 4 **Example of an Athlete With Increased LV Trabeculation**



Echocardiographic and cardiac magnetic resonance visualization **(A, B)** of excess left and right ventricular trabeculation and late gadolinium enhancement imaging **(C)** showed no myocardial fibrosis in this individual. LV = left ventricular.

FIGURE 5 Assessment of an Athlete With Myocarditis



(A) Flow diagram to aid assessment of an athlete with myocarditis. **(B)** Cardiac magnetic resonance (CMR) example of an athlete with myocarditis: **(1, 2)** HLA and mid-ventricular SAX cine still; **(3, 4)** positive T_2-short tau inversion recovery of HLA and SAX demonstrating myocardial edema/inflammation; **(5, 6)** late gadolinium enhancement showing subepicardial and mid-myocardial patchy fibrosis. ETT = exercise treadmill test; HLA = horizontal long axis; LGE = late gadolinium enhancement; SAX = short axis.

origin of the coronary arteries is possible with echocardiography using the short-axis views of the aorta (48). Although visualization of the left coronary artery is possible in up to 97% cases, identification of the origin of the right coronary artery may not be possible in as many as 20% of athletes (49). The spatial resolution for imaging the coronary arteries with CMR angiography is inferior to CT coronary angiography although CMR angiography has the capability of visualizing the origins and proximal course of the arteries (**Figure 6**) (50). Furthermore, CMR stress perfusion allows for assessment of inducible ischemia, which has an important role in decisions relating to surgical intervention in asymptomatic right coronary origin from the left sinus of Valsalva.

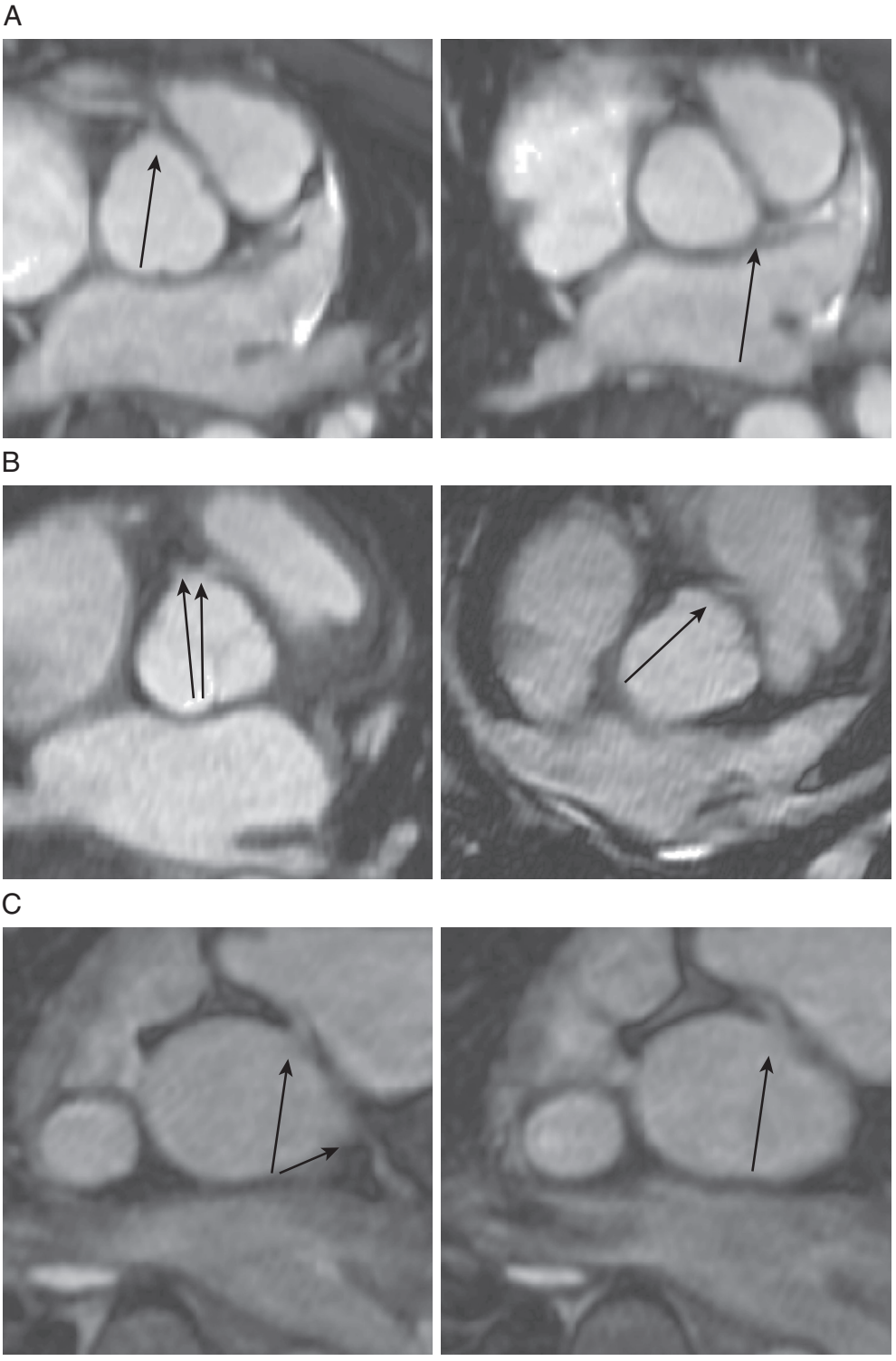
VETERAN ATHLETES

Over the past few decades, endurance events such as marathons, triathlons, and iron-mans have become increasingly popular with individuals in their fifth decade onward. Indeed, such veteran athletes comprise almost 40% of major marathoners and many have exercised intensively for decades. In parallel, there have been several reports demonstrating high concentration of biomarkers of cardiac damage and transient reduction in ventricular function after exercise.

It has been postulated that such biochemical and functional profiles (albeit transient) may reflect a subclinical myocarditis that may ultimately result in a substrate for arrhythmogenesis. Animal studies in rats forced to exercise for 1 h per day for 16 weeks have shown fibrosis in the atria and RV, impaired LV relaxation, and ease of inducibility of both atrial fibrillation and ventricular tachycardia (51). Although no study in humans who have exercised intensively has been able to link troponin leak with myocardial inflammation (52), there are emerging reports that lifelong athletes reveal an increased prevalence of myocardial fibrosis compared with sedentary counterparts of similar age (53).

The initial studies in veteran athletes were conducted by Breuckmann et al. (54). The investigators assessed 102 healthy asymptomatic veteran male marathon runners who were 50 to 72 years old and who had completed at least 5 marathons during the past 3 years and revealed a nonsignificant increase in prevalence of LGE between athletes and age-matched control subjects (12% vs. 4%, $p = 0.07$). Of the 12 athletes with LGE, 5 had a subendocardial distribution typical of coronary artery disease pattern infarction and 7 had nonspecific mid-myocardial patchy pattern of LGE. An important limitation of this study was that over 50% of athletes were previous smokers and a further 4.6% were current

FIGURE 6 **CMR Demonstrating Examples of Coronary Artery Anomaly**



(A) Normal left and right coronary origins. **(B)** Anomalous left coronary artery arising from the right coronary origin with a malignant course between the aorta and pulmonary trunk. **(C)** Anomalous right coronary artery arising from the left coronary origin and coursing between the aorta and pulmonary trunk. CMR = cardiac magnetic resonance.

smokers, raising the possibility that the subendocardial LGE was the result of coronary disease and endothelial dysfunction. The 7 individuals with noncoronary artery disease LGE pattern raised the possibility that lifelong distance running may cause myocardial scarring. Wilson et al. (55) also assessed 12 lifelong veteran endurance athletes, all of whom had run over 100 marathons with CMR and LGE, and identified myocardial fibrosis in 6 athletes (50%) compared with 20 age-matched veteran control subjects and 17 younger male endurance athletes. Four athletes had a nonspecific LGE pattern, 1 had findings consistent with previous myocarditis, and 1 with features of myocardial infarction. The investigators demonstrated that LGE is associated with the number of years of training ($p < 0.001$) and number of competitive marathons ($p < 0.001$) completed.

A CMR study of 158 veteran athletes (28 young athletes, 71 veteran control subjects, and 21 young control subjects) demonstrated that both young and veteran athletes have greater LV mass on CMR than their sedentary counterparts (53,56). The myocardial native T_1 signal, which is a measure of the interstitial space and its constitution and the ECV compartment, was lower in athletes than in control subjects, suggesting that the increased LV mass in athletes is due to cellular hypertrophy rather than expansion of interstitial space. Comparison of young athletes with older athletes showed that younger athletes were capable of developing a greater LV mass than older athletes; however, T_1 mapping and ECV measurements were no different between younger and older athletes. These findings suggest that lifelong exercise results in expansion in interstitial space or diffuse fibrosis. Furthermore, veteran athletes that ran long distance compared with those who participated in short distances had larger end-diastolic volumes, greater LV mass, but smaller T_1 signal and lower ECV. The investigators also identified minor fibrosis within RV insertion points, papillary muscles, or RV trabeculae in 44% of athletes and 10% of control subjects. There were no differences in the prevalence of minor focal fibrosis between veteran athletes and young athletes; however, focal fibrosis was more common in male athletes than in female athletes. Major fibrosis within the compacted myocardium was almost exclusively present in 11.4% of veteran male athletes with age being the only independent predictor. An ischemic LGE pattern was identified in one-third of veterans, 56% showed a nonischemic pattern, and 11% demonstrated both patterns. This study was cross-sectional; therefore, the significance of myocardial fibrosis in veteran athletes is uncertain and larger prospective studies are required.

CONCLUSIONS

CMR has a pivotal role in evaluating cardiac structural changes in competitive athletes who often present with challenging and diagnostic dilemmas. CMR enables the detection of athletes at risk of SCD by providing precise assessment of the LV and RV function and tissue characterization. Recent advances in T_1 mapping provide a valuable opportunity to study the significance of lifelong exercise on the myocardium.

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