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European Association of Preventive Cardiology (EAPC) and European Association of Cardiovascular Imaging (EACVI) joint position statement: recommendations for the indication and interpretation of cardiovascular imaging in the evaluation of the athlete's heart

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European Association of Preventive Cardiology (EAPC) and European Association of Cardiovascular Imaging (EACVI) joint position statement: recommendations for the indication and interpretation of cardiovascular imaging in the evaluation of the athlete's heart

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1. Introduction

Athletic training is associated with a spectrum of morphologic and functional cardiac adaptations known as 'the athlete's heart'.^{1,2} To the purpose of the present document an athlete is defined as an individual of young or adult age, either amateur or professional, who is engaged in regular exercise training and participate in official sports competition. Official sports competition is defined as an organized team or individual sports event that place a high premium on athletic excellence and achievement and is organized and scheduled in the agenda of Athletic Associations.³

A vast amount of literature has been assembled over the last two decades improving our understanding of the characteristics of physiologic cardiac remodelling in athletes. However, there are still areas of uncertainty regarding the differential diagnosis of the most marked expression of the athlete's heart, with certain inherited cardiac diseases, such as hypertrophic (HCM), dilated (DCM), or arrhythmogenic cardiomyopathy (AC) and left ventricular non-compaction (LVNC) cardiomyopathy.⁴⁻⁷

Indeed, in the more recent times, advances in technology, including three-dimensional (3D) echocardiography, speckle tracking echocardiography (STE), cardiac magnetic resonance (CMR), and multi-detector computed tomography (CT) have largely improved the diagnostic capabilities of the modern imaging modalities and made possible the correct identification of a broader spectrum of pathologic cardiovascular conditions that might occur in the athlete's population.

In 2015, an initial effort has been carried out by the European Association of Cardiovascular Imaging (EACVI) in order to guide appropriate interpretation of imaging in the context of athletes' evaluation.⁸ After the initial interest raised by this document, further advances have been carried out in this field, including new international criteria for electrocardiogram (ECG) interpretation, updated recommendations for sport eligibility from the American College of Cardiology and American Heart Association, and further research in this field.⁹⁻¹⁶

Therefore, we believed it timely and appropriate to expand previous work and assemble a novel recommendation document with combined effort of experts from both the European Association of Preventive Cardiology (EAPC) and EACVI in order to properly address the determinants of cardiac remodelling, indications for imaging and clues for differential diagnosis with cardiac pathology. In addition, in this revised document we addressed number of pathologic conditions that are relevant to the cardiovascular evaluation of the athletes (and were not included in previous document), such as left-ventricular non-compaction, myocarditis, mitral valve prolapse, and bicuspid aortic valve (BAV).

2 Cardiovascular adaptations in athletes

2.1 Impact of gender, age, race, and body size

The quest for excellence in sports is associated with a plethora of electrical, structural and functional cardiac adaptations termed the 'athlete's heart'. Manifestations of the athlete's heart include a higher prevalence of electrocardiographic anomalies, balanced increase in the

left and right cardiac cavity sizes, increased left ventricular (LV) wall thickness and superior indices of systolic and diastolic function, compared with sedentary individuals.^{4,17-19} Such cardiac adaptations are usually modest and fall within accepted normal limits. Occasionally, however, athletes reveal marked electrical and structural expressions that overlap with those observed in cardiac diseases.

It is imperative that clinicians adopt an individualized approach to the interpretation of an athlete's evaluation, as expression of the athlete's heart is influenced by several factors (Figure 1). Body size has an important influence on cardiac dimensions, accounting for about 50% of the variability of LV cavity size and mass in highly trained athletes.^{4,20} Therefore, when assessing the extent of cardiac remodeling, the absolute LV dimensions in an athlete should be viewed in the context of the body size.⁴ Despite these observations, indexing the structural and functional parameters is still limited in the clinical practice. The limitations of current scaling methods is underscored by the fact that the most widely used method for calculation of the body surface area (BSA; the Dubois regression) is an empirically derived formula that was developed from nine cadaveric subjects and prone to significant errors. Contemporary studies have suggested the use of fat free mass, or (if impractical) the use of height for normalization of cardiovascular variables.²¹

Women who regularly engage in sports show similar cardiac adaptations compared with male counterparts but commonly to a lesser extent, in term of absolute values. Female athletes exhibit modest absolute increases in LV wall thickness and cavity size, as well as modest increases of right ventricular (RV) and bi-atrial cavity size when compared with sedentary women.^{4,19,22,23}

Ethnicity has emerged as a major determinant of cardiac adaptation to exercise, with black athletes exhibiting a higher prevalence of electrocardiographic anomalies and significantly more LV hypertrophy in response to exercise training.^{17,23-25} Electrocardiographic anomalies are present in up to 40% of black athletes with T-wave inversions being present in a fifth of the cohort.²⁶ Papadakis et al.¹⁷ demonstrated that 13% of black athletes exhibit anterior T-wave inversion (V1-V4), which when associated with ST-segment elevation is likely to represent a feature of the 'black athlete's heart'. In addition, 12% black athletes exhibit a wall thickness >12 mm compared with only 2% of white athletes.¹⁷ The challenge of differentiating between physiological LV

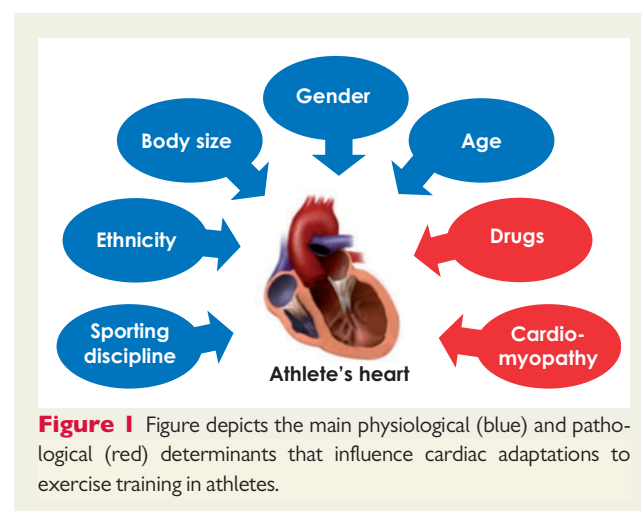


Figure 1 Figure depicts the main physiological (blue) and pathological (red) determinants that influence cardiac adaptations to exercise training in athletes.

hypertrophy and HCM in black athletes is further complicated by the fact that they exhibit similar LV cavity sizes to white athletes and a higher wall thickness to cavity ratio. Preliminary data from Arabic and Asian athletes suggest a similar or even lower prevalence of LV hypertrophy than in white athletes^{27,28} (Figure 2).

With regard to age, some differences have been reported in senior compared with younger athletes; master athletes show lower LV volumes and mass compared with the younger counterpart by both echocardiography and CMR, even though both these parameters are still higher compared with age-matched untrained controls.^{29–31} Systolic function, in terms ejection fraction and two-dimensional (2D) echocardiography strain imaging is usually preserved in master athletes and not different from younger ones; conversely, with aging, changes in diastolic function have been reported in master athletes with smaller E and e' waves and higher A and d' waves.³⁰ These changes in diastolic function reflect the normal aging process of the left ventricle and are similar to what occurs in untrained individual, therefore, it has accepted that exercise activity, while providing prolonged diastolic time associated with lower heart rate, however does not reduce the impairment of early diastolic filling induced by age.^{32,33}

2.2 Impact of type of sport on cardiovascular adaptations

Cardiac adaptations in athletes mainly depend upon the characteristics, intensity, and cumulative duration of training protocols, with a 'dose-effect' relation. Usually, in professional athletes, training schedules involve >10–15 h/week of intensive exercise conditioning. In detail, isotonic (dynamic) exercise is associated with a substantial increase in cardiac output and reduction in peripheral vascular resistance; therefore, endurance training mainly results in volume overload; conversely, isometric (static) exercise is characterized by less increase in cardiac output and by a transient increase in peripheral resistances; therefore, it training is characterized by a pressure overload.^{2,34–36} The first observation describing differences in cardiac adaptations in relation to the type of sport was reported in 1975 by

Morganroth, who observed a concentric LV hypertrophy in isometric sports and an eccentric LV hypertrophy in isotonic disciplines.³⁶ This hypothesis was subsequently expanded after 40 years of investigations and a vast literature has been assembled so far on the athlete's heart, including more recent studies with 3D echocardiography and CMR.^{20,37,38} Most sports disciplines are characterized by a varying degree of both isometric and isotonic components, and therefore the original dichotomic classification in strength (isometric) or endurance (isotonic) disciplines is not applicable for most athletes. Therefore, we suggest a simple classification of sports in four major groups based on the main physiologic characteristics of the exercise training: endurance, power, skill, and mixed (Figure 3). Pelliccia *et al.*¹ demonstrated that the highest impact on LV mass (with both enlarged LV cavity and increased wall thickness) is associated with some endurance disciplines such as cycling, rowing, swimming, and cross-country skiing, that are all characterized by a high degree of both dynamic and static components. In these athletes the substantial degree of cardiac remodelling shows a close relation to the superior exercise performance (as expressed by maximal oxygen consumption).^{39,40} On the other side, predominantly strength disciplines are characterized by only a mild absolute increase in LV wall thickness, which only rarely exceeds the upper range of normalcy.⁴¹ Consequently, LV mass is only mildly increased but, when normalized to athlete's lean body mass, may not be altered.^{41–45} This is justified by the fact that strength training consists in short bursts of intensive exercise and pressure overload, but of relatively short cumulative duration. In addition, there are certain disciplines in which the success is mostly based on athlete's technical or bodily skill (skill disciplines) that have only mild cardiovascular demand and characterized by only mild or even absent cardiac adaptations (no significant changes of LV dimensions and mass). Finally, mixed sports are those with alternate phases of work (either dynamic or static exercise) and recovery. Typical examples are the ball and team activities. In such athletes, the cardiac remodelling shows increase in LV cavity and modest change in LV wall thickness and LV mass.

Recently, Caselli *et al.*²⁰ demonstrated that regardless of the type of sport participated, the ratio between LV mass and end-diastolic volume remains constant, reflecting the balanced and harmonic remodelling of physiologic LV hypertrophy in most sport disciplines. In clinical practice, the relative wall thickness (calculated as twice the left ventricular posterior wall thickness divided by LV diastolic diameter) may be used to characterize the morphologic remodelling of the left ventricle, with values between 0.30 and 0.45 compatible with physiologic remodelling.⁴⁶ Similar adaptations also occur in the other cardiac chambers. The haemodynamic overload caused by endurance training is also responsible for the observed increase in left and right atrial volume and right ventricular size. On the contrary, strength training does not seem to change left atrial (LA) or right ventricular size substantially.^{19,47–49} In addition, other data suggest that endurance disciplines are also associated with a significant but mild increase in aortic root dimensions, while power disciplines have only a trivial impact.⁵⁰ A practical consequence of these observations is that the heart of an athlete is always characterized by a harmonic and consistent increase in the dimension of all cardiac chambers, while a non-harmonic (disproportionate) remodelling potentially suggests a non-physiologic process.

Finally, in the presence of unusual or disproportionate cardiac remodelling in relation to the sport participated and described physiologic determinants, the potential impact of doping substances

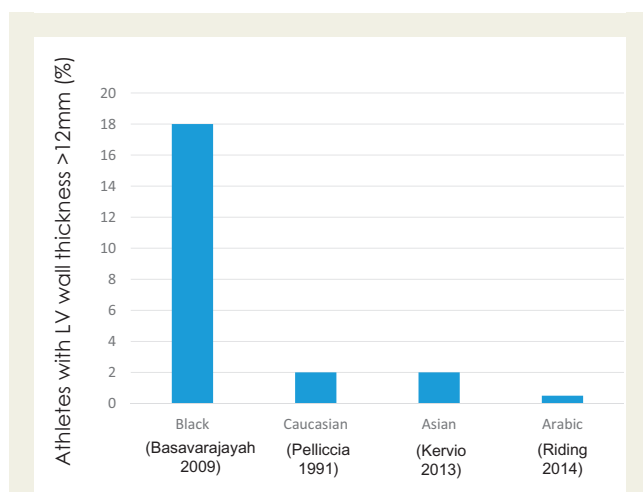
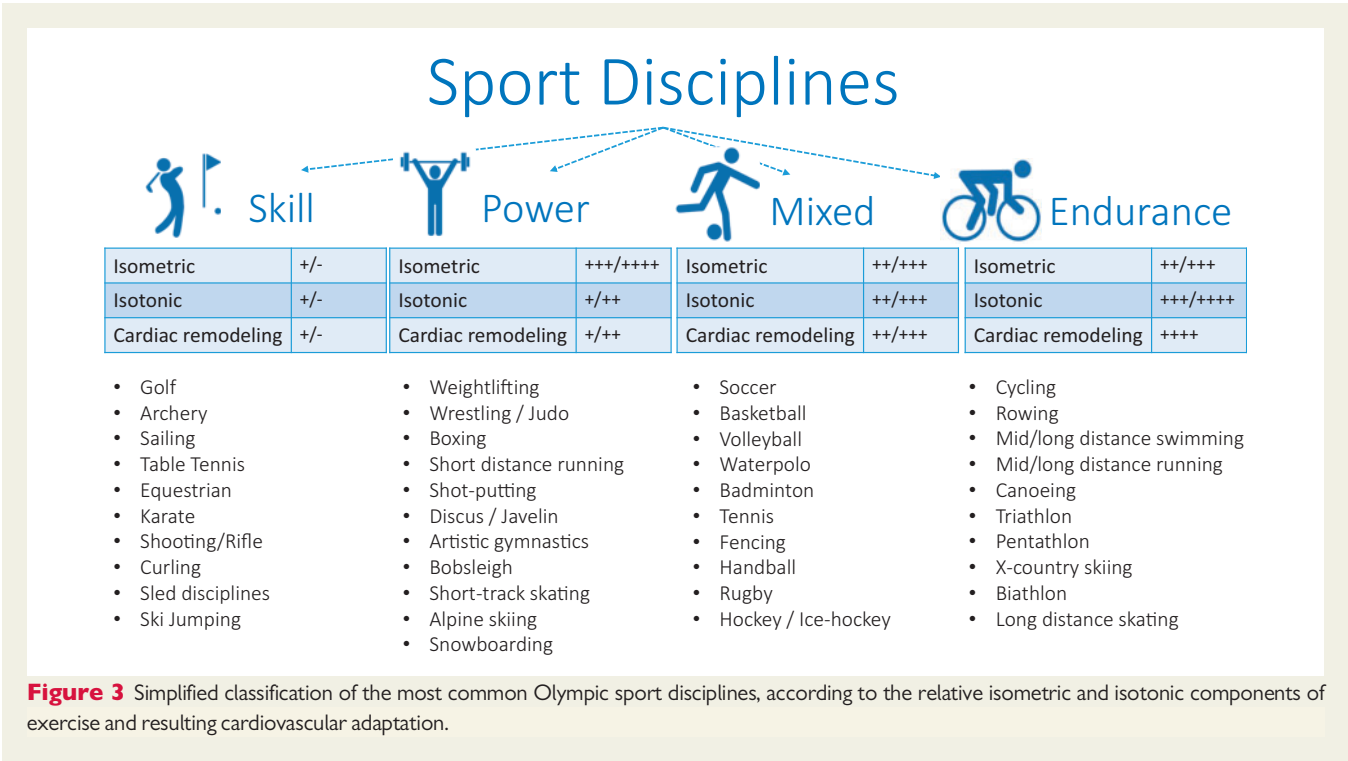


Figure 2 Ethnic-related differences of left ventricular hypertrophy in athletes. The bars represent the percentage of athletes showing left ventricular wall thickness >12mm on echocardiography in Black, Caucasian, Asian and Arabic ethnicities, respectively.



(mostly anabolic androgenic hormones, peptide hormones, growth factors, erythropoietin or its derived, and stimulants) should always be considered.^{8,42,43,51–53} A list of banned drugs is reported and annually updated by the World Anti-Doping Agency. However, in this setting, scientific evidence is lacking (because of the concealed use of the drugs and obvious clinical and ethical limitations to perform a controlled study) and only inconsistent and circumstantial observations have been reported so far. Most of the informations are limited to anabolic androgenic hormones. Few studies demonstrated that power athletes using these hormones typically show concentric LV hypertrophy compared with non-user athletes.^{42,43,53–55} Specifically, anabolic androgenic steroids stimulate cellular protein synthesis and promote the growth of all organs, including the heart; cardiac effects can include the development of concentric hypertrophy and myocardial fibrosis which can persist after deconditioning and years after discontinuation of drug abuse.^{51,56} On cardiac imaging, concentric hypertrophy and impaired systolic and diastolic LV function, which are typically not present in non-user athletes, are suspicious for drug abuse.^{54,55} Anabolic androgenic hormones users have shown a higher mortality compared with clean athletes and postmortem studies confirmed the existence of a drug-induced cardiomyopathy, characterized by greater cardiac mass, increased left ventricular wall thickness, and a large prevalence of extracellular fibrosis.^{51,57,58}

3. Indications for imaging testing and normal findings in athletes

3.1 Clinical and electrocardiogram abnormalities requiring cardiac imaging

Cardiovascular imaging usually represents an advanced step of athlete's evaluation and is preceded by physical examination and/or

12-leads ECG. Table 1 shows the most important clinical indications to perform cardiovascular imaging in athletes. The ability to make diagnosis of an abnormal cardiovascular condition in athletes mainly depends on the clear understanding of the clinical context, on the knowledge of the physiologic limits of cardiac adaptations, and on being able to seek those conditions that are at potential risk for cardiac arrest/sudden death (SCD) or adverse cardiac outcome. Most of the cardiovascular diseases observed in athletes may be suspected on the basis of an abnormal ECG (with the remarkable exception of coronary artery disease (CAD)/anomalies and valvular heart disease). Thanks to the large amount of data collected over the last decade, our understanding and interpretation of the athlete's ECG has evolved and contemporary criteria have reduced the false positives, improving the diagnostic efficacy. Specifically, after the initial work by Corrado et al. in 2010, new refined criteria for ECG interpretation have been subsequently published.^{16,26,59,60} These refined criteria demonstrated to improve specificity up to 84% in black athletes and 94% in white athletes, without compromising the sensitivity of ECG in detecting major cardiac pathologies (100%).²⁶

According to contemporary recommendations for interpretation of the athlete's ECG, the ECG abnormalities are divided in three groups according to their prevalence, relation to exercise training, association with an increased cardiovascular risk, and need for further clinical investigation to confirm (or exclude) presence of underlying cardiovascular disease.⁵⁹ The athlete's heart is commonly (up to 80%) associated with ECG changes such as sinus bradycardia, first-degree AV block, and early repolarization resulting from physiologic adaptation of the cardiac autonomic nervous system to training, i.e. increased vagal tone and/or reduced sympathetic activity. Moreover, the ECG of trained athletes often exhibits pure voltage criteria for LV hypertrophy that reflect the physiological LV remodelling, consisting of increased LV wall thickness and chamber size. Although these

Table 1 Clinical indications to perform cardiovascular imaging studies in athletes

Clinical history:	Imaging tests of choice	Heart disease	Additional testing
SCD in the family	Echocardiography	Cardiomyopathies	Clinical and genetic family screening in selected cases
Known cardiomyopathy in the family	CMR	Mitral valve prolapse	
Palpitations	Echocardiography	Cardiomyopathies	Consider 24-h and/or long-term ambulatory ECG monitoring and/or electrophysiological study in selected cases
Syncope	CMR	Coronary artery disease/anomalies	CT according to clinical suspicion Consider stress echo to rule out LV outflow obstruction
Chest pain	Echocardiography	Coronary artery disease/anomalies	Consider the risk profile, age and radiation exposure
	CMR CT Nuclear imaging		Consider exercise stress imaging
Physical examination	Imaging tests of choice	Heart disease	Additional testing
Cardiac murmurs	Echocardiography	Valvular heart disease	Additional tests on the basis of echocardiographic findings and clinical suspicion (e.g. CMR)
Abnormal cardiac sound		Congenital heart defects	
Marfanoid habitus	Echocardiography CT CMR	Marfan disease	Clinical and genetic family screening Accurate evaluation of thoracic aorta
12-leads electrocardiogram	Imaging tests of choice	Heart disease	Additional testing
T-wave inversion	Echocardiogram CMR	Cardiomyopathies Myocarditis	Clinical and genetic family screening Annual follow-up with imaging tests in athletes with normal findings at initial evaluation
ST-segment depression	Echocardiogram CMR	Cardiomyopathies Myocarditis Coronary artery disease Valve disease	Consider exercise stress imaging Coronary CT or nuclear imaging in athletes with clinical suspicion of coronary artery disease
Pathologic Q-waves	Echocardiogram CMR	Cardiomyopathies Myocarditis Coronary artery disease	Consider exercise stress imaging Coronary CT or nuclear imaging in athletes with clinical suspicion of coronary artery disease
Complete LBBB	Echocardiogram CMR CT Nuclear imaging	Cardiomyopathies Myocarditis Cardiac sarcoidosis Valve disease Coronary artery disease/anomalies	Comprehensive cardiac evaluation for exclusion of heart disease Consider exercise stress imaging
Bifascicular block (RBBB and left anterior hemiblock)	Echocardiogram	Cardiomyopathies Myocarditis Cardiac sarcoidosis Coronary artery disease	Additional tests on the basis of echocardiographic findings and clinical suspicion
Non-specific intraventricular conduction delay	Echocardiogram	Cardiomyopathies Coronary artery disease/anomalies	Additional tests on the basis of echocardiographic findings and clinical suspicion
Minor non-voltage criteria for LV or RV hypertrophy (atrial enlargement and QRS axis deviation)	Echocardiogram	Cardiomyopathies Valve disease Congenital heart disease Pulmonary hypertension	Additional tests on the basis of echocardiographic findings and clinical suspicion
Abnormal exercise testing (repolarization abnormalities/symptoms/arrhythmias)	Echocardiography CMR CT Nuclear imaging	Coronary artery disease/anomalies Cardiomyopathies Myocarditis	Consider the cardiovascular risk profile and age Consider also exercise stress imaging Low-radiation examinations advised in young individuals

CMR, cardiac magnetic resonance; CT, computed tomography; LBBB, left bundle branch block; LV, left ventricle; RBBB, right bundle branch block; RV, right ventricle; SCD, sudden cardiac death.

ECG changes (i.e. training related) may be considered 'abnormal', they do not imply the presence of cardiovascular disorders or an increased cardiovascular risk in the athlete. These ECG abnormalities should be clearly separated from training unrelated ECG patterns (present in <5%), such as ST-segment depression and T-wave inversion, pathologic Q waves, major intraventricular conduction defects, ventricular pre-excitation, long or short QT interval, and ventricular arrhythmias, which may be an expression of cardiovascular disorders, notably cardiomyopathies and cardiac ion channel diseases, with potential risk of SCD during sports.

Finally some borderline ECG variants (left and right atrial enlargement, left and right axis deviation, and right ventricular hypertrophy) are considered of uncertain significance in athletes and, in the setting of cardiac evaluation, should not require additional investigation if not associated with positive family history and present in isolation.²⁶

The ECG should be evaluated in relation with the athlete's gender, age and race, family history of cardiovascular disease and/or SCD, clinical symptoms, physical examination, and intensity/duration of physical exercise. In asymptomatic athletes with a negative family history, ECG changes due to cardiac adaptation to physical exertion should not cause alarm and do not represent indication for additional evaluation. Further diagnostic work-up, instead, should be reserved to the limited subset of athletes with ECG changes potentially reflecting underlying heart disease.

Genotype-phenotype correlation studies in cardiomyopathies reveal that ECG abnormalities may represent the only sign of disease expression in mutation carriers in the absence of any morphologic typical features and even before structural changes in the heart may become evident. Abnormal ECG repolarization in young and apparently healthy athletes may represent initial expression of underlying cardiomyopathy that may not be evident until many years later and that may ultimately be associated with adverse outcomes. The observation that T-wave inversion may identify subjects at risk of subsequent development of structural heart disease underscores the importance of continued clinical surveillance and follow-up. We suggest that athletes with repolarization abnormalities, even in the absence of structural heart disease at first evaluation (after comprehensive and multi-modality imaging), should have imaging studies on a regular basis; usually echocardiography is sufficient on annual basis but when images are suboptimal, other imaging modalities should be considered.⁶¹

3.2 Echocardiography

Standard echocardiography helps to define the upper limits of athlete's LV hypertrophy. In a reference study of 1309 athletes, 55% had an increased LV end-diastolic diameter and, of interest 14% had an LV end-diastolic diameter >60 mm (mostly endurance athletes) in the presence of normal ejection fraction (EF) and normal or increased stroke volume (Table 2). Left ventricular size should therefore be considered in the context of exercise capacity, given its robust association with VO_2 max.^{1,40} Left ventricular cavity is also strongly related to body size, therefore scaling measurements to BSA is advised in the clinical practice (upper limits in athletes have been reported as: <35 mm/m² in male and 40 mm/m² in female).⁴

Maximal LV wall thickness is <12 mm in the majority of Caucasian athletes, with only 2% ranging from 13 to 16 mm, and none >16 mm.^{1,62} Septal wall thickness is thinner in women (average = 9 mm, upper

limit = 11 mm) than in men of the same age and body size.⁶³ Conversely, in black athletes LV hypertrophy (LV wall thickness ≥ 13 mm) is detected in 18% of males and (LV wall thickness > 11 mm) in 3% of females^{23,64} (Table 2; Figure 2).

In adolescent athletes, LV end-diastolic diameter and LV wall thickness exceed values of age- and sex-matched sedentary controls, but are lower than those of adult athletes (LV end-diastolic diameter <60 mm; LV wall thickness <11 mm).⁶⁵

Most of the adaptations induced by physical training seem to regress after temporary training suspension (deconditioning) of only few weeks (9–12), while LV dilatation persists in 20% of the cases, even after an average of 5 years of inactivity, without eliciting adverse cardiovascular events during the follow-up.⁶⁶

Left ventricular ejection fraction is usually unchanged in athletes. Several studies and a meta-analysis confirmed that LV function in athletes is not different from untrained subjects and EF is consistently 50%; therefore, the finding of a reduced EF (<50%) cannot be considered uniquely as a benign consequence of athletic training and deserves careful clinical investigation.^{20,67}

With regard to diastolic function, transmitral pulse wave Doppler inflow pattern demonstrates a normal pattern, with an increased contribution of early filling velocity at rest (E/A ratio >2)^{68,69} (Figure 4). Pulsed tissue Doppler imaging (TDI) provides additional information showing normal s' peak velocity at rest (>8 cm/s) and e' peak velocity of the mitral annulus (>10 cm/s).^{68,70,71} Conversely, individuals with mild morphological expression of HCM exhibit lower e' velocity compared with athletes.⁵ The full spectrum of systolic and diastolic myocardial velocities has been described in large populations of competitive athletes.^{68,72}

Left atrial enlargement is common in large cohorts of athletes, proportional to biventricular enlargement and affected by the type of training. Pelliccia et al.¹⁹ reported a mild increase of LA diameter (≥ 40 mm) in 18% and a marked LA dilatation (≥ 45 mm) in 2% of the athletes. Left atrial volume is the preferred method for the assessment of LA remodelling and D'Andrea et al. confirmed a mild enlargement by using LA volume index ($\text{LAVi} \geq 34 \text{ mL/m}^2$) in 24% and moderate enlargement in 3% of athletes.^{48,73}

Elite athletes have normal aortic root diameter measured at the sinus of Valsalva and aortic valve annulus, with <1% of athletes showing increased dimensions. Clinicians evaluating athletes should therefore know that marked aortic root dilatation represents a pathological process and not a physiological adaptation to exercise.^{50,74,75}

Right atrium and right ventricle (RV) also undergo structural and functional remodelling as a result of haemodynamic challenges of exercise training.⁷⁶ Endurance sport requires very high cardiac outputs to be sustained for long periods and, as a result, the right heart undergoes substantial remodelling.^{29,47,76–78} A physiological RV enlargement (usually proportional with LV enlargement) was observed in both black and white athletes (Table 3).¹⁸ Despite significant RV enlargement, athletes usually show normal RV systolic function, without significant differences compared with untrained subjects.^{76,79} Only a small minority may present a mildly reduced RV fractional area change⁷⁶; ambiguities in the interpretation of mildly reduced RV function may be resolved by assessing RV function during exercise inducing both pressure and volume overload.^{80,81}

Exercise stress echocardiography can be considered a very reliable and non-invasive methodology to provide information on cardiac

Table 2 Athlete's left heart morphologic and functional parameters including upper or lower limits

First author	Year	No. of athletes	Type of sport	Parameter	Gender	Mean value	Cut-off value
Pelliccia	1999	1309	S P M E	LV End diastolic diameter (mm)	♂	55	70
Whyte	2004	442	P E	LV End diastolic diameter (mm)	♀	49	65
Pelliccia	1996	600	S P M E	LV End diastolic diameter (mm)	♀	49	66
Makan	2005	900	E	LV End diastolic diameter (mm)	♂ and ♀ Adolescent	51	60
Spirito	1994	947	S P M E	LV wall thickness (mm)	♂	10	16
Rawlins	2010	440	P E	LV wall thickness (mm)	♀ Black	9.5	13
Sharma	2002	720	P E	LV wall thickness (adolescent) (mm)	♂ and ♀ Adolescent	9.5	12
Basavarajaiah	2008	300	P E	LV wall thickness (black athletes) (mm)	♂ Black	11.5	16
Caselli	2015	1145	S P M E	LV mass/BSA (g/m ²)	♂ and ♀	103	146
Finocchiaro	2016	1083	P M E	LV mass/BSA (g/m ²)	♂	83	117
					♀	101	143
Pelliccia	2005	1777	S P M E	LA antero-posterior diameter (mm)	♂	37	50
					♀	32	45
D'Andrea	2010	650	P E	LA volume index (mL/m ²)	♂	28	36
					♀	26.5	33
Pelliccia	2010	2317	P E	Aortic root diameter (mm)	♂	32	40
					♀	28	34
D'Andrea	2010	615	P E	Proximal ascending aorta (mm)	♂ and ♀	28	34
Caselli	2015	1145	S P M E	LV ejection fraction (%)	♂ and ♀	64	55
				E/A		1.93	1.3
				TDI e' septal (cm/s)		13.8	10.3
				TDI e'/a' septal (cm/s)		2.04	1.23
				E/e' septal		6.4	8.5
D'Andrea	2010	650	P E	TDI s' septal (cm/s)	♂ and ♀	13	8
				TDI e' septal (cm/s)		24	10
				TDI s' lateral (cm/s)		15	9
				TDI e' lateral (cm/s)		16	11
				TDI e'/a' lateral		1.45	1.2
D'Andrea	2006	155	P	LV Intra-ventricular delay (ms)	♂ and ♀	9.5	45

BSA, body surface area; LA, left atrium; LV, left ventricle; TDI, tissue Doppler imaging. Type of sport: S, skill; P, power; M, mixed; E, endurance. ♀, female; ♂, male.

function, contractile reserve, exercise capabilities, and arrhythmias, which can be combined with clinical and ECG data and contribute to detect cardiac abnormalities. Being a safe and well-tolerated test, it is generally better accepted than pharmacological stress by individual athletes.^{8,82} Typical indication of exercise echocardiography is the evaluation of global and regional cardiac function during exercise in cases of suspect CAD or anomalies, in individuals with chest pain symptoms, abnormal ECG or doubtful ECG stress test. In some elite endurance athletes, both LV and RV dilatation has been reported to be associated with a mild impairment of systolic function. In these cases, exercise echocardiography enables the assessment of contractile reserve of the dilated ventricles, with a significant improvement in contractility during physical exertion, suggesting a physiological response.^{8,80,82} Finally, a special mention deserve the evaluation of athletes with valvular heart disease (i.e. haemodynamically significant valvular regurgitation, BAV, and mitral valve prolapse); in these cases exercise echocardiography may give complementary information on exercise tolerance, biventricular contractile reserve, and changes of haemodynamic and valvular functional parameters (such as valvular gradients, regurgitations, pulmonary artery pressure, and diastolic function).⁸²

3.3 Novel echocardiographic techniques

Speckle tracking (STE) and 3D echocardiography are not part of the routine evaluation of the athlete, but may become useful in specific circumstances to clarify the nature of cardiovascular adaptations. The indications to complete a routine echocardiographic examination in an athlete with these advanced technologies are summarized in Table 4.

Left ventricular global longitudinal strain (GLS) obtained by STE is currently the most used parameter in clinical practice. Main echocardiographic studies using 2 STE in the athlete's heart are summarized in Table 5. These studies demonstrate that a reduction in LV GLS is an uncommon feature in athlete's heart and cannot be considered a physiological adaptation to training. The current normal value for the general population varied from -16% to -22%, mean -20%.^{83,84} Similar values have been found in athletes, suggesting that a measure <15% should raise the suspicion of an underlying myocardial disease, particularly in case of other concomitant subclinical anomalies (Figure 5).⁸³⁻⁸⁹

Speckle tracking echocardiography has been recently applied to the investigation of the RV in athletes, providing new insights into the mechanisms of its physiologic remodelling and the assessment of the

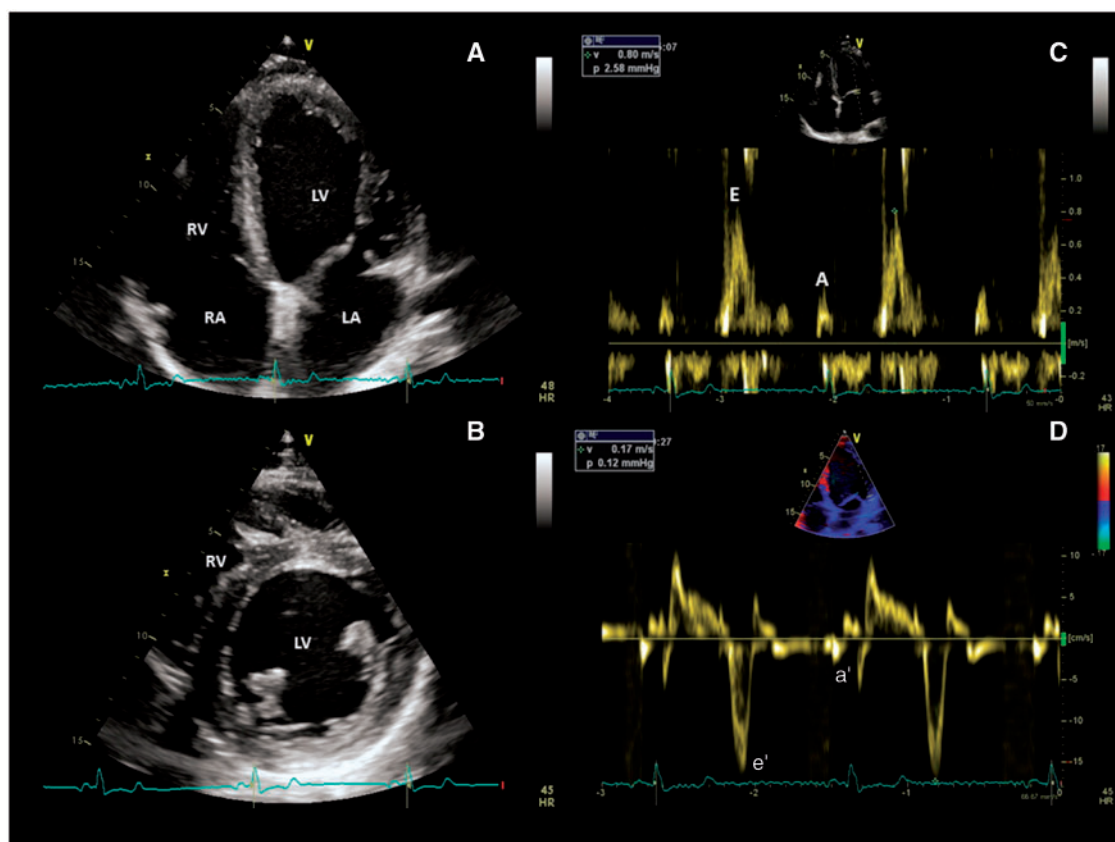


Figure 4 Twenty-two years-old male competitive endurance athlete (swimmer). Panel A: Apical 4-chamber and (Panel B) parasternal short-axis views, showing left ventricular (LV) hypertrophy, with symmetric increase of both wall thickness and LV internal cavity diameters. Panel C: Standard Doppler transmitral inflow pattern, showing a 'supranormal' early-diastolic function, with increased E velocity and E/A ratio. Panel D: Pulsed Tissue Doppler pattern of LV lateral wall, highlighting the enhanced early-diastolic myocardial function, i.e. increased e' velocity. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

possible detrimental effects of strenuous and chronic exercise training on RV function, particularly in endurance athletes.^{33,49,90–96} Strain and strain rate imaging, being able to objectively quantify regional RV dysfunction, have demonstrated to improve the ability to diagnose AC and to distinguish between physiology and pathology.^{33,97,98} However, studies investigating RV function in athletes by STE remain limited and there is lack of universally accepted cut-off values (Table 5).

Three-dimensional echocardiography has added quantitative information on the assessment of the athlete's heart, indeed cardiac volumes and mass can be estimated more precisely without the use of geometric assumptions and with very fast acquisition times.^{99–101} Three-dimensional derived information on LV geometry are very close to those obtained by CMR while 2D echocardiography routinely underestimates these measurements.^{99,102} The geometric pattern of LV adaptation to different training protocols have been investigated with 3D echocardiography. In athletes, regardless to the sport discipline, a balanced ratio between LV mass and end-diastolic volume has been described by 3D echocardiography as opposed to what typically occurs in cardiomyopathies.^{20,102,103} Additionally, the distribution of hypertrophy within the LV has been further investigated by the mass dispersion index (MDI; the standard deviation of

segmental LV mass) which is able to differentiate the homogeneous segmental distribution of LV mass typical of athletes or hypertensive patients compared with the non-homogeneous hypertrophy which is usually expression of HCM.¹⁰⁴

3.4 Cardiac magnetic resonance

Due to its diagnostic versatility, CMR imaging represents the second most valuable imaging method in the routine screening of active athletes and has definitely a role in the assessment of suspected cardiac disease. Studies reporting the systematic use of CMR as screening tool for cardiac abnormalities in athletes are, so far, scant and none have reported malignant arrhythmias or SCD as outcomes related to CMR findings.^{105–107} Additionally, it is worthy to consider that CMR shows systematically larger atrial and ventricular dimensions and volumes, and smaller wall thickness and mass, compared with echocardiography.¹⁰⁸ Therefore it should be advised to use some caution in applying echocardiographic derived reference values when performing CMR in athletes.

The main diagnoses relevant for a CMR study are: HCM, DCM, AC, LVNC, BAV, aortic root diseases, myocarditis, pericarditis, and ischaemic heart disease (see specific paragraphs). Figure 6 describes the main patterns of relevant diseases associated with risk of SCD in

Table 3 Athlete's right heart morphologic and functional parameters including upper or lower limits

First author	Year	No. of athletes	Type of sport	Parameter	Gender	Mean value	Cut-off value
D'Andrea	2013	650	P E	RV diameter basal (mm)	♂	43.5	55
					♀	39	49
				RV diameter middle-ventricle (mm)	♂	34	47
					♀	32	43
				RV longitudinal diameter (base-to-apex; mm)	♂	89	109
					♀	82	100
Zaidi	2013	675	P E	RVOT proximal (mm)	♂	32	43
					♀	30	40
				RVOT distal mm	♂	23.5	32
					♀	21.5	29
Zaidi	2013	675	E	RA area (cm ² /m ²)	♂	19.5	28
					♀	15.5	24
D'Andrea	2011	650	P E	PASP (mmHg)	♂ and ♀	24	40
D'Andrea	2013	650	P E	TAPSE (cm)	♂ and ♀	2.1	2.0
				RV FAC (%)		48.5	47
Oxborough	2012	102	E	RV TDI s' (cm/s)	♂ and ♀	11	8
				RV TDI e' (cm/s)		10	6
D'Ascenzi	2016	1009	S P M E	RVOT proximal (mm)	♂	28.4	34
				RVOT proximal index (mm/m ²)	♀	26.1	32
					♂	14.4	18
					♀	15.3	19
				RVOT distal (mm)	♂	29.8	16
				RVOT distal index (mm/m ²)	♀	27.3	34
					♂	15	19
					♀	15.9	21
				RV diameter basal (mm)	♂	40.6	49
					♀	35.2	44
				RV diameter middle ventricle (mm)	♂	27.3	35
					♀	23.9	31
				RV diastolic area (cm ²) (male)	♂	25.1	33
					♀	19.3	27
				RV systolic area (cm ²) (male)	♂	12.1	18
					♀	9.0	14
				TAPSE (mm) (male)	♂ and ♀	24	19
				RA area (cm ²) (male)	♂	18.9	25
					♀	14.8	20
				s' (cm/s)	♂	14.8	12
					♀	14.2	11
				RV FAC (%)	♂	52.0	39
	♀	53.4	38				

FAC, fractional area change; RA, right atrium; PASP, pulmonary artery systolic pressure; RV, right ventricle; RVOT, right ventricular outflow tract; TDI, tissue Doppler imaging; TAPSE, tricuspid anulus peak systolic excursion. Type of sport: S, skill; P, power; M, mixed; E, endurance. ♀, female; ♂, male.

athletes in a stepwise selection decisional algorithm using CMR findings after the whole patient's data (including symptoms, personal and familial history, electrocardiography, and echocardiography) have been interrogated.

Protocols include multiplanar cine CMR to assess morphology and function of all valves, especially the aortic valve and root whose anomalies can lead to SCD. Most importantly, cine CMR evaluates heart chambers volume and mass accurately and with high

reproducibility, and is considered the standard of reference for the assessment of global and regional contractile function.^{39,109,110}

Assessment of the RV volume, shape, and ejection fraction (EF) are main CMR criteria recognized by the task force for imaging diagnosis of AC,^{111,112} although involvement of the LV may also occur.¹¹³

The dependence of the size of the RV to the gender and the BSA highlights the need for indexing the RV parameters to the BSA. Indeed, RV remodelling and enlargement are normal adaptations to

Table 4 Indication to complete the routine echocardiographic evaluation by speckle-tracking or by 3D echocardiography

Indications for speckle-tracking echocardiography
• Identification of pre-clinical anomalies useful to the differential diagnosis between athlete's heart and early DCM (LV)
• Identification of pre-clinical anomalies useful to the differential diagnosis between athlete's heart and early HCM (LV)
• Characterization of regional wall motion abnormalities (LV and RV)
Indications for 3D echocardiography
• Better assessment of LV volumes and function
• Assessment of pattern of LV geometry
• Quantification of the extent of LV trabeculation

DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LV, left ventricle; RV, right ventricle.

Table 5 Most relevant studies assessing left (upper panel) and right (lower panel) ventricular strain by speckle-tracking echocardiography in athletes

Author	Year	Sport discipline	Nr	Longitudinal strain
				Left ventricle
Caselli et al.	2014	Olympic athletes	200	-18.1 ± 2.2%
Nottin et al.	2008	Elite cyclists	16	19.2 ± 1.9%
Cappelli et al.	2010	Endurance athletes	50	-18.4 ± 3.0%
Galderisi et al.	2010	Top level rowers	22	-22.2 ± 2.7%
Simsek et al.	2913	Marathon runners	22	-22.3 ± 2.2% (global)
Simsek et al.	2013	Wrestlers	24	-21.8 ± 1.7% (global)
Weiner et al.	2013	University Rowers	15	-16.8 ± 2.1% (pre-training) -18.3 ± 2.8% (post-training)
				Right ventricle
Teske et al.	2009	Endurance athletes/Olympic endurance athletes	58/63	-28.5 ± 2.9%/ -27.6 ± 3.1%
Oxborough et al.	2012	Endurance athletes	102	-27.0 ± 6.0%
Pagourelas et al.	2013	Endurance/Power athletes	80/28	-23.1 ± 3.7%/ -25.1 ± 3.2%
Esposito et al.	2014	Top level rowers	40	-26.3 ± 3.6% (global) -29.1 ± 4.1% (free wall)
D'Ascenzi et al.	2015	Mixed sport disciplines	29	-28.7 ± 4.9% (Pre-season) -29.2 ± 4.1% (Mid-season) -30.0 ± 3.7% (End-season)

training in amateurs and endurance athletes.^{114,115} Therefore, we recommend that RV enlargement is defined only when end-diastolic volume exceeds the major diagnostic criteria in the athletic population (i.e. ≥110 mL/m² for male and ≥100 mL/m² for males).¹¹¹ As the systolic function of the RV is usually normal in athletes, both major (RVEF <40%) and minor (RVEF < 45%) criteria should be considered in the differential diagnosis.¹¹¹

Assessment of LV hypertrophy or dilatation using cine CMR also provides paramount diagnostic information. Diagnosis of HCM is likely when myocardial hypertrophy has a focal distribution.¹¹⁶ Hypertrophic cardiomyopathy may nevertheless display a diffuse pattern, difficult to differentiate from that occurring in certain hypertensive individuals and normal athletes (especially Afro-Caribbean males).^{24,62}

Cardiac magnetic resonance is also considered as the superior method for fibrosis imaging. The assessment of late gadolinium enhancement (LGE) has excellent ability to outline myocardial replacement fibrosis and is commonly used in detection of myocardial scar and workup of cardiomyopathies,^{117–119} and differentiation between diseased and adaptive athletes, even though small spots of fibrosis have been occasionally reported in endurance athletes without other obvious disease.¹²⁰

Myocardial fibrosis can be characterized by typical ischaemic and non-ischaemic patterns, with the latter including several subpatterns with the potential to sharpen the differences between myocardial diseases. For example, in diffuse LV hypertrophy, LGE helps distinguishing potentially adaptive changes from diseases, among which the most common is HCM (especially in the absence of LV overload)

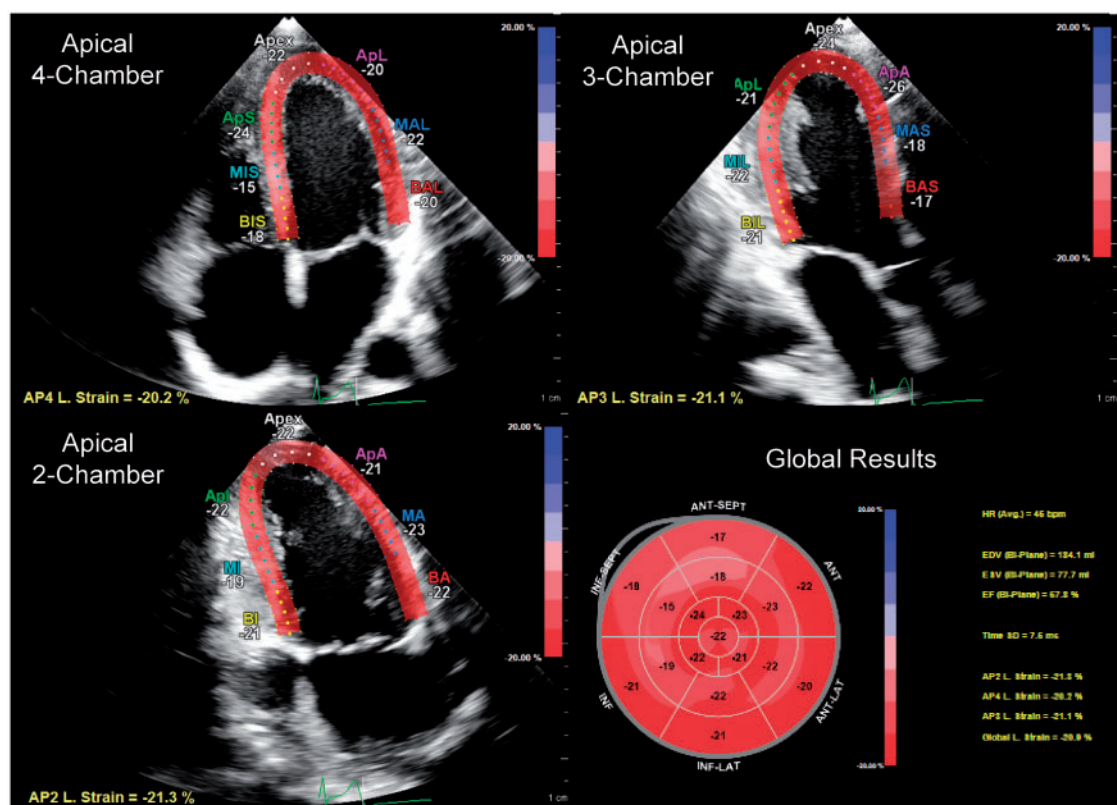


Figure 5 Left ventricular strain assessed by 2-dimensional speckle tracking echocardiography in a 20 year-old male soccer player. Global and regional longitudinal deformation is assessed from apical 4-, 3- and 2-chamber views. Peak regional values are depicted in the bull's eye plot in the lower right panel. The global longitudinal strain (GLS) is -20% (in the range of normality).

where LGE is typically patchy or confluent and occurs at the RV insertion.^{121–123} In normal-sized hearts, common non-ischaemic LGE patterns involve the mid-wall and the subepicardium, figuring inflammatory disease-related necrosis or scars (myocarditis, sarcoidosis, and collagen vascular diseases), while in dilated LV presence of LGE suggests acute or subacute inflammatory diseases like DCM or predominant left-sided AC. Rare diseases should however, be considered in LV hypertrophy,^{124–128} and even other heart shapes when the LGE pattern is atypical. Indeed, diffuse subendocardial, subepicardial basal, and intramyocardial LGE have respectively been reported in amyloidosis, Anderson-Fabry disease, and mitochondrial myopathy.^{129,130}

T1 mapping is a very promising CMR method for the assessment of the extracellular volume and diffuse fibrosis. This technique can potentially be important in myocardial diseases where LGE is less sensitive.¹³¹ Indeed, the myocardial T1 values tend to increase with the amount of extracellular matrix and aging,¹³² and decrease with fatty infiltration such as in Anderson-Fabry disease.^{133,134}

3.5 Computed tomography

Cardiac CT is characterized by a high-spatial resolution and short-scan times, but limited temporal resolution, making the technique ideal for high-resolution angiography. However before the indication to CT scan, a due consideration concerns the radiation exposure¹³⁵;

indeed, radiation dose of cardiac CT depends on the scanner type, scan protocol, and the efforts taken to limit exposure. Dynamic evaluations using older scanners can result in doses exceeding 20 mSv, while CT coronary angiography requires nowadays no more than 1 mSv in properly prepared patients using modern CT technology.¹³⁶ Although many aspects of cardiac disease can be visualized well, cardiac CT cannot be the first-choice imaging modality in young athletes. Therefore, cardiac CT should be reserved for individuals with suspected CAD (symptoms of angina, positive exercise test, arrhythmias, or syncope during exercise), aortic diseases, or pericardial pathology (Table 6). Cardiac CT is the most accurate technique for imaging anomalous coronary anatomy, including intramural course. The point of origin, course, adjacent structures, and termination (fistulas) can be evaluated (Figure 7). However, morphology is often not sufficient for interpretation of the pathophysiological relevance. Obstructive coronary disease can be excluded in case of suspected myocardial ischaemia.

Cardiac CT can also visualize most morphological features of the different cardiomyopathies, including ventricular wall dimensions and structure, cavity sizes, global contractile function, and even regional wall motion abnormalities.^{137,138} However, although cardiac CT very accurately measures global ventricular function, its practical use is limited by the radiation exposure,¹³⁹ hence, echocardiography and CMR are preferred. In case of suboptimal echocardiographic images

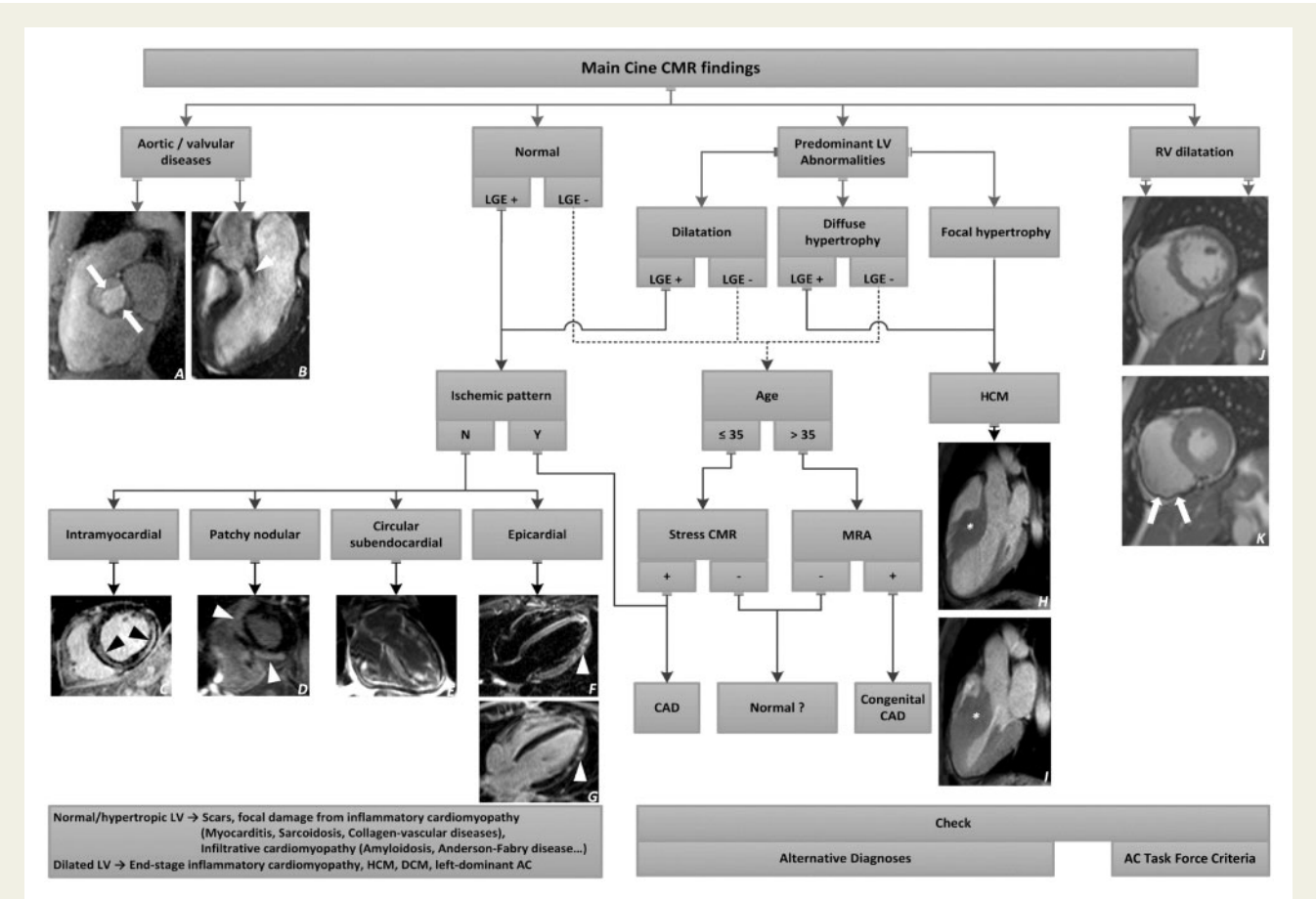


Figure 6 Stepwise diagnostic algorithm involving Cardiac Magnetic Resonance (CMR) with inserts illustrating common diseases at risk for Sudden Cardiac Death (SCD). CMR is usually performed as a second level cardiovascular examination. The first step examines cine images in order to demonstrate/exclude aortic valve and root diseases (A and B are respectively end-diastolic transverse aortic and 3-chamber views displaying bicuspid aortic (arrows) valve with regurgitation (arrowhead) and eccentric left ventricular (LV) hypertrophy, right ventricular (RV) dilatation and predominantly LV abnormalities. In case of RV dilatation, task force CMR criteria for the diagnosis of Arrhythmogenic Cardiomyopathy (AC) should be checked (J and K inserts are respectively end-diastolic and end-systolic short-axis cine views of a patient with recent onset of tachyarrhythmia, showing enlarged RV (end-diastolic volume = 115 ml/m²) and dyskinetic segments in the inferior wall (arrows). The diagnosis of hypertrophic cardiomyopathy (HCM) is usually straightforward with focal LV hypertrophy (H and I inserts respectively represent end-diastolic and end-systolic 3-chamber cine views, showing septal LV hypertrophy (asterisks). Late gadolinium enhancement (LGE) images are the next clue to the diagnosis in the remaining cases (C-G inserts represent typical patterns of non-ischemic LGE on short-axis and 4-chamber views (arrowheads). These patterns are associated to either disease-related focal myocardial damage or scar in normal-shaped LV, whereas they represent diffuse damage or end-stage cardiomyopathies when the LV is dilated. When both cine CMR and LGE patterns are normal, coronary artery disease (CAD) can be excluded using Magnetic Resonance Angiography (MRA) or stress CMR with respect to the patient age. AC, arrhythmogenic cardiomyopathy; CAD, coronary artery disease; CMR, cardiac magnetic resonance; HCM, hypertrophic cardiomyopathy; LGE, late gadolinium enhancement; LV, left ventricle; MRA, magnetic resonance angiography; N, No; RV, right ventricle; Y, Yes.

Table 6 Indications to perform coronary computed tomography based on symptoms and age. Low-radiation examinations advised in young individuals

Age category	Suspect coronary artery disease	Indication to perform CT coronary angiography
Young (<35 years)	Coronary artery anomalies (origin, course)	• Syncope • Major ventricular arrhythmias induced by exercise • Positive exercise test
Adults (>35 years)	Atherosclerotic coronary artery disease	• High risk profile • Atypical chest pain • Borderline exercise testing

CT, computed tomography.

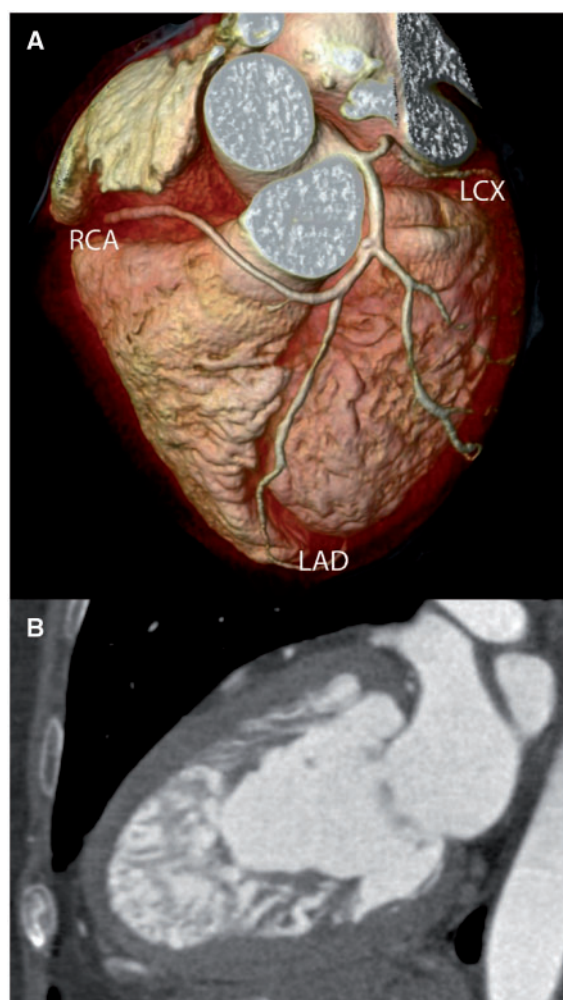


Figure 7 Cardiac Computed Tomography (CT) imaging of a patient with non-compaction cardiomyopathy (B) as well as a single coronary artery (A). LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

and contraindications to CMR, CT scan may represent the alternative imaging modality.

Left-sided valve morphology can be assessed well, while CT imaging of the right-sided valves is more challenging and requires specific attention to contrast timing. Cardiac CT offers no flow-based functional evaluation. Planimetry of stenotic valve areas has been described.¹⁴⁰ Pericardial thickening and calcification are well visualized by cardiac CT, and pericardial fluid contents may to a degree be differentiated by CT attenuation values. Finally, while cardiac CT may be considered the clinical standard for aortic imaging, 3D CMR angiography with or without contrast agent application is also of high-diagnostic value and can easily be integrated in a single session CMR examination.

3.6 Nuclear imaging

Both photon emission computed tomography (SPECT) or positron emission tomography (PET) can be used in athletes for the

assessment of myocardial ischaemia when coronary artery anomalies or disease are suspected, however ischaemia can also be related to dysbalanced myocardial perfusion (e.g. in severe LV hypertrophy) or microvascular disease. The technical details of these imaging modalities have been described in the European guidelines for cardiac nuclear imaging in 2008.¹⁴¹ In accordance with the ESC guidelines for the management of stable CAD published in 2013, exercise ECG should be the initial step in the diagnostic evaluation of athletes with suspected CAD.¹⁴² Individuals with inconclusive exercise ECG results could be referred for nuclear imaging. Similarly to CT, the indication to perform nuclear imaging should be weighted to the risk of radiation exposure.¹³⁵ The effective radiation dose for myocardial perfusion studies with novel scanners is <2 mSv for SPECT and <1 mSv for PET.¹⁴³ The accuracy of both PET and SPECT to detect CAD is very good, although PET may be preferred in balanced 3-vessel disease since PET permits absolute quantification of myocardial blood flow, representing the real added value of this technique, whereas SPECT can only provide semi-quantitative values (normalized to the maximum value), and can therefore not detect relative differences in perfusion.¹⁴⁴

4. Criteria for differential diagnosis and risk stratification of specific cardiac diseases

4.1 Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy is one of the most common causes of SCD in young athletes and represents the basis for disqualification from competitive sports according to both American and European recommendations.^{3,9} The diagnosis relies on the presence of a hypertrophied LV (i.e. LV wall thickness >15 mm) in the absence of cardiac or systemic disease capable of producing the same magnitude of LV hypertrophy.^{145,146}

The diagnosis of HCM in young competitive athletes may be challenging when the extent of LV hypertrophy is mild and LV wall thickness is in the range of 13 mm to 16 mm, which identifies the 'gray-zone' of overlap between the physiologic adaptations to training and mild phenotypic expression of the disease.^{1,5,121,147}

Cardiac imaging offers several clues for this differential diagnosis, having in mind that no single parameter may ultimately be diagnostic *per se* but final decision should always consider all clinical information available (Table 7).

The most useful morphologic criterion is the assessment of LV cavity size and geometry. Athletes in the gray zone typically show an enlarged LV cavity (end-diastolic diameter > 54 mm), while HCM athletes in the vast majority have a smaller cavity.⁵ Indeed, the shape of LV chamber is altered in most HCM patients, due to the usual asymmetric, segmental, and centripetal development of the pathologic hypertrophy. However, in a few HCM athletes, especially those with apical phenotype, the cavity size may exceed this limit.¹⁴⁷ As a general rule, the development of physiologic LV hypertrophy in the context of the athlete's heart is consistently associated with LV cavity enlargement with an eccentric pattern, at difference from HCM.^{20,103,104}

The highest degree of LV hypertrophy in athletes is seen in male gender, with values up to 15 mm in white and 16 mm in Afro-

Table 7 Cardiac imaging findings consistent with diagnosis of athlete’s heart when left ventricular wall thickness is mildly increased, ranging from 13 mm to 16 mm

Diagnosis of athlete’s heart in the gray-zone of left ventricular hypertrophy(13–16 mm)		
HCM	Findings	Athlete’s Heart
+	Family history of sudden cardiac death/HCM	–
+	Major ECG abnormalities (ST segment/T wave inversion, wide, and deep Q waves)	–
+	Normal or reduced LV cavity size (<54 mm)	–
+	Abnormal LV cavity geometry and/or segmental LV hypertrophy	–
+	LV outflow tract obstruction	–
+	Abnormal LV diastolic relaxation/filling(septal e’ velocity < 8.0 cm/s and/or E/A ratio < 1.0)	–
+	Left atrial remodelling disproportionate to LV remodelling	–
+	Positive LGE on CMR	–
+	Unchanged LV wall thickness after detraining	–

CMR, cardiac magnetic resonance; HCM, hypertrophic cardiomyopathy; ECG, electrocardiogram; LGE, late gadolinium enhancement; LV, left ventricular.

American athletes.^{1,64} Less hypertrophy is found in female athletes, with values up to 11 mm in whites and 13 mm in Afro-Americans.^{22,23} To be noticed that LV hypertrophy is typically found in sport with a combination of high volume and pressure overload, such as rowing, canoeing, and x-country skiing.^{1,20}

Athletes usually show a homogeneous distribution of wall thickness with absolute differences of <2 mm between the thickest and the thinnest segments of the LV. On the contrary, an asymmetric and heterogeneous pattern of LV hypertrophy represents a non-physiologic condition, or phenotypic expression of HCM.^{5,104}

Athletes show a preserved LV chamber geometry with mitral valve normally located. Certain mitral abnormalities may be present in HCM athletes, such as elongation of mitral chordae, with systolic anterior motion and flow acceleration in the LV outflow tract, a phenomenon that has not been described in athletes.¹⁴⁸ Additionally, while LV outflow obstruction may not be evident under resting conditions, it could be precipitated by an exercise and demonstrated on stress echocardiography in HCM patients.¹⁴⁹

Left ventricular systolic function is usually within the range of normality in both athletes and HCM patients. Only subtle differences in myocardial contraction can be detected by STE. Preliminary observations suggest that HCM with mild LV hypertrophy (12–16 mm) may have a reduction in longitudinal endocardial strain, with cut-off value <-15% able to identify pathologic hypertrophy with good accuracy (sensitivity 79%; specificity 67%). Therefore, values below this cutoff may be suggestive for pathologic LV hypertrophy.^{84,150}

One of the most consistent features of the athlete’s heart is the normal diastolic function, expression of preserved elastic, and recoil LV properties.^{68,151} Conversely, in HCM patients LV diastolic function may present impairment as an expression of myocyte alteration and interstitial fibrosis. Few individuals may show an inversion of the E/A ratio, but most frequently in HCM a subclinical impairment is associated with a reduction of the e’ velocity on TDI.^{5,147,151}

Cardiac magnetic resonance is indicated when echocardiographic images are not able to clearly identify all myocardial segments in order to exclude focal areas of hypertrophy (such as the apex and lateral wall). Indeed, CMR should be performed in all cases with associated marked ECG abnormalities and/or arrhythmias.¹⁵² The higher

contrast of CMR images between endocardial surface and the blood pool allows a better definition and distribution of LV hypertrophy and areas of focal hypertrophy. Most importantly, the use of LGE enables tissue characterization and identification of focal areas of myocardial fibrosis, commonly seen in patients with HCM.¹⁵³

When the differential diagnosis remains still unresolved, useful information may come from detraining, with serial imaging testing (echocardiograms or CMR) after temporary interruption of training. It has been demonstrated that after a short period of detraining (3-month), regression of LV hypertrophy may be observed in athletes, while this is unlikely to occur in HCM.^{66,154,155}

It is worthy to mention that left atrial size may not be particularly helpful in this specific scenario. Left atrial enlargement has been described in athletes as an expression of global cardiac adaptation to training and is typically associated with increased LV size, at difference than in HCM where LV cavity is usually of normal size or even reduced and LA appears disproportionately enlarged.^{19,48} Additionally, while in older HCM patients LA enlargement is a common finding and is considered a reliable criterion for the diagnosis and risk stratification, in young and asymptomatic HCM patients with mild expression of the disease, this finding may not be present as well, with the apparent paradox that young athletes may have larger LA compared with young HCM patients.⁵

4.2 Dilated cardiomyopathy

The sports activities most often associated with LV chamber dilation are those with high-isotonic/dynamic components, such as cycling, cross-country skiing, canoeing, and rowing.^{1,4,20}

Left ventricular cavity enlargement in athletes should always be interpreted in the context of sport discipline participated and body size (it is advised to relate LV cavity diameter to BSAs, as previously reported) and is usually associated with increased wall thickness.^{4,46,156} It has been reported that 38% of 950 elite athletes engaged in different sports disciplines showed increased LV end-diastolic diameter (>55 mm).¹ In a very large population of elite athletes, a substantial subset of 14% have a LV end-diastolic chamber markedly enlarged, with LV diameter > 60 mm, with 99th percentile corresponding to 65 mm.⁴ In a group of very elite professional cyclists

($n = 286$) participating to the Tour de France, 45% had disproportionate chamber dilatation (LV diameter > 60 mm) and a small minority also showed mildly impaired ejection fraction.¹⁵⁷ However it has been questioned whether these disproportionate cardiac adaptations were the results of illicit drug abuse.^{51,157} Therefore, these findings could theoretically be a challenge for distinguishing the physiologic LV remodelling occurring in athletes from DCM.

It is worthy to notice that LV dilation in athletes is commonly associated with normal systolic function (EF $> 50\%$). A large study involving more than 1000 Italian Olympic athletes of different sport disciplines showed normal LV ejection fraction in the entire study population, with lowest value being 53%, and fifth percentile equal to 55% (Figure 8).⁶⁸ Moreover, indices of diastolic filling and relaxation (by Doppler-echocardiography and TDI) are within normal limits.⁶⁸ In case of mildly reduced ejection fraction (i.e. EF $\geq 46\%$, $< 55\%$), it may be useful to assess LV function during exercise (by echocardiography or radionuclide imaging) (Figure 9). Absence of significant improvement of systolic function at peak exercise (i.e. an increase in ejection fraction $< 15\%$ compared with the baseline value) is in favour of a pathological dilatation. Moreover, in doubtful cases, the assessment of peak oxygen uptake, which is consistently increased in relation to total heart volume can also help us to distinguish between physiologic and pathologic LV dilatation.¹⁵⁸

Finally, STE might give additional information in terms of myocardial contraction. However, only few studies are available to date with somewhat diverse results on LV function at rest.^{86,159,160} The results are, indeed, not strikingly different from normal ranges. So far, no study has directly compared myocardial strain in athletes and DCM.

Additional value is offered by the CMR with LGE. Cardiac magnetic resonance provides accurate measurements of actual dimensions and, in this context, the presence of positive LGE could be expression of myocardial fibrosis more consistent with a diagnosis of DCM.¹⁶¹ Importantly, the absence of LGE does not exclude DCM.

4.3. Arrhythmogenic cardiomyopathy

Imaging criteria form an important part of the international diagnostic framework for arrhythmogenic cardiomyopathy (AC; previously defined arrhythmogenic right ventricular

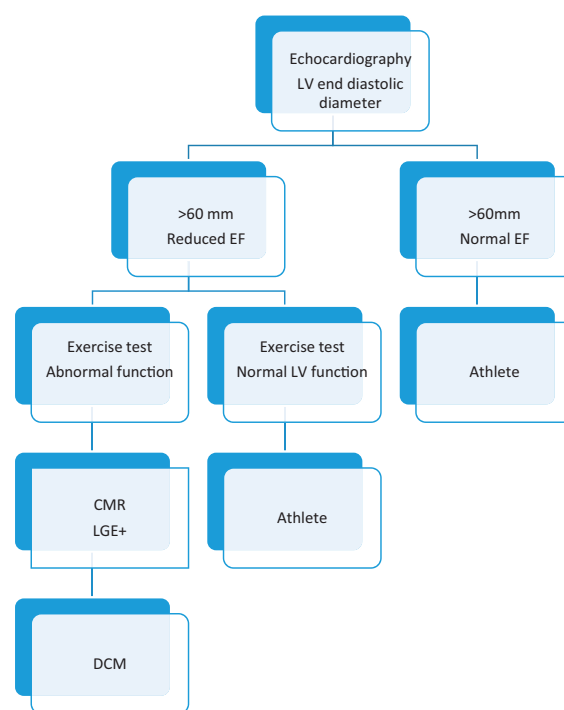


Figure 9 Proposed diagnostic algorithm for the differential diagnosis between physiological left ventricular cavity dilation in athletes and dilated cardiomyopathy. CMR, cardiac magnetic resonance; DCM, dilated cardiomyopathy; EF, ejection fraction; LGE, late gadolinium enhancement; LV, left ventricle.

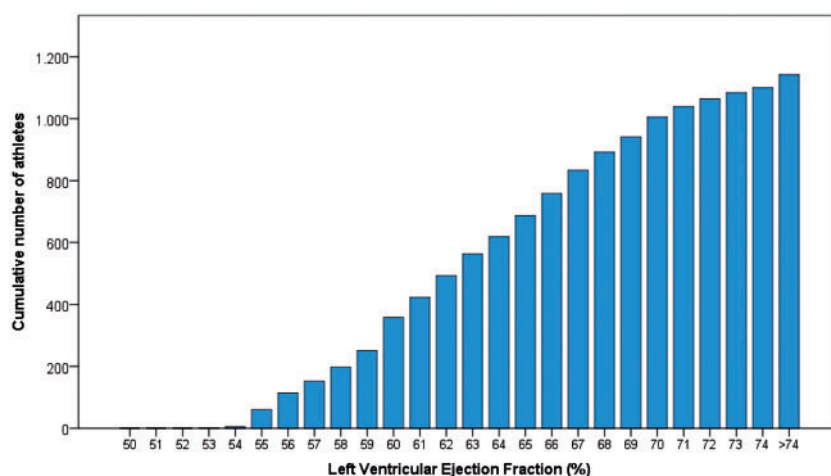


Figure 8 Left ventricular ejection fraction measured by echocardiography in a population of 1145 Olympic athletes (age 26 ± 5 years; 61% male), free of cardiovascular disease, engaged in different sport disciplines. LV ejection fraction was normal in the entire study population with the lowest value 53% and fifth percentile 55%. Data from Caselli S et al. Patterns of Left Ventricular Diastolic Function in Olympic Athletes. *J Am Soc Echocardiogr* 2015;28:236–244.

cardiomyopathy/dysplasia, ARVC/D), as outlined in the modified Task Force criteria proposed in 2010, and in the recent EACVI recommendations.^{14,111} Electrical changes, which often form the hallmark of the diagnosis of AC should be interpreted in the context of the imaging findings: these include repolarization changes in the right precordial leads (although not very specific)^{7,162}; low right precordial QRS amplitudes; epsilon waves; late potentials (especially when 3 out of 3 criteria); frequent ventricular premature beats or non-sustained ventricular tachycardia from the RV (especially when not from the RVOT)^{7,163}; or inducibility during EP study.¹⁶⁴ Of relevance, it should be noted that electrical changes in athletes could precede over long-time the morphological changes in athletes with AC.⁶¹ Although 2D echocardiography provides a readily available imaging tool, it has important limitations for visualizing the complex geometry of the RV. Therefore, modern imaging relies more on CMR.

Athlete's hearts are by definition larger than untrained hearts. Moreover, it is known that endurance exercise selectively promotes RV dilatation due to the increase in RV wall stress during high cardiac output conditions.^{76,164,165} Many endurance athletes have slightly larger RV than LV volumes.^{165,166} Physiological RV remodelling is characterized by consistent increase in RV inflow and outflow segments, at difference from the predominant increase of the outflow tract observed in AC patients.¹⁶⁷ The AC Task Force criteria proposed defined dimensional criteria in the presence of regional wall motion abnormalities.¹¹¹ With regard to RV size, the criteria are based on data derived from AC patients vs. normal controls, not including healthy athletes, which represents a potential limitation. Actually, up to 30% and 60% of athletes have RV dimensions that would match respectively the 'major' and 'minor' Task Force criteria.^{76,95} Right ventricular dilatation in athletes may be suggestive for AC only when is really extreme.^{7,96,168} Therefore, we have proposed that only major dimensional criteria, indexed by BSA should be used to define RV enlargement in athletes: specifically, RVOT > 19 mm/m² in long axis, and/or >21 mm/m² in short axis, and/or RV end-diastolic volume on CMR ≥110 mL/m² in males and ≥100 mL/m² in females.^{7,76,163} Nevertheless, RV dimensions by themselves are insufficient criteria to distinguish physiologic from pathologic RV dilatation, and need to be associated with regional wall motion abnormalities.¹¹¹ Other useful measures that have shown specificity for AC include the ratio (on echocardiography) of RV inflow dimension (in the apical view)/LV end-diastolic dimension (parasternal long-axis view) >0.9, or a ratio of RVEDV/LVEDV >1.2 on CMR.⁷

Functional measures are more important than pure dimensions. Again, CMR may perform better than echocardiography. Regional akinesia, dyskinesia, or aneurysmal deformation are important findings, since they are present in more than half of AC patients. Also measures of global dysfunction are useful: e.g. RV fractional area change on echocardiography <33%, or RVEF <40 on CMR.^{7,163} With regard to STE, RV global longitudinal strain (RV-GLS) and strain rate in athletes are comparable to non-athletes.^{95,96} On the contrary, AC patients may show a subclinical RV dysfunction with reduced RV-GLS, and further decrease is observed in those AC patients regularly engaged in sport activities.¹⁶⁹ Additionally, mechanical dispersion of right ventricular contraction detected by STE may represent an early predictor of future arrhythmic events.^{98,170} While LGE on CMR is seen in >40% of familial forms of AC (due to desmosomal mutations),

it is still not part of the current AC Task Force criteria. Often LGE is present also or exclusively in the LV, as it is recognized that LV involvement of familial AC is common.

New data indicate that morphologic and functional evaluation of the RV both with echocardiography and CMR during exercise (i.e. not at rest) can be of help in the differential diagnosis of pathologic RV remodelling.^{81,94,171} Indeed, athletes with subclinical AC may have volumetric or functional values within normal range at rest, while showing subnormal augmentation of RV systolic function during exercise.^{80,94,163,172} Table 8 summarizes the most common criteria that may help in differential diagnosis between physiologic RV adaptation in athletes as opposed to AC.

4.4 Left ventricular non-compaction

Left ventricular non-compaction is a relatively novel cardiomyopathy that is characterized by prominent myocardial trabeculations and deep inter-trabecular recesses.^{173–176} Knowledge relating to the precise stage of development and the natural history of the disorder is still incomplete, however available data are suggestive of a morphologically and clinically heterogeneous disorder. Whereas some individuals present with overt heart failure and potentially fatal arrhythmias, others may remain asymptomatic.¹⁷⁵ The clinical diagnosis is currently reliant on three proposed echocardiographic criteria and are based on the demonstration of high non-compacted to compacted ratio within the LV myocardium.^{173,174,177}

Advances in tissue harmonics and image resolution in echocardiography have coincided with increased reports of features consistent with LVNC in patients with heart failure,¹⁷⁶ as well as in low-risk cohorts including sickle cell patients¹⁷⁸ and athletes,^{179–184} particularly those of African/Afro-Caribbean origin. A study of over a 1000 asymptomatic athletes demonstrated that 18% exhibited increased LV trabeculations and 8% fulfilled echocardiographic criteria for LVNC, more commonly in black athletes.¹⁷⁹ A small proportion (0.9%) of these athletes also exhibited concomitant T-wave inversion and reduced indices of systolic function that may be considered diagnostic of LVNC, a finding that was also reported in Dutch football players.¹⁸⁰

At the moment is debated if these findings could be considered incomplete expression of LVNC phenotype that may be unmasked through intensive exercise training, or conversely, if they may represent just atypical features of cardiac adaptation. The precise mechanism for the development of increased LV trabeculations in low-risk cohorts is unclear, however, it has been observed that an increased cardiac preload is the common factor in situations associated with increased LV trabeculations, such as heart failure, chronic anaemia, and athletic training. It is therefore possible that an increase in preload may unmask a pre-existing trabeculation. The hypothesis is supported by a longitudinal study, using the pregnancy model to assess the impact of a physiological increase in cardiac loading conditions on LV trabeculations.¹⁸⁵

A multimodal diagnostic approach is recommended for the diagnosis of LVNC in athletes.¹⁸⁴ We propose the following guidance on the assessment of athletes presenting with increased LV trabeculations, here defined as showing a non-compacted to compacted (NC/C) layer ratio >2.0 in systole on echocardiography or >2.3 in diastole on CMR (Table 9).^{173,186} Cardiac symptoms or a family history of heart failure, or premature SCD in an athlete fulfilling criteria for

Table 8 Clinical and multi-modality imaging findings that may help in differential diagnosis between physiologic RV adaptation as opposed to AC

Differential diagnosis between athlete's heart and AC		
AC	Findings	Athlete
+	Family history of sudden cardiac death/AC	-
+	Anterior T wave inversion on ECG	-
+	Ventricular arrhythmias with LBBB morphology	-
+	Exercise induced VT	-
+	RV size exceeding major Task Force Criteria for echocardiography or CMR (consider only indexed values)	-
+	Regional wall motion abnormalities (akinesia or dyskinesia) on cardiac imaging.	-
+	Global RV dysfunction on echocardiography (RVFAC < 33%) or CMR (RVEF ≤ 40)	-
+	Abnormal RV function on exercise echocardiography/CMR	-

AC, arrhythmogenic cardiomyopathy; CMR, cardiac magnetic resonance; ECG, electrocardiogram; LGE, late gadolinium enhancement; LBBB, left bundle branch block; RV, right ventricle; RVEF, right ventricular ejection fraction; RVFAC, right ventricular fractional area change; VT, ventricular tachycardia.

LVNC favours cardiac pathology. Information from screening of first-degree relatives for features of LVNC is invaluable but not always practical. Additional echocardiography features of LVNC include low ejection fraction that does not improve (by at least 20%) with moderate exercise (70% of the maximum predicted heart rate), a mean $e' < 9$ cm/s at echocardiography, and a thickness of compacted layer in systole <8 mm.¹⁸⁷ During maximal exercise testing, features favouring LVNC include peak oxygen consumption less than predicted value from healthy controls, or occurrence of complex ventricular arrhythmias. Abnormal myocardial strain patterns are in the experimental phase for this condition but an abnormal parameter may suggest a disease process.¹⁸⁸ Finally, detection of areas of LGE within the LV on CMR is in favour of a cardiomyopathic process.¹⁸⁹

4.5 Aortic root disease and bicuspid aortic valve

Remodelling of the aortic root may be expected to occur in athletes as a consequence of haemodynamic overload with exercise training.^{50,74,190–192} Technically, aortic root diameter measurements should be made from the parasternal long-axis view using the leading edge-to-leading edge convention and preferring 2D measurements rather than M-mode measurements.⁷³

Measurements ideally should include: (i) the aortic valve annulus (hinge point of aortic leaflets), (ii) the sinuses of Valsalva, (iii) the sinotubular junction, and (iv) the proximal ascending aorta (Figure 10).⁷³

Several observational studies performed in the general non-athletic population reported that height and body size are the most relevant determinants of aortic root size.^{75,193–195} Iskandar and Thompson⁷⁵ in a meta-analysis including a cohort of 5580 elite athletes and 727 controls reported that athletes have greater aortic root diameters compared with control subjects; however the effect of exercise training on aortic size was small and most pronounced in those engaged in endurance disciplines. Other studies on different athletic populations reported a low prevalence of aortic enlargement (>40 mm in males) in athletes.^{50,74,190,191,196} Pelliccia et al.⁵⁰ in a large cohort of 2317 elite athletes reported 1.3% of aortic root enlargement (17 males) with the 99th percentile equal to 40 mm in males and 34 mm in females. This value is recommended as cut-off for

Table 9 Findings consistent with diagnosis of athlete's heart or left ventricular non-compaction when increased trabeculations are occasionally found on echocardiography in athletes

Athletes with increased trabeculations		
LVNC	Findings	Athlete
+	Family history of sudden cardiac death/LVNC	-
+	Symptoms	-
+	Reduced LV systolic function (EF < 50%)	-
+	Reduced thickness of compact layer	-
+	Late gadolinium enhancement on CMR	-
+	T-wave inversion on ECG	-
+	Left bundle branch block on ECG	-
+	Exercise induced VT/AF	-
+	Abnormal diastolic function	-

AF, atrial fibrillation; CMR, cardiac magnetic resonance; ECG, electrocardiogram; LV, left ventricle; LVNC, left ventricular non-compaction; VT, ventricular tachycardia.

evaluating aortic root diameters in elite athletes. In order to avoid the confounding effects of body size and age, the American College of Cardiology and the American Heart Association have recently proposed the use of Z-scores to identify subjects with significant aortic root dilation (i.e. Z-score > 2).¹¹

In athletes with an aortic root dimension above the reference values, the presence of associated pathologic conditions including Marfan Syndrome or BAV should be excluded.^{197,198} In athletes with dilated aortic root, even in the absence of recognized structural systemic/cardiac disease, a periodical clinical and diagnostic assessment with non-invasive imaging should be recommended, to monitor aortic root dimensions over time and recognize an accelerated enlargement.

Bicuspid aortic valve is one of the most common congenital cardiac anomalies, with prevalence between 0.5% and 2% in the general population.¹⁹⁹ In large athletes population the prevalence of BAV has been reported as 1%.²⁰⁰ Inherited disease is described in up to

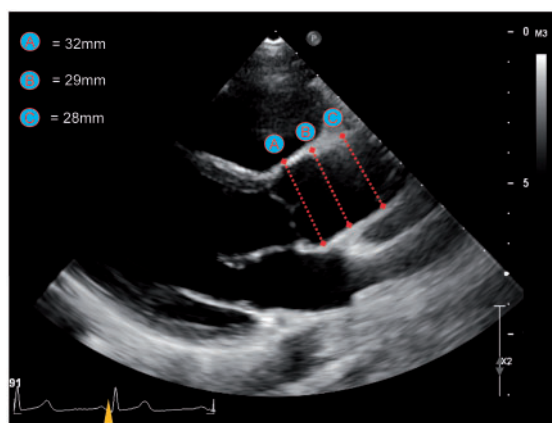


Figure 10 Parasternal long-axis view of the aortic root and ascending aorta in end-diastole in a 18 year-old male soccer player. The measurements of aortic root at sinuses of Valsalva (A), sinotubular junction (B), and proximal ascending aorta (C) are reported.

10–17% of first-degree relatives.²⁰¹ As such, early detection of this entity is of great importance, particularly due to the fact that in up to 30% various complications can interfere.²⁰² Beside possible progression to valve dysfunction (stenosis or regurgitation), individuals with BAV present with larger dimensions of the aortic sinus, ascending aorta, and aortic arch compared with those with a tricuspid aortic valve. They harbour an increased risk for progression and, in the very worst case, aortic dissection.^{203,204} However, not all individuals with BAV seem to be at risk for progressive aortic dilation, and thus it is important to identify athletes at highest risk for aortic complications.²⁰⁰ This can only be achieved by regular echocardiographic follow-up. Furthermore, BAV may be associated with additional diseases (particularly in case of an autosomal-dominant inheritance pattern). As such, coarctation of the aorta, interrupted aortic arch, patent ductus arteriosus, coronary anomaly or hypoplastic left heart, as well as Williams or Turner syndrome have to be excluded.^{205–207}

Only a few studies have addressed the outcome of BAV in the general population: in one study, 25% to 42% of subjects with BAV required surgery for symptomatic valve disease, LV dysfunction, ascending aortic dilation, or endocarditis.^{204,208} However, overall life expectancy is not decreased in patients with BAV.^{204,209} A recent international registry on BAV reported that the presence of raphe was associated with higher prevalence of valvular dysfunction and increased rates of surgery.²¹⁰ Endocarditis may complicate BAV disease in about 10–30% during life, however, antibiotic prophylaxis is currently not routinely recommended in isolated BAV.²¹¹

Outcome data on athletes are sparse but generally, adverse outcome depends on various predictors (e.g. age >30–50 years and aortic dimension of >40 mm or, at least, moderate aortic valve dysfunction at baseline).^{200,204,212,213}

Bicuspid aortic valve may be difficult to diagnose in athletes and may sometimes be missed; careful physical examination may reveal a mild murmur and/or a characteristic mid-systolic ‘click’. Echocardiography is the imaging modality of choice when BAV is suspected. The number of leaflets, leaflet fusion, and the presence of a ‘raphe’ can be reliably determined in the short-axis view, while

systolic doming and eccentric diastolic closure of the leaflets can be visualized in the long-axis view. Two- or three-dimensional transoesophageal echocardiography may further improve the accuracy for diagnosis and correct assessment of BAV (Figure 11).²¹⁴ Associated coarctation of the aorta can be suspected on echocardiography but needs to be confirmed by CT or CMR. Furthermore, Doppler echocardiography allows accurate assessment of valve dysfunction. Presence of valvular regurgitation or stenosis should be properly assessed according to most recent guidelines.^{215,216} In case of valvular regurgitation and LV cavity dilation, the latter should be interpreted in the context of sport discipline participated and body size, using normalized values as advised.^{4,12} Finally, it may be appropriate to obtain an exact assessment of the ascending aortic diameters by an additional CT or CMR scan at least as an index at ‘baseline’ and in case of aneurysmatic aortic dilation with potential indication for surgery.²¹⁷

4.6 Mitral valve prolapse

Mitral valve prolapse (MVP) is the most common valvular disease in the general population, with an estimated prevalence of 2–3%; it is defined as an abnormal systolic displacement of one or both leaflets into the left atrium below the mitral annulus, due to structural elongation or abnormal distensibility of the mitral valve.²¹⁸ The main echocardiographic characteristic is the displacement of one or both leaflets >2 mm beyond the annulus (from the parasternal long-axis view) associated with maximal leaflet thickness ≥ 5 mm (in the classic MVP) or <5 mm (in the non-classic MVP).^{219–221} Although MVP is generally regarded as a benign condition, the outcome is widely heterogeneous, and complications such as mitral regurgitation, atrial fibrillation, congestive heart failure, endocarditis, ventricular arrhythmias, and SCD have been reported.^{220,222,223} In detail, the estimated rate of SCD in MVP ranges from 0.2%/year to 0.4%/year in prospective follow-up studies and recent evidence seems to suggest that MVP is an underestimated cause of arrhythmic SCD, mostly in young adult women.^{15,220,224} Most importantly MVP has been reported to account for a large proportion (as high as 11%) of the overall causes of SCD in young competitive athletes.²²⁵

Echocardiography is the imaging technique of choice for the diagnosis and characterization of MVP and is generally indicated when the typical end-systolic murmur associated with mid-systolic click is identified on physical examination. The entity of leaflet prolapse, characteristics and quantification of mitral regurgitation jet, LV size and function, and left atrial size should be reported and periodically re-evaluated. Mitral valve regurgitation should be assessed according to most recent guidelines.²¹⁵ In presence of LV cavity dilation, the specific impact of mitral regurgitation should be interpreted in context of athlete’s type of sport participated and body size (specifically in endurance athletes LV is considered dilated when end diastolic diameter exceeds 35 mm/m² in males and 40 mm/m² in females).^{4,12} In case of ventricular arrhythmias on resting or exercise ECG (especially those with right bundle branch block morphology) a CMR should be requested in order to exclude the presence of areas of fibrosis which may be correlated with severe ventricular tachy-arrhythmias.¹⁵

4.7. Myocarditis

Myocarditis is an inflammatory disease of the heart muscle that occasionally affects young individuals including athletes. The viral aetiology

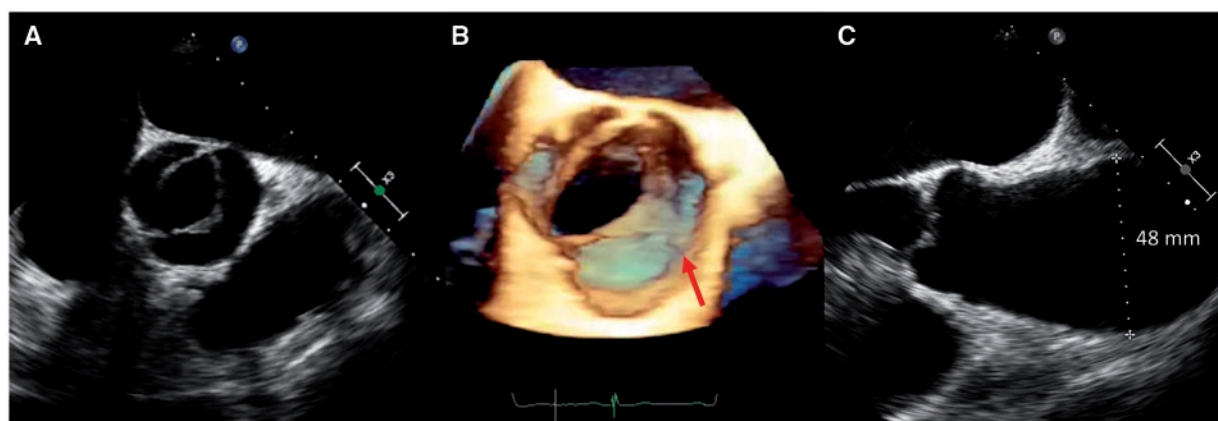


Figure 11 Transesophageal echocardiogram of a 24-year old patient with bicuspid valve. Two-dimensional imaging showing bicuspid valve in systole characterized by the antero-posterior pattern (A); Real-time three-dimensional imaging showing the raphe between right and left coronary cusps (red arrow, panel B); long-axis view of the aorta showing a marked dilation of the ascending aorta with a maximal diameter of 48 mm (C).

is largely predominant in developed countries.^{226,227} The clinical course is variable ranging from mildly symptomatic to fulminant disease. Some patients heal completely with the elimination of pathogens and resolution of the inflammatory process, but in others, the activation of autoimmunity may evolve in a chronic disease and/or DCM.^{228,229} During all the phases of the disease, the interstitial oedema, myocardial necrosis, and fibrosis represent the myocardial substrate for the electrical instability.^{225,227,228} In this scenario, the sport activity may trigger malignant arrhythmias which may ultimately culminate in SCD.^{3,225}

The clinical suspicion of myocarditis may rise from clinical history of a recent respiratory or gastrointestinal tract infection. Patients may report fever, chest pain, palpitation, and decreased physical performance; laboratory testing may reveal increased inflammatory markers (C-reactive protein and erythrocyte sedimentation rate) associated with an otherwise unexplained rise in cardiac troponin.²²⁷ However, it should be noticed that clinical presentation might be subtle and inflammatory markers only mildly elevated.

Electrocardiographic findings are not specific and include most commonly repolarization abnormalities and atrial or ventricular arrhythmias.^{3,226} Indeed, isolated or complex ventricular arrhythmias during an exercise test may be one of the first manifestations of the disease.

On echocardiography, the LV may be dilated with thin myocardial walls resembling DCM, or non-dilated with increased myocardial wall thickness due to myocardial oedema. Global systolic function may be mildly reduced and, of relevance, focal regional wall motion abnormalities may be observed. Concomitant pericardial effusion may suggest pericardial involvement.²²⁷

Over the last decade CMR has acquired an increasingly role for the diagnosis of myocarditis: an international consensus group reported that, in the appropriate clinical context, the diagnosis of myocarditis is defined by at least 2 of 3 of the following findings: (i) regional or global myocardial signal intensity increase in T₂-weighted images; (ii) increased global myocardial early gadolinium enhancement ratio between myocardium and skeletal muscle in gadolinium enhanced T₁-weighted images; (iii) at least one focal lesion

with non-ischaemic regional distribution in inversion recovery-prepared gadolinium enhanced T₁-weighted images.²³⁰

Furthermore, the identification of LGE may confer prognostic information, since it is a strong independent predictor of events during follow-up.^{231–233}

The clinical significance of persistent area of LGE in an asymptomatic athlete with clinically healed myocarditis is still unresolved; it is reasonable to assume that after clinical resolution of the disease the absence of symptoms, LV dysfunction, ECG abnormalities, and arrhythmias on 24-h Holter ECG/exercise test represent a low-risk condition and the athlete may resume training and competition under strict clinical surveillance.

4.8 Congenital coronary artery anomalies

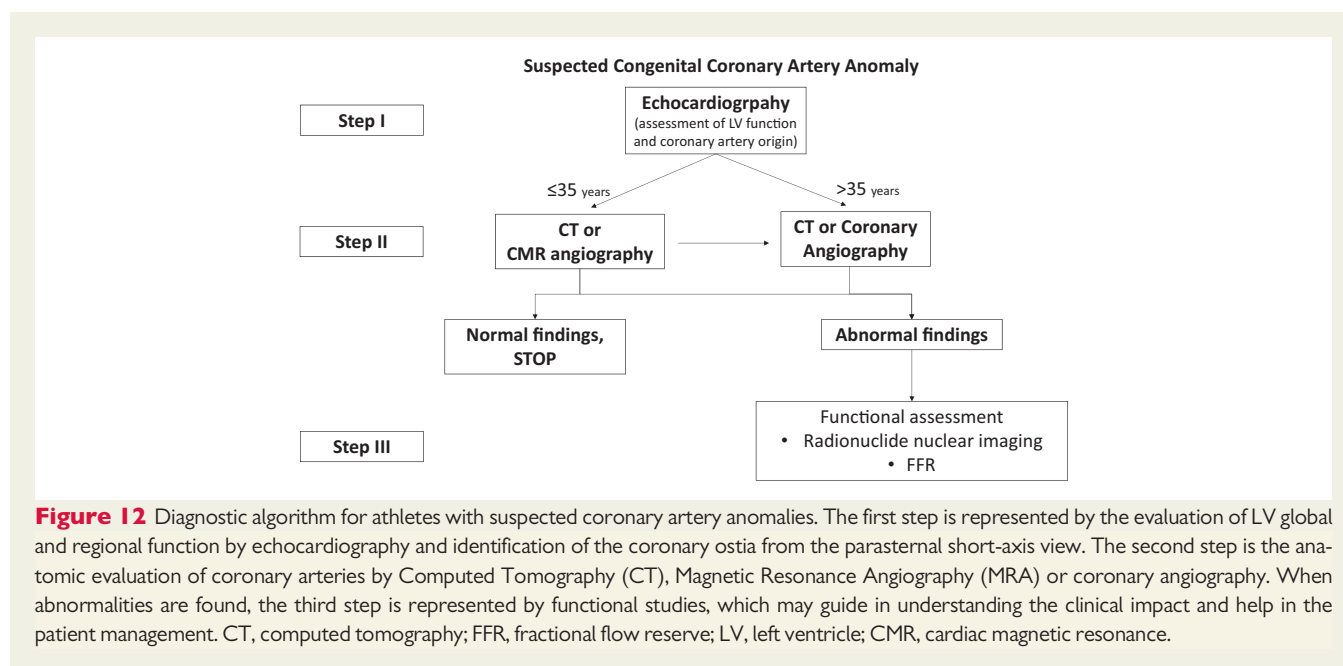
The estimated prevalence of congenital coronary artery anomalies (CCAA) in the general population is quite variable, depending on both the definition and the source of data, ranging from 0.21% to 5.79%. Despite the low prevalence, CCAA are well recognized as major cause of SCD in competitive athletes, accounting for about 17% of such deaths in the USA and for 16% in Italy.

However, not all CCAA have the same prognostic impact, the anomalies considered at risk of SCD on effort include an anomalous origin from a wrong aortic sinus, anomalous origin from the pulmonary artery and myocardial bridge (MB).

The diagnostic algorithm for athletes with suspect CCAA is shown in Figure 12.

Anomalous coronary artery origin from a wrong aortic sinus (either the right coronary artery from the left or the left coronary artery from the right sinus) can present a variable course of the proximal tract, i.e. pre-pulmonic, retro-aortic, intra-septal sub-pulmonic, or inter-arterial and the latter is considered at risk of SCD.^{234,235}

To the diagnosis, unfortunately, the ECG and even maximal exercise test are often normal. If the index of suspicion is sufficiently high, because of potential clinical markers (such as exertional syncope, chest pain, or arrhythmias), the diagnosis can be defined non-invasively by transthoracic (or transoesophageal) echocardiography as a first step.²³⁵ It has been shown that visualization of the ostium and



proximal course of the left main and right coronary arteries is possible in over 98% and 80% of athletes.²¹⁷

The failure to demonstrate that a CA originates from its proper Valsalva sinus requires further anatomic confirmation with CT, CMR angiography or coronary angiography based on age and risk profile (Table 6; Figure 12).^{235,236} In patients with a clinical suspicion of CCAA, the European Society of Cardiology recommends CT and the American Heart Association either CT or CMR angiography, the latter preferred due to radiation concerns.^{237,238}

After the diagnosis, functional assessment of CCAA for clinical management and advise relative to sport participation is challenging in asymptomatic people. Aim of the functional assessment is detection of exercise-induced ischaemia. To the scope, nuclear scintigraphy and/or stress echocardiography and coronary angiography should be performed. Intravascular ultrasound (IVUS) of the proximal vessel has been proposed to evaluate lesion severity based upon the amount of hypoplasia and the degree of lateral compression; finally, fractional flow reserve (FFR) assessment is also recommended.²³⁵ Intravascular ultrasound and FFR should be performed both at baseline and with pharmacological stress.

Myocardial bridge consists of a major epicardial CA, usually the left anterior descending CA, coursing deep within the myocardium.^{239,240} Effort-induced ischaemia has been attributed to tachycardia, which increases the myocardial oxygen requirement and reduces the coronary flow occurring in diastole. Diagnosis of MB can be achieved non-invasively by CT which can define the anatomic characteristics, such as the length and depth of the intramyocardial course of the CA, even if haemodynamic characteristics cannot be derived. Coronary angiography confirms the diagnosis by showing the classic 'milking effect' (i.e. a transient compression in systole, that can be accentuated by intracoronary nitroglycerin injection). Intravascular ultrasound can reveal the characteristic 'half-moon' sign and the extent of phasic arterial compression, besides proximal plaque and negative arterial remodelling.²³⁹

The major challenge, however, remains the criteria to guide management: crucial to risk stratification is the demonstration of exercise-induced ischaemia.^{239,240} Reversible perfusion defects can be detected by stress nuclear imaging (see Section 3.6). Alternatively, reversible ischaemia due to MB can be detected by combined stress CMR perfusion and wall motion imaging. Coronary physiological measurements across a MB during pharmacological infusion are also valuable; i.e. intracoronary Doppler can reveal the distinctive 'fingertip' phenomenon and intracoronary pressure measurement with values of fractional flow reserve (FFR) <0.75 suggests ischaemia.

5. Conclusion

This document offers a comprehensive overview of the cardiac physiologic remodelling as well as the changes associated with pathologic conditions, detectable in athletes by the most advanced imaging techniques. The correct approach to the diagnosis and management of cardiac pathologic conditions in athlete's populations represents nowadays a largely recognized clinical need for clinical cardiologists and sport medicine specialists.

This document provides the clues for a timely and correct identification of the most relevant cardiac diseases, according to the most common clinical scenarios. Adherence to this document will help clinicians to require imaging testing according to the recognized indications and provides the keys for appropriate interpretation of result, in the context of the athlete's gender, age, race, and sport participated.

Eventually, we are confident that appropriate use of cardiovascular imaging techniques in the athlete's population will facilitate a more cost-effective cardiovascular evaluation, contributing to safer competitive sport participation.

Conflict of interest: Doctors Pelliccia, Caselli, Sharma, Basso, Bax, Corrado, D'Andrea, D'Ascenzi, Di Paolo, Edvardsen, Gati, Galderisi,

Nchimi, Nieman, Papadakis, Pisicchio, Schmied, Popescu, Habib, Grobbee, and Lancellotti have nothing to disclose.

Doctor Heidebuchel reports the following relationships, outside the submitted work: Biotronik, Pfizer/BMS, Daiichi-Sankyo, Bayer, Boehringer-Ingelheim, Cardiome, St Jude Medical, Bracco Imaging Europe NV.

References

- Pelliccia A, Maron BJ, Spataro A, Proschan MA, Spirito P. The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes. *N Engl J Med* 1991;**324**:295–301.
- Maron BJ, Pelliccia A. The heart of trained athletes: cardiac remodeling and the risks of sports, including sudden death. *Circulation* 2006;**114**:1633–1644.
- Pelliccia A, Fagard R, Bjornstad HH, Anastassakis A, Arbustini E, Assanelli D, Biffi A, Borjesson M, Carre F, Corrado D, Delise P, Dorwarth U, Hirth A, Heidebuchel H, Hoffmann E, Mellwig KP, Panhuyzen-Goedkoop N, Pisani A, Solberg EE, van-Buuren F, Vanhees L, Blomstrom-Lundqvist C, Deligiannis A, Dugmore D, Glikson M, Hoff PI, Hoffmann A, Hoffmann E, Horstkotte D, Nordrehaug JE, Oudhof J, McKenna WJ, Penco M, Priori S, Reybrouck T, Senden J, Spataro A, Thiene G. Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the Study Group of Sports Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J* 2005;**26**:1422–1445.
- Pelliccia A, Culasso F, Di Paolo FM, Maron BJ. Physiologic left ventricular cavity dilatation in elite athletes. *Ann Intern Med* 1999;**130**:23–31.
- Caselli S, Maron MS, Urbano-Moral JA, Pandian NG, Maron BJ, Pelliccia A. Differentiating left ventricular hypertrophy in athletes from that in patients with hypertrophic cardiomyopathy. *Am J Cardiol* 2014;**114**:1383–1389.
- Caselli S, Attenhofer Jost CH, Jenni R, Pelliccia A. Left ventricular noncompaction diagnosis and management relevant to pre-participation screening of athletes. *Am J Cardiol* 2015;**116**:801–808.
- Zaidi A, Sheikh N, Jongman JK, Gati S, Panoulas VF, Carr-White G, Papadakis M, Sharma R, Behr ER, Sharma S. Clinical differentiation between physiological remodeling and arrhythmogenic right ventricular cardiomyopathy in athletes with marked electrocardiographic repolarization anomalies. *J Am Coll Cardiol* 2015;**65**:2702–2711.
- Galderisi M, Cardim N, D'Andrea A, Bruder O, Cosyns B, Davin L, Donal E, Edvardsen T, Freitas A, Habib G, Kitsiou A, Plein S, Petersen SE, Popescu BA, Schroeder S, Burgstahler C, Lancellotti P, Sicari R, Muraru D, Lombardi M, Dulgheru R, Gerche AL. The multi-modality cardiac imaging approach to the Athlete's heart: an expert consensus of the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015;**16**:353.
- Maron BJ, Udelson JE, Bonow RO, Nishimura RA, Ackerman MJ, Estes NA 3rd, Cooper LT Jr, Link MS, Maron MS. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 3: hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and other cardiomyopathies, and myocarditis: a scientific statement from the American Heart Association and American College of Cardiology. *Circulation* 2015;**132**:e273–e280.
- Maron BJ, Levine BD, Washington RL, Baggish AL, Kovacs RJ, Maron MS. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 2: preparticipation screening for cardiovascular disease in competitive athletes: a scientific statement from the American Heart Association and American College of Cardiology. *J Am Coll Cardiol* 2015;**66**:2356–2361.
- Braverman AC, Harris KM, Kovacs RJ, Maron BJ. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 7: aortic diseases, including Marfan syndrome: a scientific statement from the American Heart Association and American College of Cardiology. *J Am Coll Cardiol* 2015;**66**:2398–2405.
- Bonow RO, Nishimura RA, Thompson PD, Udelson JE. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 5: valvular heart disease: a scientific statement from the American Heart Association and American College of Cardiology. *J Am Coll Cardiol* 2015;**66**:2385–2392.
- Thompson PD, Myerburg RJ, Levine BD, Udelson JE, Kovacs RJ. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 8: coronary artery disease: a scientific statement from the American Heart Association and American College of Cardiology. *J Am Coll Cardiol* 2015;**66**:2406–2411.
- Haugaa KH, Basso C, Badano LP, Bucciarelli-Ducci C, Cardim N, Gaemperli O, Galderisi M, Habib G, Knuuti J, Lancellotti P, McKenna W, Neglia D, Popescu BA, Edvardsen T. Comprehensive multi-modality imaging approach in arrhythmogenic cardiomyopathy—an expert consensus document of the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2017;**18**:237–253.
- Basso C, Perazzolo Marra M, Rizzo S, De Lazzari M, Giorgi B, Cipriani A, Frigo AC, Rigato I, Migliore F, Pilichou K, Bertaglia E, Cacciavillani L, Baucé B, Corrado D, Thiene G, Iliceto S. Arrhythmic mitral valve prolapse and sudden cardiac death. *Circulation* 2015;**132**:556–566.
- Sharma S, Drezner JA, Baggish A, Papadakis M, Wilson MG, Prutkin JM, La Gerche A, Ackerman MJ, Borjesson M, Salerno JC, Asif IM, Owens DS, Chung EH, Emery MS, Froelicher VF, Heidebuchel H, Adamczuk C, Asplund CA, Cohen G, Harmon KG, Marek JC, Molossi S, Niebauer J, Pelto HF, Perez MV, Riding NR, Saarel T, Schmied CM, Shipon DM, Stein R, Vetter VL, Pelliccia A, Corrado D. International recommendations for electrocardiographic interpretation in athletes. *Eur Heart J* 2017; doi: 10.1093/eurheartj/ehw631.
- Papadakis M, Carre F, Kervio G, Rawlins J, Panoulas VF, Chandra N, Basavarajiah S, Carby L, Fonseca T, Sharma S. The prevalence, distribution, and clinical outcomes of electrocardiographic repolarization patterns in male athletes of African/Afro-Caribbean origin. *Eur Heart J* 2011;**32**:2304–2313.
- Zaidi A, Ghani S, Sharma R, Oxborough D, Panoulas VF, Sheikh N, Gati S, Papadakis M, Sharma S. Physiological right ventricular adaptation in elite athletes of African and Afro-Caribbean origin. *Circulation* 2013;**127**:1783–1792.
- Pelliccia A, Maron BJ, Di Paolo FM, Biffi A, Quattrini FM, Pisicchio C, Roselli A, Caselli S, Culasso F. Prevalence and clinical significance of left atrial remodeling in competitive athletes. *J Am Coll Cardiol* 2005;**46**:690–696.
- Caselli S, Di Paolo FM, Pisicchio C, Di Pietro R, Quattrini FM, Di Giacinto B, Culasso F, Pelliccia A. Three-dimensional echocardiographic characterization of left ventricular remodeling in Olympic athletes. *Am J Cardiol* 2011;**108**:141–147.
- Dewey FE, Rosenthal D, Murphy DJ Jr, Froelicher VF, Ashley EA. Does size matter? Clinical applications of scaling cardiac size and function for body size. *Circulation* 2008;**117**:2279–2287.
- Pelliccia A, Maron BJ, Culasso F, Spataro A, Caselli G. Athlete's heart in women. Echocardiographic characterization of highly trained elite female athletes. *JAMA* 1996;**276**:211–215.
- Rawlins J, Carre F, Kervio G, Papadakis M, Chandra N, Edwards C, Whyte GP, Sharma S. Ethnic differences in physiological cardiac adaptation to intense physical exercise in highly trained female athletes. *Circulation* 2010;**121**:1078–1085.
- Di Paolo FM, Schmied C, Zerguini YA, Junge A, Quattrini F, Culasso F, Dvorak J, Pelliccia A. The athlete's heart in adolescent Africans: an electrocardiographic and echocardiographic study. *J Am Coll Cardiol* 2012;**59**:1029–1036.
- Sheikh N, Papadakis M, Carre F, Kervio G, Panoulas VF, Ghani S, Zaidi A, Gati S, Rawlins J, Wilson MG, Sharma S. Cardiac adaptation to exercise in adolescent athletes of African ethnicity: an emergent elite athletic population. *Br J Sports Med* 2013;**47**:585–592.
- Sheikh N, Papadakis M, Ghani S, Zaidi A, Gati S, Adami PE, Carre F, Schnell F, Wilson M, Avila P, McKenna W, Sharma S. Comparison of electrocardiographic criteria for the detection of cardiac abnormalities in elite black and white athletes. *Circulation* 2014;**129**:1637–1649.
- Kervio G, Pelliccia A, Nagashima J, Wilson MG, Gauthier J, Murayama M, Uzan L, Ville N, Carre F. Alterations in echocardiographic and electrocardiographic features in Japanese professional soccer players: comparison to African-Caucasian ethnicities. *Eur J Prev Cardiol* 2013;**20**:880–888.
- Riding NR, Salah O, Sharma S, Carre F, George KP, Farooq A, Hamilton B, Chalabi H, Whyte GP, Wilson MG. ECG and morphologic adaptations in Arabic athletes: are the European Society of Cardiology's recommendations for the interpretation of the 12-lead ECG appropriate for this ethnicity? *Br J Sports Med* 2014;**48**:1138–1143.
- Bohm P, Schneider G, Linneweber L, Rentzsch A, Kramer N, Abdul-Khalik H, Kindermann W, Meyer T, Scharhag J. Right and left ventricular function and mass in male elite master athletes: a controlled contrast-enhanced cardiovascular magnetic resonance study. *Circulation* 2016;**133**:1927–1935.
- Donal E, Rozoy T, Kervio G, Schnell F, Mabo P, Carre F. Comparison of the heart function adaptation in trained and sedentary men after 50 and before 35 years of age. *Am J Cardiol* 2011;**108**:1029–1037.
- Prakken NH, Cramer MJ, Teske AJ, Arend M, Mali WP, Velthuis BK. The effect of age in the cardiac MRI evaluation of the athlete's heart. *Int J Cardiol* 2011;**149**:68–73.
- Fleg JL, Shapiro EP, O'Connor F, Taube J, Goldberg AP, Lakatta EG. Left ventricular diastolic filling performance in older male athletes. *JAMA* 1995;**273**:1371–1375.
- Teske AJ, Cox MG, De Boeck BW, Doevendans PA, Hauer RN, Cramer MJ. Echocardiographic tissue deformation imaging quantifies abnormal regional right ventricular function in arrhythmogenic right ventricular dysplasia/cardiomyopathy. *J Am Soc Echocardiogr* 2009;**22**:920–927.

34. Gielen S, Schuler G, Adams V. Cardiovascular effects of exercise training: molecular mechanisms. *Circulation* 2010;**122**:1221–1238.
35. Kovacs R, Baggish AL. Cardiovascular adaptation in athletes. *Trends Cardiovasc Med* 2016;**26**:46–52.
36. Morganroth J, Maron BJ, Henry WL, Epstein SE. Comparative left ventricular dimensions in trained athletes. *Ann Intern Med* 1975;**82**:521–524.
37. D'Andrea A, Riegler L, Morra S, Scarafie R, Salerno G, Cocchia R, Golia E, Martone F, Di Salvo G, Limongelli G, Pacileo G, Bossone E, Calabro R, Russo MG. Right ventricular morphology and function in top-level athletes: a three-dimensional echocardiographic study. *J Am Soc Echocardiogr* 2012;**25**:1268–1276.
38. Spence AL, Naylor LH, Carter HH, Buck CL, Dembo L, Murray CP, Watson P, Oxborough D, George KP, Green DJ. A prospective randomised longitudinal MRI study of left ventricular adaptation to endurance and resistance exercise training in humans. *J Physiol* 2011;**589**:5443–5452.
39. Scharf M, Brem MH, Wilhelm M, Schoepf UJ, Uder M, Lell MM. Atrial and ventricular functional and structural adaptations of the heart in elite triathletes assessed with cardiac MR imaging. *Radiology* 2010;**257**:71–79.
40. Steding K, Engblom H, Buhre T, Carlsson M, Mosen H, Wohlfart B, Arheden H. Relation between cardiac dimensions and peak oxygen uptake. *J Cardiovasc Magn Reson* 2010;**12**:8.
41. Pelliccia A, Spataro A, Caselli G, Maron BJ. Absence of left ventricular wall thickening in athletes engaged in intense power training. *Am J Cardiol* 1993;**72**:1048–1054.
42. Urhausen A, Holpes R, Kindermann W. One- and two-dimensional echocardiography in bodybuilders using anabolic steroids. *Eur J Appl Physiol Occup Physiol* 1989;**58**:633–640.
43. Urhausen A, Kindermann W. Sports-specific adaptations and differentiation of the athlete's heart. *Sports Med* 1999;**28**:237–244.
44. Urhausen A, Monz T, Kindermann W. Sports-specific adaptation of left ventricular muscle mass in athlete's heart. II: an echocardiographic study with 400-m runners and soccer players. *Int J Sports Med* 1996;**17** Suppl 3:S152–S156.
45. Urhausen A, Kindermann W. Echocardiographic findings in strength- and endurance-trained athletes. *Sports Med* 1992;**13**:270–284.
46. Douglas PS, O'Toole ML, Katz SE, Ginsburg GS, Hiller WD, Laird RH. Left ventricular hypertrophy in athletes. *Am J Cardiol* 1997;**80**:1384–1388.
47. D'Andrea A, La Gerche A, Golia E, Teske AJ, Bossone E, Russo MG, Calabro R, Baggish AL. Right heart structural and functional remodeling in athletes. *Echocardiography* 2015;**32** Suppl 1:S11–S22.
48. D'Andrea A, Riegler L, Cocchia R, Scarafie R, Salerno G, Gravino R, Golia E, Vriz O, Citro R, Limongelli G, Calabro P, Di Salvo G, Caso P, Russo MG, Bossone E, Calabro R. Left atrial volume index in highly trained athletes. *Am Heart J* 2010;**159**:1155–1161.
49. Pagourelas ED, Koudi E, Efthimiadis GK, Deligiannis A, Geleris P, Vassilikos V. Right atrial and ventricular adaptations to training in male Caucasian athletes: an echocardiographic study. *J Am Soc Echocardiogr* 2013;**26**:1344–1352.
50. Pelliccia A, Di Paolo FM, De Blasis E, Quattrini FM, Piscichio C, Guerra E, Culasso F, Maron BJ. Prevalence and clinical significance of aortic root dilation in highly trained competitive athletes. *Circulation* 2010;**122**:698–706; 3pfollowing706.
51. La Gerche A, Brosnan MJ. Cardiovascular effects of performance-enhancing drugs. *Circulation* 2017;**135**:89–99.
52. Deligiannis A, Björnstad H, Carre F, Heidbüchel H, Koudi E, Panhuyzen-Goedkoop NM, Pigozzi F, Schänzer W, Vanhees L. ESC study group of sports cardiology position paper on adverse cardiovascular effects of doping in athletes. *Eur J Cardiovasc Prev Rehabil* 2006;**13**:687–694.
53. De Piccoli B, Giada F, Benettin A, Sartori F, Piccolo E. Anabolic steroid use in body builders: an echocardiographic study of left ventricle morphology and function. *Int J Sports Med* 1991;**12**:408–412.
54. Luijckx T, Velthuis BK, Backx FJ, Buckens CF, Prakken NH, Rienks R, Mali WP, Cramer MJ. Anabolic androgenic steroid use is associated with ventricular dysfunction on cardiac MRI in strength trained athletes. *Int J Cardiol* 2013;**167**:664–668.
55. Nottin S, Nguyen LD, Terbah M, Obert P. Cardiovascular effects of androgenic anabolic steroids in male bodybuilders determined by tissue Doppler imaging. *Am J Cardiol* 2006;**97**:912–915.
56. Urhausen A, Albers T, Kindermann W. Are the cardiac effects of anabolic steroid abuse in strength athletes reversible? *Heart* 2004;**90**:496–501.
57. Darke S, Torok M, Dufjou J. Sudden or unnatural deaths involving anabolic-androgenic steroids. *J Forensic Sci* 2014;**59**:1025–1028.
58. Far HR, Agren G, Thiblin L. Cardiac hypertrophy in deceased users of anabolic androgenic steroids: an investigation of autopsy findings. *Cardiovasc Pathol* 2012;**21**:312–316.
59. Corrado D, Pelliccia A, Heidbüchel H, Sharma S, Link M, Basso C, Biffi A, Buja G, Delise P, Gussac I, Anastakis A, Borjesson M, Björnstad HH, Carre F, Deligiannis A, Dugmore D, Fagard R, Hoogsteen J, Mellwig KP, Panhuyzen-Goedkoop N, Solberg E, Vanhees L, Drezner J, Estes NA 3rd, Illiceto S, Maron BJ, Peidro R, Schwartz PJ, Stein R, Thiene G, Zeppilli P, McKenna WJ. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. *Eur Heart J* 2010;**31**:243–259.
60. Drezner JA, Fischbach P, Froelicher V, Marek J, Pelliccia A, Prutkin JM, Schmied CM, Sharma S, Wilson MG, Ackerman MJ, Anderson J, Ashley E, Asplund CA, Baggish AL, Borjesson M, Cannon BC, Corrado D, DiFiori JP, Harmon KG, Heidbüchel H, Owens DS, Paul S, Salerno JC, Stein R, Vetter VL. Normal electrocardiographic findings: recognising physiological adaptations in athletes. *Br J Sports Med* 2013;**47**:125–136.
61. Pelliccia A, Di Paolo FM, Quattrini FM, Basso C, Culasso F, Popoli G, De Luca R, Spataro A, Biffi A, Thiene G, Maron BJ. Outcomes in athletes with marked ECG repolarization abnormalities. *N Engl J Med* 2008;**358**:152–161.
62. Spirito P, Pelliccia A, Proschan MA, Granata M, Spataro A, Bellone P, Caselli G, Biffi A, Vecchio C, Maron BJ. Morphology of the "athlete's heart" assessed by echocardiography in 947 elite athletes representing 27 sports. *Am J Cardiol* 1994;**74**:802–806.
63. Pelliccia A, Dipaolo FM. Cardiac remodeling in women athletes and implications for cardiovascular screening. *Med Sci Sports Exerc* 2005;**37**:1436–1439.
64. Basavarajiah S, Boraita A, Whyte G, Wilson M, Carby L, Shah A, Sharma S. Ethnic differences in left ventricular remodeling in highly-trained athletes relevance to differentiating physiologic left ventricular hypertrophy from hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2008;**51**:2256–2262.
65. Sharma S, Maron BJ, Whyte G, Firooz S, Elliott PM, McKenna WJ. Physiologic limits of left ventricular hypertrophy in elite junior athletes: relevance to differential diagnosis of athlete's heart and hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002;**40**:1431–1436.
66. Pelliccia A, Maron BJ, De Luca R, Di Paolo FM, Spataro A, Culasso F. Remodeling of left ventricular hypertrophy in elite athletes after long-term deconditioning. *Circulation* 2002;**105**:944–949.
67. Pluim BM, Zwinderman AH, van der Laarse A, van der Wall EE. The athlete's heart. A meta-analysis of cardiac structure and function. *Circulation* 2000;**101**:336–344.
68. Caselli S, Di Paolo FM, Piscichio C, Pandian NG, Pelliccia A. Patterns of left ventricular diastolic function in Olympic athletes. *J Am Soc Echocardiogr* 2015;**28**:236–244.
69. D'Andrea A, Limongelli G, Caso P, Sarubbi B, Della Pietra A, Brancaccio P, Cice G, Scherillo M, Limongelli F, Calabro R. Association between left ventricular structure and cardiac performance during effort in two morphological forms of athlete's heart. *Int J Cardiol* 2002;**86**:177–184.
70. Cardim N, Oliveira AG, Longo S, Ferreira T, Pereira A, Reis RP, Correia JM. Doppler tissue imaging: regional myocardial function in hypertrophic cardiomyopathy and in athlete's heart. *J Am Soc Echocardiogr* 2003;**16**:223–232.
71. Vinereanu D, Florescu N, Sculthorpe N, Tweddell AC, Stephens MR, Fraser AG. Differentiation between pathologic and physiologic left ventricular hypertrophy by tissue Doppler assessment of long-axis function in patients with hypertrophic cardiomyopathy or systemic hypertension and in athletes. *Am J Cardiol* 2001;**88**:53–58.
72. D'Andrea A, Cocchia R, Riegler L, Scarafie R, Salerno G, Gravino R, Golia E, Pezzullo E, Citro R, Limongelli G, Pacileo G, Cuomo S, Caso P, Russo MG, Bossone E, Calabro R. Left ventricular myocardial velocities and deformation indexes in top-level athletes. *J Am Soc Echocardiogr* 2010;**23**:1281–1288.
73. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;**28**:1–39.e14.
74. D'Andrea A, Cocchia R, Riegler L, Scarafie R, Salerno G, Gravino R, Vriz O, Citro R, Limongelli G, Di Salvo G, Cuomo S, Caso P, Russo MG, Calabro R, Bossone E. Aortic root dimensions in elite athletes. *Am J Cardiol* 2010;**105**:1629–1634.
75. Iskandar A, Thompson PD. A meta-analysis of aortic root size in elite athletes. *Circulation* 2013;**127**:791–798.
76. D'Ascenzi F, Piscichio C, Caselli S, Di Paolo FM, Spataro A, Pelliccia A. RV remodeling in olympic athletes. *JACC Cardiovasc Imaging* 2017;**10**:385–393.
77. D'Ascenzi F, Caselli S, Solari M, Pelliccia A, Cameli M, Focardi M, Padeletti M, Corrado D, Bonifazi M, Mondillo S. Novel echocardiographic techniques for the evaluation of athletes' heart: a focus on speckle-tracking echocardiography. *Eur J Prev Cardiol* 2016;**23**:437–446.
78. Scharhag J, Schneider G, Urhausen A, Rochette V, Kramann B, Kindermann W. Athlete's heart: right and left ventricular mass and function in male endurance athletes and untrained individuals determined by magnetic resonance imaging. *J Am Coll Cardiol* 2002;**40**:1856–1863.
79. D'Andrea A, Riegler L, Golia E, Cocchia R, Scarafie R, Salerno G, Pezzullo E, Nunziata L, Citro R, Cuomo S, Caso P, Di Salvo G, Cittadini A, Russo MG, Calabro R, Bossone E. Range of right heart measurements in top-level athletes: the training impact. *Int J Cardiol* 2013;**164**:48–57.

80. Claessen G, La Gerche A, Voigt JU, Dymarkowski S, Schnell F, Petit T, Willems R, Claus P, Delcroix M, Heidebuchel H. Accuracy of echocardiography to evaluate pulmonary vascular and RV function during exercise. *JACC Cardiovasc Imaging* 2016;**9**:532–543.
81. La Gerche A, Claessen G, Van de Bruene A, Pattyn N, Van Cleemput J, Gewillig M, Bogaert J, Dymarkowski S, Claus P, Heidebuchel H. Cardiac MRI: a new gold standard for ventricular volume quantification during high-intensity exercise. *Circ Cardiovasc Imaging* 2013;**6**:329–338.
82. Lancellotti P, Pelliccia PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, Edvardsen T, Garbi M, Ha JW, Kane GC, Kreeger J, Mertens L, Pibarot P, Picano E, Ryan T, Tsutsui JM, Varga A. The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr* 2017;**30**:101–138.
83. Cappelli F, Toncelli L, Cappelli B, De Luca A, Stefani L, Maffulli N, Galanti G. Adaptive or maladaptive hypertrophy, different spatial distribution of myocardial contraction. *Clin Physiol Funct Imaging* 2010;**30**:6–12.
84. Caselli S, Montesanti D, Autore C, Di Paolo FM, Pisicchio C, Squeo MR, Musumeci B, Spataro A, Pandian NG, Pelliccia A. Patterns of left ventricular longitudinal strain and strain rate in Olympic athletes. *J Am Soc Echocardiogr* 2015;**28**:245–253.
85. Galderisi M, Lomoriello VS, Santoro A, Esposito R, Olibet M, Raia R, Di Minno MN, Guerra G, Mele D, Lombardi G. Differences of myocardial systolic deformation and correlates of diastolic function in competitive rowers and young hypertensives: a speckle-tracking echocardiography study. *J Am Soc Echocardiogr* 2010;**23**:1190–1198.
86. Nottin S, Doucende G, Schuster-Beck I, Dauzat M, Obert P. Alteration in left ventricular normal and shear strains evaluated by 2D-strain echocardiography in the athlete's heart. *J Physiol* 2008;**586**:4721–4733.
87. Simsek Z, Hakan Tas M, Degirmenci H, Gokhan Yazici A, Ipek E, Duman H, Gundogdu F, Karakelleoglu S, Senocak H. Speckle tracking echocardiographic analysis of left ventricular systolic and diastolic functions of young elite athletes with eccentric and concentric type of cardiac remodeling. *Echocardiography* 2013;**30**:1202–1208.
88. Soullier C, Obert P, Doucende G, Nottin S, Cade S, Perez-Martin A, Messner-Pellenc P, Schuster I. Exercise response in hypertrophic cardiomyopathy: blunted left ventricular deformational and twisting reserve with altered systolic-diastolic coupling. *Circ Cardiovasc Imaging* 2012;**5**:324–332.
89. Weiner RB, Hutter AM Jr, Wang F, Kim J, Weyman AE, Wood MJ, Picard MH, Bagish AL. The impact of endurance exercise training on left ventricular torsion. *JACC Cardiovasc Imaging* 2010;**3**:1001–1009.
90. D'Ascenzi F, Pelliccia A, Corrado D, Cameli M, Curci V, Alvino F, Natali BM, Focardi M, Bonifazi M, Mondillo S. Right ventricular remodeling induced by exercise training in competitive athletes. *Eur Heart J Cardiovasc Imaging* 2016;**17**:301–307.
91. Esposito R, Galderisi M, Schiano-Lomoriello V, Santoro A, De Palma D, Ippolito R, Muscarello R, Santoro C, Guerra G, Cameli M, Mondillo S, De Simone G. Nonsymmetric myocardial contribution to supranormal right ventricular function in the athlete's heart: combined assessment by speckle tracking and real time three-dimensional echocardiography. *Echocardiography* 2014;**31**:996–1004.
92. Heidebuchel H, La Gerche A. The right heart in athletes. Evidence for exercise-induced arrhythmogenic right ventricular cardiomyopathy. *Herzschrittmacherther Elektrophysiol* 2012;**23**:82–86.
93. La Gerche A, Burns AT, D'Hooge J, Maclsaac AI, Heidebuchel H, Prior DL. Exercise strain rate imaging demonstrates normal right ventricular contractile reserve and clarifies ambiguous resting measures in endurance athletes. *J Am Soc Echocardiogr* 2012;**25**:253–262.e1.
94. La Gerche A, Burns AT, Mooney DJ, Inder WJ, Taylor AJ, Bogaert J, Macisaac AI, Heidebuchel H, Prior DL. Exercise-induced right ventricular dysfunction and structural remodeling in endurance athletes. *Eur Heart J* 2012;**33**:998–1006.
95. Oxenburgh D, Sharma S, Shave R, Whyte G, Birch K, Artis N, Batterham AM, George K. The right ventricle of the endurance athlete: the relationship between morphology and deformation. *J Am Soc Echocardiogr* 2012;**25**:263–271.
96. Oxenburgh D, Shave R, Warburton D, Williams K, Oxenburgh A, Charlesworth S, Foulds H, Hoffman MD, Birch K, George K. Dilatation and dysfunction of the right ventricle immediately after ultraendurance exercise: exploratory insights from conventional two-dimensional and speckle tracking echocardiography. *Circ Cardiovasc Imaging* 2011;**4**:253–263.
97. Teske AJ, Cox MG, Te Riele AS, De Boeck BV, Doevedans PA, Hauer RN, Cramer MJ. Early detection of regional functional abnormalities in asymptomatic ARVD/C gene carriers. *J Am Soc Echocardiogr* 2012;**25**:997–1006.
98. Sarvari SI, Haugaa KH, Anfinson OG, Leren TP, Smiseth OA, Kongsgaard E, Amlie JP, Edvardsen T. Right ventricular mechanical dispersion is related to malignant arrhythmias: a study of patients with arrhythmogenic right ventricular cardiomyopathy and subclinical right ventricular dysfunction. *Eur Heart J* 2011;**32**:1089–1096.
99. Lang RM, Badano LP, Tsang W, Adams DH, Agricola E, Buck T, Faletra FF, Franke A, Hung J, de Isla LP, Kamp O, Kasprzak JD, Lancellotti P, Marwick TH, McCulloch ML, Monaghan MJ, Nihoyannopoulos P, Pandian NG, Pelliccia PA, Pepi M, Roberson DA, Shernan SK, Shirali GS, Sugeng L, Ten Cate FJ, Vannan MA, Zamorano JL, Zoghbi WA. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. *Eur Heart J Cardiovasc Imaging* 2012;**13**:1–46.
100. Muraru D, Badano LP, Peluso D, Dal Bianco L, Casablanca S, Kocabay G, Zoppellaro G, Illiceto S. Comprehensive analysis of left ventricular geometry and function by three-dimensional echocardiography in healthy adults. *J Am Soc Echocardiogr* 2013;**26**:618–628.
101. Caselli S, Di Pietro R, Di Paolo FM, Pisicchio C, di Giacinto B, Guerra E, Cusano F, Pelliccia A. Left ventricular systolic performance is improved in elite athletes. *Eur J Echocardiogr* 2011;**12**:514–519.
102. De Castro S, Pelliccia A, Caselli S, Di Angelantonio E, Papetti F, Cavarretta E, Carbone I, Francione M, Passariello R, Pandian NG, Fedele F. Remodelling of the left ventricle in athlete's heart: a three dimensional echocardiographic and magnetic resonance imaging study. *Heart* 2006;**92**:975–976.
103. De Castro S, Caselli S, Maron M, Pelliccia A, Cavarretta E, Maddukuri P, Cartoni D, Di Angelantonio E, Kuvlin JT, Patel AR, Pandian NG. Left ventricular remodelling index (LVRI) in various pathophysiological conditions: a real-time three-dimensional echocardiographic study. *Heart* 2007;**93**:205–209.
104. Caselli S, Pelliccia A, Maron M, Santini D, Puccio D, Marcantonio A, Pandian NG, De Castro S. Differentiation of hypertrophic cardiomyopathy from other forms of left ventricular hypertrophy by means of three-dimensional echocardiography. *Am J Cardiol* 2008;**102**:616–620.
105. Hendel RC, Patel MR, Kramer CM, Poon M, Hendel RC, Carr JC, Gerstad NA, Gillam LD, Hodgson JM, Kim RJ, Kramer CM, Lesser JR, Martin ET, Messer JV, Redberg RF, Rubin GD, Rumsfeld JS, Taylor AJ, Weigold WG, Woodard PK, Brindis RG, Hendel RC, Douglas PS, Peterson ED, Wolk MJ, Allen JM, Patel MR. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. *J Am Coll Cardiol* 2006;**48**:1475–1497.
106. Pennell DJ, Sechtem UP, Higgins CB, Manning WJ, Pohost GM, Rademakers FE, van Rossum AC, Shaw LJ, Yucel EK. Clinical indications for cardiovascular magnetic resonance (CMR): consensus panel report. *Eur Heart J* 2004;**25**:1940–1965.
107. Yoon YE, Hong YJ, Kim HK, Kim JA, Na JO, Yang DH, Kim YJ, Choi EY. The Korean Society of Cardiology and the Korean Society of Radiology. 2014 Korean guidelines for appropriate utilization of cardiovascular magnetic resonance imaging: a joint report of the Korean Society of Cardiology and the Korean Society of Radiology. *Korean J Radiol* 2014;**15**:659–688.
108. Prakken NH, Teske AJ, Cramer MJ, Mosterd A, Bosker AC, Mali WP, Doevedans PA, Velthuis BK. Head-to-head comparison between echocardiography and cardiac MRI in the evaluation of the athlete's heart. *Br J Sports Med* 2012;**46**:348–354.
109. O'Donnell DH, Abbata S, Chaitiraphan V, Yared K, Killeen RP, Martos R, Keane D, Cury RC, Dodd JD. Cardiac MR imaging of nonischemic cardiomyopathies: imaging protocols and spectra of appearances. *Radiology* 2012;**262**:403–422.
110. Bluemke DA, Krupinski EA, Ovitt T, Gear K, Unger E, Axel L, Boxt LM, Casolo G, Ferrari VA, Funaki B, Globits S, Higgins CB, Julsrud P, Lipton M, Mawson J, Nygren A, Pennell DJ, Stillman A, White RD, Wichter T, Marcus F. MR Imaging of arrhythmogenic right ventricular cardiomyopathy: morphologic findings and interobserver reliability. *Cardiology* 2003;**99**:153–162.
111. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA, Calkins H, Corrado D, Cox MG, Daubert JP, Fontaine G, Gear K, Hauer R, Nava A, Picard MH, Protonotarios N, Saffitz JE, Sanborn DM, Steinberg JS, Tandri H, Thiene G, Towbin JA, Tsatsopoulou A, Wichter T, Zareba W. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. *Circulation* 2010;**121**:1533–1541.
112. Luijckx T, Velthuis BK, Prakken NH, Cox MG, Bots ML, Mali WP, Hauer RN, Cramer MJ. Impact of revised task force criteria: distinguishing the athlete's heart from ARVC/D using cardiac magnetic resonance imaging. *Eur J Prev Cardiol* 2012;**19**:885–891.
113. Sen-Chowdhry S, Syrris P, Prasad SK, Hughes SE, Merrifield R, Ward D, Pennell DJ, McKenna WJ. Left-dominant arrhythmogenic cardiomyopathy: an under-recognized clinical entity. *J Am Coll Cardiol* 2008;**52**:2175–2187.

114. Zilinski JL, Contursi ME, Isaacs SK, Deluca JR, Lewis GD, Weiner RB, Hutter AM Jr, D'Hemecourt PA, Troyanos C, Dyer KS, Baggish AL. Myocardial adaptations to recreational marathon training among middle-aged men. *Circ Cardiovasc Imaging* 2015;**8**:e002487.
115. Utomi V, Oxborough D, Whyte GP, Somauroo J, Sharma S, Shave R, Atkinson G, George K. Systematic review and meta-analysis of training mode, imaging modality and body size influences on the morphology and function of the male athlete's heart. *Heart* 2013;**99**:1727–1733.
116. Chun EJ, Choi SI, Jin KN, Kwag HJ, Kim YJ, Choi BW, Lee W, Park JH. Hypertrophic cardiomyopathy: assessment with MR imaging and multidetector CT. *Radiographics* 2010;**30**:1309–1328.
117. Kim RJ, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O, Bundy J, Finn JP, Klocke FJ, Judd RM. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation* 1999;**100**:1992–2002.
118. Fieno DS, Kim RJ, Chen EL, Lomasney JW, Klocke FJ, Judd RM. Contrast-enhanced magnetic resonance imaging of myocardium at risk: distinction between reversible and irreversible injury throughout infarct healing. *J Am Coll Cardiol* 2000;**36**:1985–1991.
119. Moon JC, Reed E, Sheppard MN, Elkington AG, Ho SY, Burke M, Petrou M, Pennell DJ. The histologic basis of late gadolinium enhancement cardiovascular magnetic resonance in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2004;**43**:2260–2264.
120. Breuckmann F, Mohlenkamp S, Nassenstein K, Lehmann N, Ladd S, Schmermund A, Sievers B, Schlosser T, Jockel KH, Heusch G, Erbel R, Barkhausen J. Myocardial late gadolinium enhancement: prevalence, pattern, and prognostic relevance in marathon runners. *Radiology* 2009;**251**:50–57.
121. Maron BJ, Pelliccia A, Spirito P. Cardiac disease in young trained athletes. Insights into methods for distinguishing athlete's heart from structural heart disease, with particular emphasis on hypertrophic cardiomyopathy. *Circulation* 1995;**91**:1596–1601.
122. Petersen SE, Selvanayagam JB, Francis JM, Myerson SG, Wiesmann F, Robson MD, Ostman-Smith I, Casadei B, Watkins H, Neubauer S. Differentiation of athlete's heart from pathological forms of cardiac hypertrophy by means of geometric indices derived from cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2005;**7**:551–558.
123. Waterhouse DF, Ismail TF, Prasad SK, Wilson MG, O'Hanlon R. Imaging focal and interstitial fibrosis with cardiovascular magnetic resonance in athletes with left ventricular hypertrophy: implications for sporting participation. *Br J Sports Med* 2012;**46**:i69–i77.
124. Bruder O, Wagner A, Jensen CJ, Schneider S, Ong P, Kispert EM, Nassenstein K, Schlosser T, Sabin GV, Sechtem U, Mahrholdt H. Myocardial scar visualized by cardiovascular magnetic resonance imaging predicts major adverse events in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2010;**56**:875–887.
125. O'Hanlon R, Grasso A, Roughton M, Moon JC, Clark S, Wage R, Webb J, Kulkarni M, Dawson D, Sulaiabeek H, Chandrasekaran B, Bucciarelli-Ducci C, Pasquale F, Cowie MR, McKenna WJ, Sheppard MN, Elliott PM, Pennell DJ, Prasad SK. Prognostic significance of myocardial fibrosis in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2010;**56**:867–874.
126. Petersen SE, Jerosch-Herold M, Hudsmith LE, Robson MD, Francis JM, Doll HA, Selvanayagam JB, Neubauer S, Watkins H. Evidence for microvascular dysfunction in hypertrophic cardiomyopathy: new insights from multiparametric magnetic resonance imaging. *Circulation* 2007;**115**:2418–2425.
127. Satoh H, Sano M, Suwa K, Saitoh T, Nobuhara M, Saotome M, Urushida T, Katoh H, Hayashi H. Distribution of late gadolinium enhancement in various types of cardiomyopathies: significance in differential diagnosis, clinical features and prognosis. *World J Cardiol* 2014;**6**:585–601.
128. Moravsky G, Ofek E, Rakowski H, Butany J, Williams L, Ralph-Edwards A, Wintersperger BJ, Crean A. Myocardial fibrosis in hypertrophic cardiomyopathy: accurate reflection of histopathological findings by CMR. *JACC Cardiovasc Imaging* 2013;**6**:587–596.
129. Yilmaz A, Sechtem U. Diagnostic approach and differential diagnosis in patients with hypertrophied left ventricles. *Heart* 2014;**100**:662–671.
130. Maron MS. Clinical utility of cardiovascular magnetic resonance in hypertrophic cardiomyopathy. *J Cardiovasc Magn Reson* 2012;**14**:13.
131. Moon JC, Messroghli DR, Kellman P, Piechnik SK, Robson MD, Ugander M, Gatehouse PD, Arai AE, Friedrich MG, Neubauer S, Schulz-Menger J, Schelbert EB; Society for Cardiovascular Magnetic Resonance Imaging; Cardiovascular Magnetic Resonance Working Group of the European Society of Cardiology. Myocardial T1 mapping and extracellular volume quantification: a Society for Cardiovascular Magnetic Resonance (SCMR) and CMR Working Group of the European Society of Cardiology consensus statement. *J Cardiovasc Magn Reson* 2013;**15**:92.
132. Liu CY, Liu YC, Wu C, Armstrong A, Volpe GJ, van der Geest RJ, Liu Y, Hundley WG, Gomes AS, Liu S, Nacif M, Bluemke DA, Lima JA. Evaluation of age-related interstitial myocardial fibrosis with cardiac magnetic resonance contrast-enhanced T1 mapping: MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol* 2013;**62**:1280–1287.
133. Sado DM, White SK, Piechnik SK, Bannypersad SM, Treibel T, Captur G, Fontana M, Maestrini V, Flett AS, Robson MD, Lachmann RH, Murphy E, Mehta A, Hughes D, Neubauer S, Elliott PM, Moon JC. Identification and assessment of Anderson-Fabry disease by cardiovascular magnetic resonance noncontrast myocardial T1 mapping. *Circ Cardiovasc Imaging* 2013;**6**:392–398.
134. Pica S, Sado DM, Maestrini V, Fontana M, White SK, Treibel T, Captur G, Anderson S, Piechnik SK, Robson MD, Lachmann RH, Murphy E, Mehta A, Hughes D, Kellman P, Elliott PM, Herrey AS, Moon JC. Reproducibility of native myocardial T1 mapping in the assessment of Fabry disease and its role in early detection of cardiac involvement by cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2014;**16**:99.
135. Fazel R, Krumholz HM, Wang Y, Ross JS, Chen J, Ting HH, Shah ND, Nasir K, Einstein AJ, Nallamothu BK. Exposure to low-dose ionizing radiation from medical imaging procedures. *N Engl J Med* 2009;**361**:849–857.
136. Layritz C, Schmid J, Achenbach S, Ulzheimer S, Wuest W, May M, Ropers D, Klinghammer L, Daniel WG, Pflederer T, Lell M. Accuracy of prospectively ECG-triggered very low-dose coronary dual-source CT angiography using iterative reconstruction for the detection of coronary artery stenosis: comparison with invasive catheterization. *Eur Heart J Cardiovasc Imaging* 2014;**15**:1238–1245.
137. Bomma C, Dalal D, Tandri H, Prakasa K, Nasir K, Roguin A, Piccini J, Dong J, Mahadevappa M, Tichnell C, James C, Lima JA, Fishman E, Calkins H, Bluemke DA. Evolving role of multidetector computed tomography in evaluation of arrhythmogenic right ventricular dysplasia/cardiomyopathy. *Am J Cardiol* 2007;**100**:99–105.
138. Troupis JM, Singh Pasricha S, Gunaratnam K, Nasis A, Cameron J, Seneviratne S. Cardiomyopathy and cardiac computed tomography: what the radiologist needs to know. *Clin Radiol* 2013;**68**:e49–e58.
139. Sharma A, Einstein AJ, Vallakati A, Arbab-Zadeh A, Mukherjee D, Lichstein E. Meta-analysis of global left ventricular function comparing multidetector computed tomography with cardiac magnetic resonance imaging. *Am J Cardiol* 2014;**113**:731–738.
140. Feuchtnner GM, Dichtl W, Friedrich GJ, Frick M, Alber H, Schachner T, Bonatti J, Mallouhi A, Frede T, Pachinger O, Zur Nedden D, Müller S. Multislice computed tomography for detection of patients with aortic valve stenosis and quantification of severity. *J Am Coll Cardiol* 2006;**47**:1410–1417.
141. Hesse B, Lindhardt TB, Acampa W, Anagnostopoulos C, Ballinger J, Bax JJ, Edenbrandt L, Flotats A, Germano G, Stopar TG, Franken P, Kelion A, Kjaer A, Le Guludec D, Ljungberg M, Maenhout AF, Marcassa C, Marving J, McKiddie F, Schaefer WM, Stegger L, Underwood R. EANM/ESC guidelines for radionuclide imaging of cardiac function. *Eur J Nucl Med Mol Imaging* 2008;**35**:851–885.
142. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di MC, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabate M, Senior R, Taggart DP, van der Wall EE, Vrints CJ, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hämilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Ryden L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirim A, Zamorano JL. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013;**34**:2949–3003.
143. Dorbala S, Blankstein R, Skali H, Park MA, Fantony J, Mauceri C, Semer J, Moore SC, Di Carli MF. Approaches to reducing radiation dose from radionuclide myocardial perfusion imaging. *J Nucl Med* 2015;**56**:592–599.
144. Kajander S, Joutsiniemi E, Saraste M, Pietila M, Ukkonen H, Saraste A, Sipilä HT, Teras M, Maki M, Airaksinen J, Hartiala J, Knuuti J. Cardiac positron emission tomography/computed tomography imaging accurately detects anatomically and functionally significant coronary artery disease. *Circulation* 2010;**122**:603–613.
145. Elliott PM, Anastakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, Hagege AA, Lafont A, Limongelli G, Mahrholdt H, McKenna WJ, Mogensen J, Nihoyannopoulos P, Nistri S, Pieper PG, Pieske B, Rapezzi C, Rutten FH, Tillmanns C, Watkins H. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the task force for the diagnosis and management of hypertrophic cardiomyopathy of the European Society of Cardiology (ESC). *Eur Heart J* 2014;**35**:2733–2779.
146. Cardim N, Galderisi M, Edvardsen T, Plein S, Popescu BA, D'Andrea A, Bruder O, Cosyns B, Davin L, Donal E, Freitas A, Habib G, Kitsiou A, Petersen SE, Schroeder S, Lancellotti P, Camici P, Dulgheru R, Hagendorff A, Lombardi M, Muraru D, Sicari R. Role of multimodality cardiac imaging in the management of

- patients with hypertrophic cardiomyopathy: an expert consensus of the European Association of Cardiovascular Imaging Endorsed by the Saudi Heart Association. *Eur Heart J Cardiovasc Imaging* 2015;**16**:280.
147. Sheikh N, Papadakis M, Schnell F, Panoulas V, Malhotra A, Wilson M, Carre F, Sharma S. Clinical profile of athletes with hypertrophic cardiomyopathy. *Circ Cardiovasc Imaging* 2015;**8**:e003454.
 148. Maron MS, Olivetto I, Harrigan C, Appelbaum E, Gibson CM, Lesser JR, Haas TS, Udelson JE, Manning WJ, Maron BJ. Mitral valve abnormalities identified by cardiovascular magnetic resonance represent a primary phenotypic expression of hypertrophic cardiomyopathy. *Circulation* 2011;**124**:40–47.
 149. Maron MS, Olivetto I, Zenovich AG, Link MS, Pandian NG, Kuvlin JT, Nistri S, Cecchi F, Udelson JE, Maron BJ. Hypertrophic cardiomyopathy is predominantly a disease of left ventricular outflow tract obstruction. *Circulation* 2006;**114**:2232–2239.
 150. Kansal MM, Lester SJ, Surapaneni P, Sengupta PP, Appleton CP, Ommen SR, Ressler SW, Hurst RT. Usefulness of two-dimensional and speckle tracking echocardiography in “Gray Zone” left ventricular hypertrophy to differentiate professional football player’s heart from hypertrophic cardiomyopathy. *Am J Cardiol* 2011;**108**:1322–1326.
 151. Lewis JF, Spirito P, Pelliccia A, Maron BJ. Usefulness of Doppler echocardiographic assessment of diastolic filling in distinguishing “athlete’s heart” from hypertrophic cardiomyopathy. *Br Heart J* 1992;**68**:296–300.
 152. Schnell F, Riding N, O’Hanlon R, Axel Lentz P, Donal E, Kervio G, Matelot D, Leurent G, Doutreleau S, Chevalier L, Guerard S, Wilson MG, Carré F. Recognition and significance of pathological T-wave inversions in athletes. *Circulation* 2015;**131**:165–173.
 153. Maron MS, Appelbaum E, Harrigan CJ, Buross J, Gibson CM, Hanna C, Lesser JR, Udelson JE, Manning WJ, Maron BJ. Clinical profile and significance of delayed enhancement in hypertrophic cardiomyopathy. *Circ Heart Fail* 2008;**1**:184–191.
 154. Maron BJ, Pelliccia A, Spataro A, Granata M. Reduction in left ventricular wall thickness after deconditioning in highly trained Olympic athletes. *Br Heart J* 1993;**69**:125–128.
 155. Weiner RB, Wang F, Berkstresser B, Kim J, Wang TJ, Lewis GD, Hutter AM Jr, Picard MH, Baggish AL. Regression of “gray zone” exercise-induced concentric left ventricular hypertrophy during prescribed detraining. *J Am Coll Cardiol* 2012;**59**:1992–1994.
 156. Finocchiaro G, Dhutia H, D’Silva A, Malhotra A, Steriotis A, Millar L, Prakash K, Narain R, Papadakis M, Sharma R, Sharma S. Effect of sex and sporting discipline on LV adaptation to exercise. *JACC Cardiovasc Imaging* 2016; doi: 10.1016/j.jcmg.2016.08.011.
 157. Abergel E, Chatellier G, Hagege AA, Oblak A, Linhart A, Ducardonnet A, Menard J. Serial left ventricular adaptations in world-class professional cyclists: implications for disease screening and follow-up. *J Am Coll Cardiol* 2004;**44**:144–149.
 158. Engholm H, Steding K, Carlsson M, Mosen H, Heden B, Buhre T, Ekmeheg B, Arheden H. Peak oxygen uptake in relation to total heart volume discriminates heart failure patients from healthy volunteers and athletes. *J Cardiovasc Magn Reson* 2010;**12**:74.
 159. Poulsen SH, Hjortshøj S, Korup E, Poenitz V, Espersen G, Sogaard P, Suder P, Egeblad H, Kristensen BO. Strain rate and tissue tracking imaging in quantitation of left ventricular systolic function in endurance and strength athletes. *Scand J Med Sci Sports* 2007;**17**:148–155.
 160. Richard V, Lafitte S, Reant P, Serri K, Lafitte M, Brette S, Kerouani A, Chalabi H, Dos Santos P, Douard H, Roudaut R. An ultrasound speckle tracking (two-dimensional strain) analysis of myocardial deformation in professional soccer players compared with healthy subjects and hypertrophic cardiomyopathy. *Am J Cardiol* 2007;**100**:128–132.
 161. Mahrholdt H, Wagner A, Judd RM, Sechtem U, Kim RJ. Delayed enhancement cardiovascular magnetic resonance assessment of non-ischaemic cardiomyopathies. *Eur Heart J* 2005;**26**:1461–1474.
 162. Brosnan M, La Gerche A, Kalman J, Lo W, Fallon K, MacIsaac A, Prior DL. Comparison of frequency of significant electrocardiographic abnormalities in endurance versus nonendurance athletes. *Am J Cardiol* 2014;**113**:1567–1573.
 163. La Gerche A, Claessen G, Dymarkowski S, Voigt JU, De Buck F, Vanhees L, Droogne W, Van Cleemput J, Claus P, Heidbuchel H. Exercise-induced right ventricular dysfunction is associated with ventricular arrhythmias in endurance athletes. *Eur Heart J* 2015;**36**:1998–2010.
 164. Heidbuchel H, Hoogsteen J, Fagard R, Vanhees L, Ector H, Willems R, Van Lierde J. High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias. Role of an electrophysiologic study in risk stratification. *Eur Heart J* 2003;**24**:1473–1480.
 165. La Gerche A, Heidbuchel H, Burns AT, Mooney DJ, Taylor AJ, Pfluger HB, Inder WJ, MacIsaac AJ, Prior DL. Disproportionate exercise load and remodeling of the athlete’s right ventricle. *Med Sci Sports Exerc* 2011;**43**:974–981.
 166. Arbab-Zadeh A, Perhonen M, Howden E, Peshock RM, Zhang R, Adams-Huet B, Haykowsky MJ, Levine BD. Cardiac remodeling in response to 1 year of intensive endurance training. *Circulation* 2014;**130**:2152–2161.
 167. Baucé B, Frigo G, Benini G, Michieli P, Basso C, Folino AF, Rigato I, Mazzotti E, Daliento L, Thiene G, Nava A. Differences and similarities between arrhythmogenic right ventricular cardiomyopathy and athlete’s heart adaptations. *Br J Sports Med* 2010;**44**:148–154.
 168. La Gerche A, Robberecht C, Kuiperi C, Nuyens D, Willems R, de Ravel T, Matthijs G, Heidbuchel H. Lower than expected desmosomal gene mutation prevalence in endurance athletes with complex ventricular arrhythmias of right ventricular origin. *Heart* 2010;**96**:1268–1274.
 169. Saberniak J, Hasselberg NE, Borgquist R, Platonov PG, Sarvari SI, Smith HJ, Ribe M, Holst AG, Edvardsen T, Haugaa KH. Vigorous physical activity impairs myocardial function in patients with arrhythmogenic right ventricular cardiomyopathy and in mutation positive family members. *Eur J Heart Fail* 2014;**16**:1337–1344.
 170. Leren IS, Saberniak J, Haland TF, Edvardsen T, Haugaa KH. Combination of ECG and echocardiography for identification of arrhythmic events in early ARVC. *JACC Cardiovasc Imaging* 2017;**10**:503–513.
 171. Claessen G, Claus P, Ghysels S, Vermeersch P, Dymarkowski S, La Gerche A, Heidbuchel H. Right ventricular fatigue developing during endurance exercise: an exercise cardiac magnetic resonance study. *Med Sci Sports Exerc* 2014;**46**:1717–1726.
 172. Stewart GM, Yamada A, Haseler LJ, Kavanagh JJ, Koerbin G, Chan J, Sabapathy S. Altered ventricular mechanics after 60 min of high-intensity endurance exercise: insights from exercise speckle-tracking echocardiography. *Am J Physiol Heart Circ Physiol* 2015;**308**:H875–H883.
 173. Jenni R, Oechslin E, Schneider J, Attenhofer Jost C, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: a step towards classification as a distinct cardiomyopathy. *Heart* 2001;**86**:666–671.
 174. Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium. A study of eight cases. *Circulation* 1990;**82**:507–513.
 175. Oechslin E, Jenni R. Left ventricular non-compaction revisited: a distinct phenotype with genetic heterogeneity? *Eur Heart J* 2011;**32**:1446–1456.
 176. Kohli SK, Pantazis AA, Shah JS, Adeyemi B, Jackson G, McKenna WJ, Sharma S, Elliott PM. Diagnosis of left-ventricular non-compaction in patients with left-ventricular systolic dysfunction: time for a reappraisal of diagnostic criteria? *Eur Heart J* 2008;**29**:89–95.
 177. Stollberger C, Winkler-Dworak M, Blazek G, Finsterer J. Prognosis of left ventricular hypertrabeculation/noncompaction is dependent on cardiac and neuromuscular comorbidity. *Int J Cardiol* 2007;**121**:189–193.
 178. Gati S, Papadakis M, Van Niekerk N, Reed M, Yeghen T, Sharma S. Increased left ventricular trabeculation in individuals with sickle cell anaemia: physiology or pathology? *Int J Cardiol* 2013;**168**:1658–1660.
 179. Gati S, Chandra N, Bennett RL, Reed M, Kervio G, Panoulas VF, Ghani S, Sheikh N, Zaidi A, Wilson M, Papadakis M, Carre F, Sharma S. Increased left ventricular trabeculation in highly trained athletes: do we need more stringent criteria for the diagnosis of left ventricular non-compaction in athletes? *Heart* 2013;**99**:401–408.
 180. Luijckx T, Cramer MJ, Zaidi A, Rienks R, Senden PJ, Sharma S, van Hellemond FJ, Buckens CF, Mali WP, Velthuis BK. Ethnic differences in ventricular hypertrabeculation on cardiac MRI in elite football players. *Neth Heart J* 2012;**20**:389–395.
 181. Martinoli R, Papetti F, Dofcaci A, Mercurio V, Pirruccio G, Pirelli M, Piccirilli S, Greci G, Lanzillo C, Sansoni L, Saccucci P, Banci M. Isolated left ventricular non compaction as possible cause of athletic training suspension: a preliminary study on screened athletes. *J Sports Med Phys Fitness* 2013;**53**:240–247.
 182. Ganga HV, Thompson PD. Sports participation in non-compaction cardiomyopathy: a systematic review. *Br J Sports Med* 2014;**48**:1466–1471.
 183. Luijckx T, Cramer MJ, Zaidi A, Rienks R, Senden PJ, Sharma S, van Hellemond FJ, Buckens CF, Mali WP, Velthuis BK. Ethnic differences in ventricular hypertrabeculation on cardiac MRI in elite football players. *Neth Heart J* 2012;**20**:389–395.
 184. Caselli S, Ferreira D, Kanawati E, Di Paolo F, Piscicchio C, Attenhofer Jost C, Spataro A, Jenni R, Pelliccia A. Prominent left ventricular trabeculations in competitive athletes: a proposal for risk stratification and management. *Int J Cardiol* 2016;**223**:590–595.
 185. Gati S, Papadakis M, Papamichael ND, Zaidi A, Sheikh N, Reed M, Sharma R, Thilaganathan B, Sharma S. Reversible de novo left ventricular trabeculations in pregnant women: implications for the diagnosis of left ventricular noncompaction in low-risk populations. *Circulation* 2014;**130**:475–483.
 186. Petersen SE, Selvanayagam JB, Wiesmann F, Robson MD, Francis JM, Anderson RH, Watkins H, Neubauer S. Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging. *J Am Coll Cardiol* 2005;**46**:101–105.

187. Gebhard C, Stahli BE, Greutmann M, Biaggi P, Jenni R, Tanner FC. Reduced left ventricular compacta thickness: a novel echocardiographic criterion for non-compaction cardiomyopathy. *J Am Soc Echocardiogr* 2012;**25**:1050–1057.
188. Haland TF, Saberniak J, Leren IS, Edvardsen T, Haugaa KH. Echocardiographic comparison between left ventricular non-compaction and hypertrophic cardiomyopathy. *Int J Cardiol* 2017;**228**:900–905.
189. Nucifora G, Aquaro GD, Pingitore A, Masci PG, Lombardi M. Myocardial fibrosis in isolated left ventricular non-compaction and its relation to disease severity. *Eur J Heart Fail* 2011;**13**:170–176.
190. Babaee Bigi MA, Aslani A. Aortic root size and prevalence of aortic regurgitation in elite strength trained athletes. *Am J Cardiol* 2007;**100**:528–530.
191. Kinoshita N, Mimura J, Obayashi C, Katsukawa F, Onishi S, Yamazaki H. Aortic root dilatation among young competitive athletes: echocardiographic screening of 1929 athletes between 15 and 34 years of age. *Am Heart J* 2000;**139**:723–728.
192. Pelliccia A, Di Paolo FM, Quattrini FM. Aortic root dilatation in athletic population. *Prog Cardiovasc Dis* 2012;**54**:432–437.
193. Gardin JM, Arnold AM, Polak J, Jackson S, Smith V, Gottdiener J. Usefulness of aortic root dimension in persons ≥ 65 years of age in predicting heart failure, stroke, cardiovascular mortality, all-cause mortality and acute myocardial infarction (from the Cardiovascular Health Study). *Am J Cardiol* 2006;**97**:270–275.
194. Gautier M, Detaint D, Fermanian C, Aegerter P, Delorme G, Arnoult F, Milleron O, Raoux F, Stheneur C, Boileau C, Vahanian A, Jondeau G. Nomograms for aortic root diameters in children using two-dimensional echocardiography. *Am J Cardiol* 2010;**105**:888–894.
195. Roman MJ, Devereux RB, Kramer-Fox R, O'Loughlin J. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. *Am J Cardiol* 1989;**64**:507–512.
196. Maron BJ, Ackerman MJ, Nishimura RA, Pyeritz RE, Towbin JA, Udelson JE. Task force 4: HCM and other cardiomyopathies, mitral valve prolapse, myocarditis, and Marfan syndrome. *J Am Coll Cardiol* 2005;**45**:1340–1345.
197. Biner S, Rafique AM, Ray I, Cuk O, Siegel RJ, Tolstrup K. Aortopathy is prevalent in relatives of bicuspid aortic valve patients. *J Am Coll Cardiol* 2009;**53**:2288–2295.
198. Yetman AT, Graham T. The dilated aorta in patients with congenital cardiac defects. *J Am Coll Cardiol* 2009;**53**:461–467.
199. Siu SC, Silversides CK. Bicuspid aortic valve disease. *J Am Coll Cardiol* 2010;**55**:2789–2800.
200. Spataro A, Pelliccia A, Rizzo M, Biffi A, Masazza G, Pigozzi F. The natural course of bicuspid aortic valve in athletes. *Int J Sports Med* 2008;**29**:81–85.
201. Beppu S, Suzuki S, Matsuda H, Ohmori F, Nagata S, Miyatake K. Rapidity of progression of aortic stenosis in patients with congenital bicuspid aortic valves. *Am J Cardiol* 1993;**71**:322–327.
202. Ward C. Clinical significance of the bicuspid aortic valve. *Heart* 2000;**83**:81–85.
203. Bonow RO. Bicuspid aortic valves and dilated aortas: a critical review of the ACC/AHA practice guidelines recommendations. *Am J Cardiol* 2008;**102**:111–114.
204. Michelena HI, Khanna AD, Mahoney D, Margaryan E, Topolsky Y, Suri RM, Eidem B, Edwards WD, Sundt TM 3rd, Enriquez-Sarano M. Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA* 2011;**306**:1104–1112.
205. Cripe L, Andelfinger G, Martin LJ, Shooner K, Benson DW. Bicuspid aortic valve is heritable. *J Am Coll Cardiol* 2004;**44**:138–143.
206. Gelb BD, Zhang J, Sommer RJ, Wasserman JM, Reitman MJ, Willner JP. Familial patent ductus arteriosus and bicuspid aortic valve with hand anomalies: a novel heart-hand syndrome. *Am J Med Genet* 1999;**87**:175–179.
207. Hallidie-Smith KA, Karas S. Cardiac anomalies in Williams-Beuren syndrome. *Arch Dis Child* 1988;**63**:809–813.
208. Della Corte A, Bancone C, Quarto C, Dialetto G, Covino FE, Scardone M, Caianiello G, Cotrufo M. Predictors of ascending aortic dilatation with bicuspid aortic valve: a wide spectrum of disease expression. *Eur J Cardiothorac Surg* 2007;**31**:397–404; discussion 404–5.
209. Tzemos N, Therrien J, Yip J, Thanassoulis G, Tremblay S, Jamorski MT, Webb GD, Siu SC. Outcomes in adults with bicuspid aortic valves. *JAMA* 2008;**300**:1317–1325.
210. Kong WK, Delgado V, Poh KK, Regeer MV, Ng AC, McCormack L, Yeo TC, Shanks M, Parent S, Enache R, Popescu BA, Liang M, Yip JW, Ma LC, Kamperidis V, van Rosendaal PJ, van der Velde ET, Ajmone Marsan N, Bax JJ. Prognostic implications of raphe in bicuspid aortic valve anatomy. *JAMA Cardiol* 2017;**2**:285.
211. Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, Bolger A, Cabell CH, Takahashi M, Baltimore RS, Newburger JW, Strom BL, Tani LY, Gerber M, Bonow RO, Pallasch T, Shulman ST, Rowley AH, Burns JC, Ferrieri P, Gardner T, Goff D, Durack DT. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2007;**116**:1736–1754.
212. Michelena HI, Desjardins VA, Avierinos JF, Russo A, Nkomo VT, Sundt TM, Pelliccia PA, Tajik AJ, Enriquez-Sarano M. Natural history of asymptomatic patients with normally functioning or minimally dysfunctional bicuspid aortic valve in the community. *Circulation* 2008;**117**:2776–2784.
213. De Mozzi P, Longo UG, Galanti G, Maffulli N. Bicuspid aortic valve: a literature review and its impact on sport activity. *Br Med Bull* 2008;**85**:63–85.
214. Muraru D, Badano LP, Vannan M, Iliceto S. Assessment of aortic valve complex by three-dimensional echocardiography: a framework for its effective application in clinical practice. *Eur Heart J Cardiovasc Imaging* 2012;**13**:541–555.
215. Lancellotti P, Tribouilloy C, Hagendorff A, Popescu BA, Edvardsen T, Pierard LA, Badano L, Zamorano JL. Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2013;**14**:611–644.
216. Baumgartner H, Hung J, Bermejo J, Chambers JB, Edvardsen T, Goldstein S, Lancellotti P, LeFebvre M, Miller F Jr, Otto CM. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr* 2017;**30**:372–392.
217. Freeman RV, Otto CM. Bicuspid aortic valve and aortopathy: see the first, then look at the second. *JACC Cardiovasc Imaging* 2013;**6**:162–164.
218. Delling FN, Vasan RS. Epidemiology and pathophysiology of mitral valve prolapse: new insights into disease progression, genetics, and molecular basis. *Circulation* 2014;**129**:2158–2170.
219. Levine RA, Stathogiannis E, Newell JB, Harrigan P, Weyman AE. Reconsideration of echocardiographic standards for mitral valve prolapse: lack of association between leaflet displacement isolated to the apical four chamber view and independent echocardiographic evidence of abnormality. *J Am Coll Cardiol* 1988;**11**:1010–1019.
220. Nishimura RA, McGoon MD, Shub C, Miller FA Jr, Ilstrup DM, Tajik AJ. Echocardiographically documented mitral-valve prolapse. Long-term follow-up of 237 patients. *N Engl J Med* 1985;**313**:1305–1309.
221. Perloff JK, Child JS. Mitral valve prolapse. Evolution and refinement of diagnostic techniques. *Circulation* 1989;**80**:710–711.
222. Freed LA, Benjamin EJ, Levy D, Larson MG, Evans JC, Fuller DL, Lehman B, Levine RA. Mitral valve prolapse in the general population: the benign nature of echocardiographic features in the Framingham Heart Study. *J Am Coll Cardiol* 2002;**40**:1298–1304.
223. Freed LA, Levy D, Levine RA, Larson MG, Evans JC, Fuller DL, Lehman B, Benjamin EJ. Prevalence and clinical outcome of mitral-valve prolapse. *N Engl J Med* 1999;**341**:1–7.
224. Sriram CS, Syed FF, Ferguson ME, Johnson JN, Enriquez-Sarano M, Cetta F, Cannon BC, Asirvatham SJ, Ackerman MJ. Malignant bileaflet mitral valve prolapse syndrome in patients with otherwise idiopathic out-of-hospital cardiac arrest. *J Am Coll Cardiol* 2013;**62**:222–230.
225. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol* 2003;**42**:1959–1963.
226. Adler Y, Charron P, Imazio M, Badano L, Baron-Esquivias G, Bogaert J, Brucato A, Guertel P, Klingel K, Lionis C, Maisch B, Mayosi B, Pavie A, Ristic AD, Sabate Tenas M, Seferovic P, Swedberg K, Tomkowski W, Achenbach S, Agewall S, Al-Attar N, Angel FJ, Arad M, Asteggiano R, Bueno H, Caforio AL, Carerj S, Ceconi C, Evangelista A, Flachskampf F, Giannakoulas G, Gielen S, Habib G, Kolh P, Lambrinou E, Lancellotti P, Lazaros G, Linhart A, Meurin P, Nieman K, Piepoli MF, Price S, Roos-Hesselink J, Roubille F, Ruschitzka F, Sagrista Saulea J, Sousa-Uva M, Uwe Voigt J, Luis Zamorano J. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: the task force for the diagnosis and management of pericardial diseases of the European Society of Cardiology (ESC) Endorsed by: the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2015;**36**:2921–2964.
227. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, Fu M, Helio T, Heymans S, Jahns R, Klingel K, Linhart A, Maisch B, McKenna W, Mogensen J, Pinto YM, Ristic A, Schultheiss HP, Seggewiss H, Tavazzi L, Thiene G, Yilmaz A, Charron P, Elliott PM. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J* 2013;**34**:2636–2648, 2648a–2648d.
228. Basso C, Carturan E, Corrado D, Thiene G. Myocarditis and dilated cardiomyopathy in athletes: diagnosis, management, and recommendations for sport activity. *Cardiol Clin* 2007;**25**:423–429.vi.
229. Sagar S, Liu PP, Cooper LT Jr. Myocarditis. *Lancet* 2012;**379**:738–747.
230. Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, White JA, Abdel-Aty H, Gutberlet M, Prasad S, Aletras A, Laissy JP, Paterson I,

- Filipchuk NG, Kumar A, Pauschinger M, Liu P. Cardiovascular magnetic resonance in myocarditis: a JACC White Paper. *J Am Coll Cardiol* 2009;**53**: 1475–1487.
231. Dawson DK, Hawlisch K, Prescott G, Roussin I, Di Pietro E, Deac M, Wong J, Frenneaux MP, Pennell DJ, Prasad SK. Prognostic role of CMR in patients presenting with ventricular arrhythmias. *JACC Cardiovasc Imaging* 2013;**6**:335–344.
232. Grun S, Schumm J, Greulich S, Wagner A, Schneider S, Bruder O, Kispert EM, Hill S, Ong P, Klingel K, Kandolf R, Sechtem U, Mahrholdt H. Long-term follow-up of biopsy-proven viral myocarditis: predictors of mortality and incomplete recovery. *J Am Coll Cardiol* 2012;**59**:1604–1615.
233. Schumm J, Greulich S, Wagner A, Grun S, Ong P, Bentz K, Klingel K, Kandolf R, Bruder O, Schneider S, Sechtem U, Mahrholdt H. Cardiovascular magnetic resonance risk stratification in patients with clinically suspected myocarditis. *J Cardiovasc Magn Reson* 2014;**16**:14.
234. Angelini P. Coronary artery anomalies: an entity in search of an identity. *Circulation* 2007;**115**:1296–1305.
235. Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *J Am Coll Cardiol* 2000;**35**:1493–1501.
236. Pelliccia A, Spataro A, Maron BJ. Prospective echocardiographic screening for coronary artery anomalies in 1,360 elite competitive athletes. *Am J Cardiol* 1993;**72**:978–979.
237. Bluemke DA, Achenbach S, Budoff M, Gerber TC, Gersh B, Hillis LD, Hundley WG, Manning WJ, Printz BF, Stuber M, Woodard PK. Noninvasive coronary artery imaging: magnetic resonance angiography and multidetector computed tomography angiography: a scientific statement from the American Heart Association committee on cardiovascular imaging and intervention of the council on cardiovascular radiology and intervention, and the councils on clinical cardiology and cardiovascular disease in the young. *Circulation* 2008;**118**: 586–606.
238. Schroeder S, Achenbach S, Bengel F, Burgstahler C, Cademartiri F, de Feyter P, George R, Kaufmann P, Kopp AF, Knuuti J, Ropers D, Schuijf J, Tops LF, Bax JJ. Cardiac computed tomography: indications, applications, limitations, and training requirements: report of a Writing Group deployed by the Working Group Nuclear Cardiology and Cardiac CT of the European Society of Cardiology and the European Council of Nuclear Cardiology. *Eur Heart J* 2008;**29**:531–556.
239. Corban MT, Hung OY, Eshtehardi P, Rasoul-Arzrumly E, McDaniel M, Mekonnen G, Timmins LH, Lutz J, Guyton RA, Samady H. Myocardial bridging: contemporary understanding of pathophysiology with implications for diagnostic and therapeutic strategies. *J Am Coll Cardiol* 2014;**63**:2346–2355.
240. Schwarz ER, Gupta R, Haager PK, Vom Dahl J, Klues HG, Minartz J, Uretsky BF. Myocardial bridging in absence of coronary artery disease: proposal of a new classification based on clinical-angiographic data and long-term follow-up. *Cardiology* 2009;**112**:13–21.