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RECOMMENDATION PAPER

The multi-modality cardiac imaging approach to the Athlete's heart: an expert consensus of the European Association of Cardiovascular Imaging

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The term 'athlete's heart' refers to a clinical picture characterized by a slow heart rate and enlargement of the heart. A multi-modality imaging approach to the athlete's heart aims to differentiate physiological changes due to intensive training in the athlete's heart from serious cardiac diseases with similar morphological features. Imaging assessment of the athlete's heart should begin with a thorough echocardiographic examination. Left ventricular (LV) wall thickness by echocardiography can contribute to the distinction between athlete's LV hypertrophy and hypertrophic cardiomyopathy (HCM). LV end-diastolic diameter becomes larger (>55 mm) than the normal limits only in end-stage HCM patients when the LV ejection fraction is <50%. Patients with HCM also show early impairment of LV diastolic function, whereas athletes have normal diastolic function. When echocardiography cannot provide a clear differential diagnosis, cardiac magnetic resonance (CMR) imaging should be performed. With CMR, accurate morphological and functional assessment can be made. Tissue characterization by late gadolinium enhancement may show a distinctive, non-ischaemic pattern in HCM and a variety of other myocardial conditions such as idiopathic dilated cardiomyopathy or myocarditis. The work-up of athletes with suspected coronary artery disease should start with an exercise ECG. In athletes with inconclusive exercise ECG results, exercise stress echocardiography should be considered. Nuclear cardiology techniques, coronary cardiac tomography (CCT) and/or CMR may be performed in selected cases. Owing to radiation exposure and the young age of most athletes, the use of CCT and nuclear cardiology techniques should be restricted to athletes with unclear stress echocardiography or CMR.

Keywords Athlete's heart • Left ventricular hypertrophy • Hypertrophic cardiomyopathy • Idiopathic dilated cardiomyopathy • Arrhythmogenic right ventricular cardiomyopathy • Echocardiography • Cardiac magnetic resonance • Coronary cardiac CT • Nuclear cardiology

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The approach to the athlete's heart

Definition of the athlete's heart and physiological left ventricular hypertrophy

The term 'athlete's heart' refers to a clinical picture characterized by two distinct and specific cardiac effects induced by a sustained and regular physical training programme, namely, slow heart rate (HR) and enlargement of the heart.[1,2] This is the result of haemodynamic changes corresponding to HR reduction and stroke volume (SV) increase along with the reduction in systemic vascular resistance. Further haemodynamic changes include a slight elevation of cardiac output (=SV × HR) during exercise and a more pronounced increase in blood pressure. From a physiological point of view, in the long-run haemodynamic changes during exercise lead to an increase in both left ventricular (LV) internal size (LV dilation) and LV hypertrophy (LVH) which is generated in order to normalize LV wall stress. Cardiac response to training is also influenced by additional factors including hormonal stimuli and genetic susceptibility. LV dilation and LVH may be pronounced enough to mimic a pathological state, but LV systolic and diastolic function are normal or even supranormal, a feature which is the very nature of the athlete's heart.

Of interest, in the athlete's heart ejection fraction (EF), i.e. the percentage of blood in the left ventricle at-end-diastole, which is ejected per beat, remains normal or can be even marginally reduced at rest.[3] This perhaps surprising finding can be ascribed to different factors. First of all, the formula used to calculate EF (100 × SV/LV end-diastolic volume) is designed for individuals with normal sized LV and can produce an intrinsic mathematical underestimation of LV performance in the hearts of the athletes who generally have increased LV end-diastolic volume. Furthermore, EF is an estimate of the LV chamber function and not of myocardial contractility itself: it can therefore underestimate LV ability to increase SV during strenuous exercise. Finally and more importantly, EF of the athletes increases markedly during effort when larger LV end-diastolic volume allows to best utilize the Frank–Starling mechanism (the higher preload, the more rapid diastolic filling, and the smaller LV end-systolic volume) and increase SV compared with non-athletes.[3,4] Accordingly, a truly comprehensive assessment of LV systolic function in athletes should be performed not only at rest but also during exercise with standard echocardiography, advanced ultrasound techniques and other non-invasive cardiac imaging modalities. However, despite these theoretical incentives to measure LV function and myocardial mechanics during exercise, the majority of the studies have evaluated the athlete's heart only at rest.

Differential impact of endurance and strength training on the heart (Morganroth hypothesis)

Endurance sports [dynamic (isotonic) exercise, e.g., running, walking, cycling, swimming, rowing, and skiing) imply an aerobic training in which the goal is prolonged athletic output over an extended distance or for a long period of time. *Strength training* (isometric exercise, e.g., wrestling, weightlifting) is a type of physical exercise specializing in the use of resistance to induce muscular contraction which builds the strength, anaerobic endurance, and size of skeletal muscles.

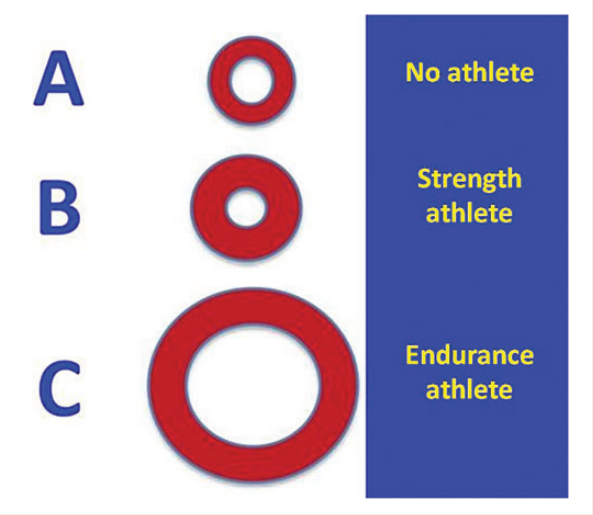

Figure 1: The 'Morganroth hypothesis'. A = no athlete, B = Strength training athlete: concentric LV hypertrophy, C = Endurance athlete: eccentric LV hypertrophy.

Morganroth *et al.*[5] hypothesized that morphological adaptations in athletes correspond with the type of haemodynamic overload imposed on the heart during exercise (*Figure 1*). Endurance training would lead, as a consequence of volume overload and increased diastolic wall stress, to eccentric LVH (LV mass increase with increased LV cavity dimension). In contrast, strength training leads, as a consequence of pressure overload and increased systolic wall stress, to concentric LVH (increased wall thickness with no change in cavity size). The 'Morganroth hypothesis' is not without its critics. Plenty of evidence supported this hypothesis for endurance training, while several studies failed to support the cardiac phenotype expected in strength training.[6] This may at least in part be explained by the fact that some sports (soccer, rugby, hockey, etc.) include both endurance and strength training programmes. Other factors include the absence of standardized measurements, some degree of inaccuracy of M-mode and 2D echocardiographic measurements and the confounding effect of the performance-enhancing substances abuse. In addition, most of the studies challenging the 'Morganroth hypothesis' are cross-sectional by design. *Figure 2* depicts two different types of echocardiographically detected LVH in an endurance athlete and in an athlete exerting mixed training, respectively. The 'Morganroth hypothesis' needs therefore to be retested in longitudinal studies, assessing well-defined exercise protocols and using standardized measurements ideally with cardiac magnetic resonance (CMR) and/or 3D echocardiography. It is noteworthy that a meta-analysis of 66 echocardiographic studies comparing 1451 athletes and 813 control subjects showed significantly larger LV diameters and greater wall thickness, with a relatively balanced LVH, in endurance as well as in strength and combined (endurance + strength) training athletes.[7]

Data from the Italian pre-participation screening programmes reported LV dilatation and LVH in large cohorts of young athletes assessed by echocardiography. LV end-diastolic diameters varied widely, but were found to be above normal in the majority of athletes, whereas LV wall thickness >12 mm was found only in a small percentage.[1] LV EF is preserved (i.e. >50%) in the most of but not in

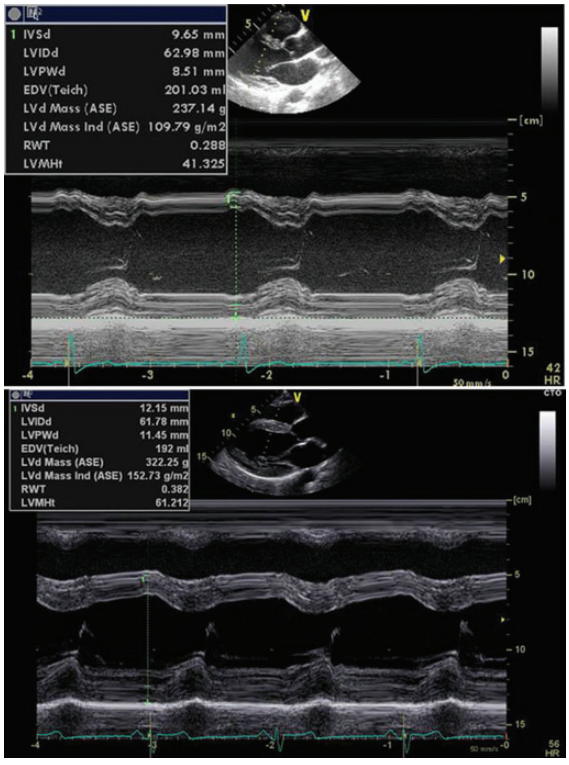

Figure 2: Different kinds of LVH in two athletes with different training patterns. LV mass index (indexation for both BSA and height powered to 2.7) defines the presence of clear-cut LVH (cut-off values in men: >115 g/m^2 or >48 g/m$^{2.7}$) whereas relative wall thickness (2 × posterior wall thickness/LV internal end-diastolic diameter) (eccentric ≤ 0.42, concentric > 0.42) (see Lang RM *et al.*[81]). The upper panel depicts an eccentric type of LV hypertrophy (LV mass increase with increased LV cavity dimension) in an endurance athlete (swimming). The cut-off point of LVH is achieved by indexing LVM for BSA not for height;[2.7] relative wall thickness defines a concentric geometry. The lower panel depicts a LVH, which is still eccentric (LV mass with increased LV cavity dimension) but also mild increased LV wall thickness) in an athlete with 'mixed' training (combined endurance and strength training in rugby). The cut-off point for LVH is achieved by indexing LV mass for both BSA and height[2.7]; relative wall thickness shows an eccentric geometry. IVSd, interventricular septal thickness in diastole; LViDd, LV internal end-diastolic diameter; LVPWD, LV posterior wall thickness in diastole; EDV, End-diastolic volume, LVd Mass (ASE); LV mass in diastole according to ASE, LVd mass index (for BSA); RWT, relative wall thickness; LVMHt, LV mass index for height.[2.7]

all endurance athletes,[8] and marginally low EF at rest does not equal LV systolic dysfunction in athletes. LV diastolic function remains also normal, independent of the training type.[9] The volume load of endurance training also influences the right ventricle, which is commonly enlarged in endurance athletes.[10]

EACVI expert consensus key points

- The original Morganroth hypothesis differentiates eccentric LVH seen in athletes performing endurance training from concentric LVH in athletes undergoing strength training.

Table 1 Most common aetiologies of sudden cardiac death in athletes

Heritability	Structurally abnormal heart	Structurally normal heart
Inherited	Cardiomyopathies	Channelopathies
	HCM	Long QT syndrome
	ARVC	Brugada syndrome
	IDCM	Cathecol-aminergic polimorphic ventricular tachycardia
	Congenital coronary anomalies	
	Bridged coronary arteries	Wolff–Parkinson–White
	Aortic diseases	
Acquired	Myocardial ischaemia	Commotio cordis
	Myocarditis	Drugs and stimulants
	Cardiac sarcoidosis	Electrolyte imbalance
	Valvular heart disease	

- The 'Morganroth hypothesis' for endurance training is well supported by evidence, while several studies failed to support the cardiac phenotype expected in strength training.

Sudden cardiac death in athletes

The cardiovascular benefits of regular exercise are established[11] and most sports activities are presumed to be good for health. The effects of competitive sports and vigorous exercise training and longevity are, however, uncertain.[12,13] Excessive training should, therefore, not be regarded as a negligible risk. Although sudden cardiac death (SCD) in athletes is rare, sport activity in adolescent and young athletes is associated with an increased risk of SCD, which has a variable incidence (0.5–2.3 per 100 000 person-years) and is more common in males.[14–16] However, incidence and numbers might be underestimated. The aetiology of SCD in athletes <35 years is mostly inherited and caused by structural heart disease, such as hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC). In contrast, in athletes >35 years the vast majority of SCD is a consequence of acquired disease, in particular coronary artery disease (CAD).[17] *Table 1* shows an overview of the most common aetiologies of SCD. More widespread use of genetic analysis following autopsies now allows to reveal previously undiscovered causes of SCD at ordinary autopsies.[18,19]

EACVI expert consensus key points:

- Intense sport activity in adolescent and young athletes is associated with an increased risk of SCD, which has an incidence ranging between 0.5 and 2.3 per 100 000 person-years and is more common in males. However, incidence and numbers might be underestimated.
- The aetiology of SCD in athletes <35 years is mostly inherited, it being due to structural heart disease (mainly HCM and ARVC). In contrast, the vast majority of SCD in athletes >35 years is a consequence of acquired disease, in particular CAD.

Cardiovascular effects of performance-enhancing substances

The use of performance enhancing, illicit substances is an important problem not only in competitive athletes.[20] The list of drugs which are banned is annually updated by the World Anti-Doping Agency and includes anabolic agents and corticosteroids, peptide hormones, growth factors and erythropoietin, β-2 agonists, hormone and metabolic modulators, diuretics and masking agents, stimulants (amphetamine, cocaine), and cannabinoids. The majority of these drugs interfere with training induced adrenergic hyperactivation and may lead to unfavourable effects, such as arrhythmias, CAD, myocarditis, pericarditis, heart failure, and SCD.

Drugs increasing lean muscle mass and enhancing performance include testosterone and anabolic androgenic steroids. They stimulate cellular protein synthesis through adrenergic receptors and promote the growth of all organs, including the heart, which have receptors similar to those of androgens. Their cardiac effects can include the development of myocardial fibrosis[21] and blunt the deconditioning effect on LVH usually observed in athletes, thus misleading to the diagnosis of HCM. Accordingly, echocardiography shows alterations of LV diastolic function,[22] which are typically not present in athletes who do not use steroids. Reduction of EF by both standard echo[23] and CMR[24] as well as reduction of myocardial strain by both Doppler-derived strain rate imaging[25] and speckle tracking echocardiography (STE)[26] have been also observed in steroids users.

Non-steroid agents producing anabolic effects include β-2 agonist, clenbuterol (used also to reduce body fat), human growth hormone and insulin/insulin-like growth factors, human chorionic gonadotropin, erythropoietin, and selective androgen receptor modulators. Although it is well known that the chronic use of these drugs can induce LVH and LV diastolic dysfunction,[27] their effects in competitive athletes is poorly investigated by cardiac imaging. All stimulants structurally related to amphetamine can cause catecholamine-mediated cardiotoxicity (vasospasm, vasoconstriction, tachycardia, arterial hypertension). As a consequence, the heart is compromised resulting in LVH, myocardial fibrosis, and necrosis.[27] The use of cocaine is associated with acute and/or chronic cardiac disease, but it may also induce regional wall motion abnormalities mimicking premature CAD, aortic dissection, vasculitis, and stroke.[28,29]

Generally, screening of athletes by cardiac imaging can raise suspicion about this kind of cardiotoxicity (*Table 2*) but cannot reliably unmask the cardiotoxic effects of banned substances. This lack of reliability is also related to the fact that the use of these drugs is often characterized by periods of abuse and intervals of abstinence in order to maximize their performance-enhancing effects while limiting the negative cardiac consequences. Furthermore, additional drugs can be used to limit side effects and mask the doping effects. However, the combination of LVH with diastolic dysfunction and/or subclinical alteration of systolic function may raise suspicion of a doping effect on the heart when other primary pathologies, mainly HCM and arterial hypertension, have been excluded. In this context, CMR can provide further information about the presence of myocardial fibrosis as a main determinant of diastolic dysfunction but cannot be considered conclusive.

Table 2 Power of cardiac imaging for suspected diagnosis performance-enhancing substances involvement

Prohibited substances	Cardiac effect	Demonstration by cardiac imaging
Anabolic androgenic substances	LVH, LV diastolic dysfunction, reduction of EF, reduction of longitudinal strain	+++
Non-steroids anabolic agents (B2 agonists, peptide hormones, growth factors, recombinant human erythropoietin)	LVH, LV diastolic dysfunction	+
Stimulants (amphetamines, methamphetamine and cocaine)	Acute and chronic CAD, Aortic dissection	++

+++, largely demonstrated; ++, well demonstrated; +, poorly demonstrated.

EACVI expert consensus key points:

- Drugs increasing lean muscle mass and enhancing performance as well as non-steroid agents producing anabolic effects may induce myocardial fibrosis, which is consistent with LVH and alterations of LV diastolic function.
- The use of cocaine is associated with acute and chronic cardiac disease but may also induce regional wall motion abnormalities suggestive of premature CAD.
- Cardiac imaging cannot prove or rule out illicit substance abuse. However, the combination of clear-cut LVH with diastolic dysfunction and/or subclinical alteration of systolic function may raise the suspicion of illicit substance abuse when other primary pathologies (HCM or arterial hypertension) are excluded. CMR can provide additional information about the presence of myocardial fibrosis but cannot be considered always conclusive.

The assessment of anatomy and function

Differential diagnosis of athlete's heart from pathological remodelling of the left ventricle

The role of echocardiography

Standard echocardiography has a pivotal role in differentiating physiological and pathological LVH. In a series of 1309 athletes of different disciplines, 55% had increased LV end-diastolic diameter and only 15% of the endurance athletes demonstrated values >60 mm, always in the presence of a normal EF.[2,6] However, in a study of Abergel *et al.*[3] the majority of elite cyclists had LV end-diastolic diameter >60 mm. Cardiac size should be therefore considered in the

context of exercise capacity given its robust association with VO_2 max.[30] A LV end-diastolic diameter >60 mm should therefore raise the suspicion of an idiopathic dilated cardiomyopathy (IDCM) when the LV dilation is out of proportion to the athlete's conditioning. In 947 elite athletes, maximal end-diastolic septal wall thickness was ≤12 mm in most. Only 1.7% had septal thickness >13 mm (range = 13–16 mm).[31] Septal thickness was lower in women (average = 9 mm, upper limits = 12 mm) compared with men of the same age and body size.[31] Moreover, LV remodelling in Afro-caribbean athletes is characterized by similar cavity size but a disproportionate wall thickening compared with Caucasians.[32] In athletes LVH involves equally the septal and the other LV walls. Conversely, in HCM increased wall thickness (>15 mm) involves mainly the basal septum, and in 20% of HCM cases is associated with additional features, i.e. systolic anterior motion (SAM) of the mitral valve or aortic valve mid-systolic closure.[33] After cessation of exercise training ('physical deconditioning') for about 3 months a reduction of maximum septal wall thickness (of about 15–33%) can be observed in healthy athletes,[34] whereas the reduction involving both septal thickness (by 15%) and LV cavity dimension (by 7%) occurs after 1–13 years of training cessation.[35] However, In 20% of the athletes increased LV end-diastolic diameter was persistent even after an average of 5 years of inactivity, despite normal LV function and no occurrence of adverse cardiac events.[36] Conversely, reverse LV remodelling (both LV wall thickness and LV cavity dilation) does not occur in pathological LVH. Likewise, LVH related to anabolic substance abuse is typically not reversible even after 12 months of deconditioning.[37]

In athletes, LV mass increase is usually combined with normal EF at rest, whereas SV is normal or even augmented, as a result of increased preload (LV end-diastolic volume).[1,5,37–39] Pulsed tissue Doppler provides additional information for a comprehensive assessment of functional properties of the athlete's heart showing normal[37] or supranormal[40,41] myocardial systolic performance at rest. Accordingly, a cut-off value <9 cm/s of systolic peak velocity (s′, average of four mitral annular sites) demonstrated 87% sensitivity and 97% specificity in distinguishing pathological LVH (arterial hypertension or HCM) from athlete's LVH.[42]

Also LV diastolic function at rest can appear normal but is often supranormal when compared with no trained individuals, in particular in endurance-trained athletes.[37,43] Typically, the transmitral E/A ratio is >2 in athletes (*Figure 3*). This feature helps to distinguish physiological from pathological LVH, which is characterized by an

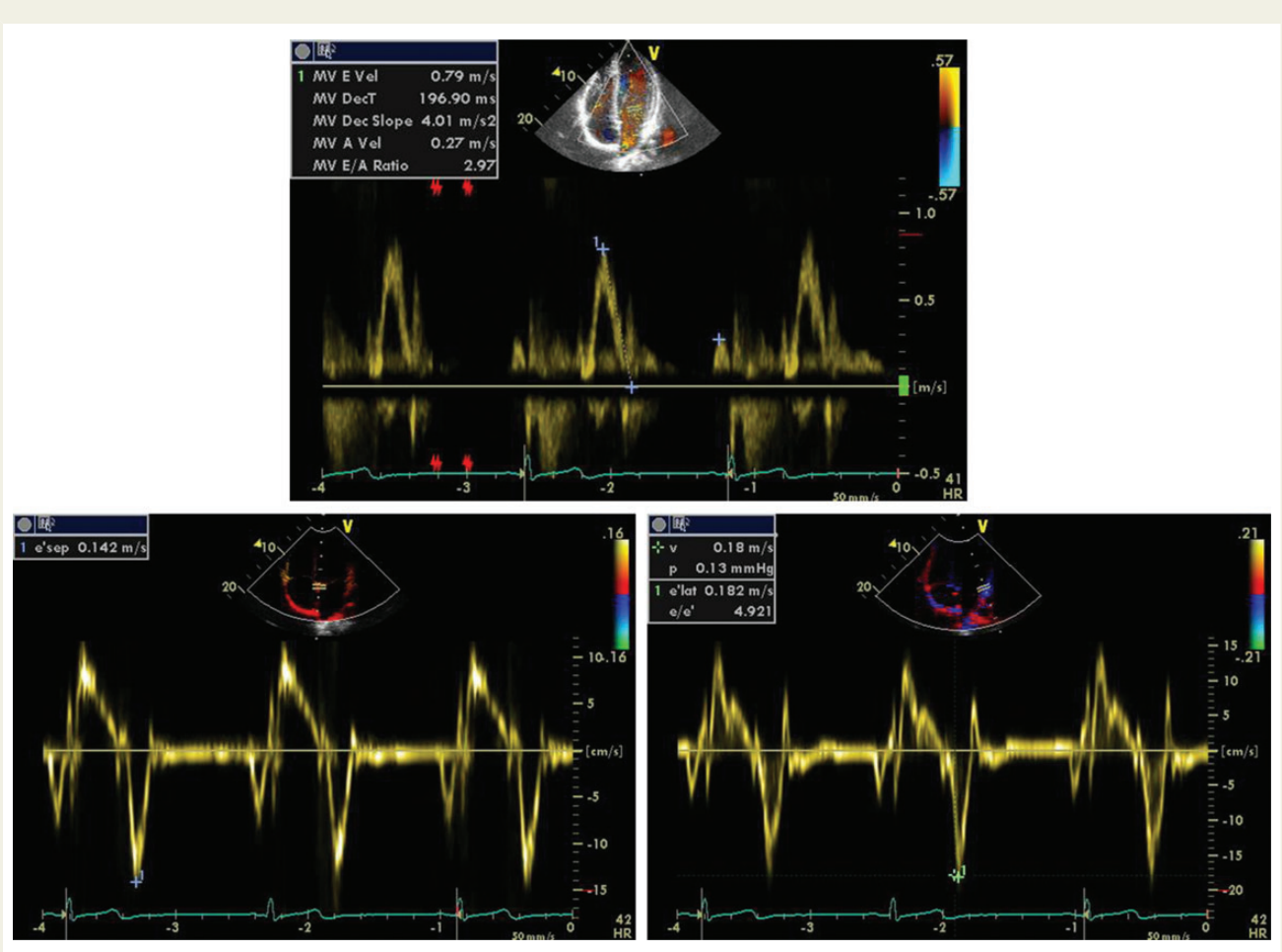

Figure 3: Supranormal LV diastolic function in a competitive runner. In the upper panel, standard Doppler-derived transmitral patterns shows an E/A ratio = 2.97. In the lower panel, pulsed tissue Doppler-derived e′ velocity is very high at both septal (left) and lateral mitral annulus (right) and E/e′ ratio (= 4.9) is consistent with a normal diastolic function.

Table 3 Key echocardiographic measurements to be measured in athletes

Left ventricle	Right ventricle
LV mass index (g/m^2)	RV free wall (mm)
LV end-diastolic volume (mL)	RV basal diameter (mm)
Septal wall thickness (mm)	RV base to apex diameter (mm)
LV EF (%)	TAPSE (mm)
LV SV (mL)	IVC size (mm)
LV CO (L/min)	IVC respiratory reactivity (%)
Transmitral E/A ratio	
E velocity deceleration time (ms)	
Annular s′ velocity (ms)	
Annular e′ velocity (cm/s)	
E/e′ ratio	
e′/a′ ratio	

A, transmitral atrial velocity; a′, annular atrial velocity (pulsed tissue Doppler); CO, cardiac output; E, transmitral early-diastolic velocity; e′, annular early-diastolic velocity (pulsed tissue Doppler); EF, = ejection fraction; IVC, inferior vena cava; LV, left ventricular. RV, right ventricular; s′, annular systolic velocity (pulsed tissue Doppler) TAPSE, tricuspid annular plane systolic excursion.

E/A ratio <1 and a prolonged E velocity deceleration time. Pulsed tissue Doppler-derived early-diastolic myocardial velocity (e′) (*Figure 3*) and e′/a′ ratio of basal septal and basal lateral wall were found to be increased in athletes.[6,44] Of interest, e′ velocity of the LV inferior wall was positively correlated with LV end-diastolic diameter in endurance athletes since the predominant pre-load increase of isotonic training induces a proportional improvement of myocardial relaxation.[9] Conversely, in patients with HCM, e′ velocity reduction occurred in both the hypertrophic septum and the normal thickness of lateral wall.[45] Regional diastolic dysfunction (e′/a′ <1) was detected in 25% of the myocardial segments of HCM patients (including the non-hypertrophic walls) but was not present in any segments of athletes.[46] Also in hypertensive patients a reduction of the septal e′/a′ ratio was observed, in particular in those with clear-cut LVH.[47] Increased E/e′ ratio at rest was found to correlate with NYHA class and exercise capacity in HCM patients,[48] whereas it was found to be normal in athletes.[39] However, there are few descriptions of athletes with pathology and we cannot assume that athletes with cardiomyopathies will exhibit the typical pathological features seen in non-athletes with cardiomyopathies. *Table 3* summarizes LV key parameters, which should be measured by standard echo Doppler examination in the athletes.

Advanced echocardiographic technologies have been used to characterize the athlete's heart and to distinguish physiological and pathological LVH. Some studies analysed athlete's heart by STE.[49–52] One of these studies found a slight reduction in global longitudinal strain (GLS) at rest that was compensated by an increase of radial and circumferential strain in professional soccer players.[48] Lower apical radial strain and lower LV twisting at rest were also observed in cyclists than in sedentary controls.[49] These reports suggest LV adaptation of athletes at rest and also highlight the load dependency of strain measurement. Athlete's heart is in fact a very interesting model of strain variation at loading conditions. In another study a significant reduction of systolic and diastolic strain and strain rate was found in hypertensives—but not in athletes—with clear-cut LVH in comparison with normal sedentary controls.[51] An e′/a′ ratio >1 was found in 100% of a large population of competitive athletes, 90% of subjects had e′ ≥16 cm/s, s′ ≥10 cm/s, and GLS ≤−16%.[51] GLS was also found to be lower in 18 hypertensive patients (−17.5 ± 2.8%) than in 22 elite rowers (−22.2 ± 2.7%) and in 19 sedentary controls (−21.1 ± 2.0%) ($P < 0.0001$).[53] In a study comparing soccer players with HCM patients, radial strain—but not longitudinal strain or pulsed tissue Doppler-derived annular systolic velocities—differentiated the two groups.[54] Very recently, the combination of 2D STE and 3D volumetric assessment allowed identifying different LV remodelling patterns in endurance-trained (increased LV twisting), strength-trained, and mixed-trained athletes.[55] Albeit promising and useful to gain physiological information on the athlete's heart, the experience with STE is still preliminary and does not yet support its routine use for the differential diagnosis of athlete's heart from pathologic LVH.

EACVI expert consensus key points:

- Standard echocardiography is the first-line exam for differentiating athlete's heart from pathologic LVH.
- In elite athletes the LV end-diastolic diameter is not frequently increased >60 mm. A LV end-diastolic diameter >60 mm—when combined with reduced EF and abnormal diastolic function—should raise suspicion of IDCM.
- In elite athletes LVH involves typically all myocardial segments and the maximal septal thickness is usually ≤12 mm. Septal wall thickness is lower in female athletes and more pronounced in African than in Caucasian athletes.
- In HCM increased wall thickness (>15 mm) involves mainly the basal septum and in 20% of HCM cases is associated with additional features, such as SAM or aortic valve mid-systolic closure.
- After physical deconditioning of three months, a reduction of LV wall thickness can be observed in athletes but not in HCM.
- In athletes LVH is combined with normal EF, normal, or even increased SV and s′ velocity >9 cm/s, whereas s′ is <9 cm/s in HCM. EF is normal or high in early stages and possibly reduced in advanced stages of HCM.
- LV diastolic function is often supranormal in athletes (E/A ratio >2, increased e′ velocity, low E/e′ ratio). In the HCM E/A ratio is <1, E velocity deceleration time is prolonged, e′ velocity and e′/a′ ratio are low. However, normal LV diastolic filling pattern does not exclude pathological LVH.

The role of CMR

LV and RV volumes and mass as well as global and regional contractile function can be accurately assessed with steady state free precession (SSFP) cine CMR.[56–58] The excellent inter-study reproducibility of cine CMR can be relevant when assessing not only the features of the athlete's heart but also individual changes, such as reduction of LV wall thickness following training cessation. Quantification of LV contraction and relaxation through measurements of myocardial strain and strain-rate can be obtained by CMR tagging, but recently introduced CMR feature of tissue tracking techniques allows derivation of such parameters also from routine SSFP cine images.[59,60] Contrast enhanced CMR, using the late gadolinium enhancement (LGE) imaging, enables differentiation of ischaemic from non-ischaemic patterns of myocardial damage.[61,62] Non-ischaemic

patterns of myocardial damage include a subendocardial ring of enhancement (myocardial amyloid), patchy enhancement (HCM), or mid-myocardial and epicardial hyper-enhancement (myocarditis or Anderson Fabry's disease).[63] A more recent and promising CMR methodology, T1 mapping, provides the assessment of diffuse myocardial fibrosis either using native T1 values or through quantification of the extracellular volume from pre- and post-contrast T1 mapping, which cannot be visualized using LGE.[64] This may further increase the diagnostic accuracy to identify pathological LVH.

Cine CMR was used to differentiate athlete's heart from pathological LVH using multiple geometric measures.[65] Twenty-eight normal controls, 25 elite athletes, 35 patients with HCM, 18 hypertensive patients, and 24 patients with LVH due to aortic valve stenosis were assessed. LV diastolic wall to volume ratio, which corresponds substantially to echocardiographic derived relative wall thicknesses, had the highest area under the curve (0.993) providing a sensitivity of 80% and a specificity of 99% to distinguish athlete' heart (<0.15 mm $\times$ m^2/mL) from all forms of pathologic LVH. No false-positives and false-negatives were identified when differentiating athlete's hearts from pathological LVH using a multivariate logistic regression model with multiple geometric measures. Single or combined geometric measures using CMR were not able to differentiate various other forms of pathological LVH such as HCM or that due to arterial hypertension. The potential advantage of CMR over echocardiography was also demonstrated.[66] Compared to the reference CMR, echocardiography missed LVH in 6% of cases with suspected HCM and underestimated the maximal LV end-diastolic wall thickness by 20%; echocardiography also failed to document LV end-diastolic wall thickness $>$ 30 mm in 10% of cases. In subjects with abnormal ECGs but normal or borderline echocardiogram, CMR was able to identify patients with HCM and apical HCM (wall thickness $>$ 28 mm).[67] LGE derived non-ischaemic pattern was described in multiple studies of HCM.[68–70] Of interest, a small prevalence of LGE was demonstrated even in non-hypertrophied myocardial segments.[71,72] *Figure 4* shows a CMR image in an endurance athlete which facilitated a diagnosis of HCM, with LGE in the hypertrophied septum indicating regional fibrosis. This suggests that LGE increases the diagnostic accuracy over and above the geometric measures that one can provide and determine using CMR cines itself, but LGE absence cannot rule out HCM. On the other hand, LGE can be seen in athletes without evidence of HCM.[73] T1 mapping might be of potential use to distinguish athlete's heart from pathologic LVH but has never been systematically investigated for this differential diagnosis.

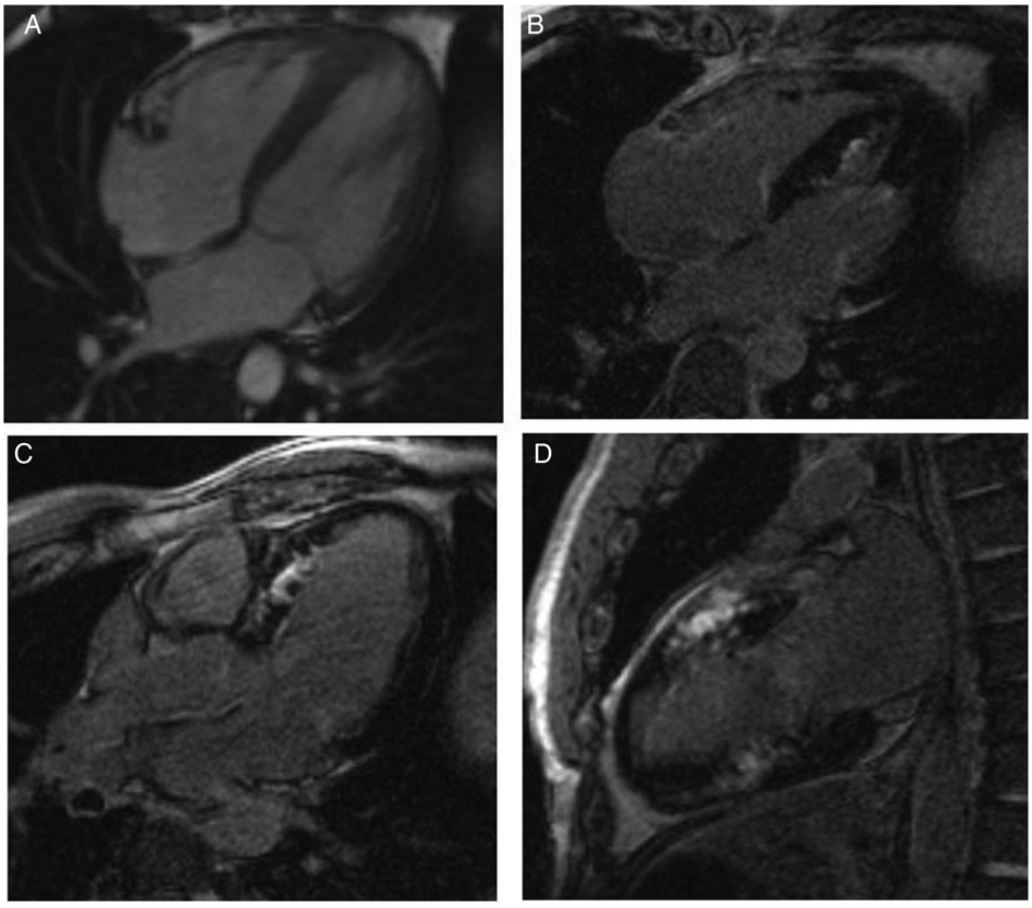

Figure 4: Diagnosis of HCM in a 41-year old male endurance athlete by CMR. (*A*) The left ventricle is enlarged (LV end-diastolic diameter = 58 mm), septal thickness is 15 mm. (*B–D*). LGE revealed myocardial fibrosis of anterior and inferior septum. Genetic analysis confirmed the diagnosis of HCM.

CMR can help to differentiate also athlete's heart from IDCM not only by providing high image quality and accurate measurements of volumes and EF of both ventricles, but also by using LGE which demonstrates mid-myocardial streaks in about one-third of subjects.[62,74,75] However, the absence of LGE cannot rule out IDCM.

Expert consensus key points:

- CMR is superior to echocardiography in differentiating athlete's heart from structural and functional changes which are related with HCM (80% sensitivity and 90% specificity of cine CMR derived LV diastolic wall to volume ratio < 0.15 mm $\times$ m^2/mL in athlete's LVH).
- LGE may provide additional diagnostic information beyond geometric measures obtained by simple cine CMR in order to differentiate athlete's heart from HCM.
- CMR can be helpful to distinguish athlete's heart from IDCM not only because of more accurate measurements of volumes and EF compared with echocardiography, but also due to additional information provided by LGE.
- The absence of LGE does not rule out HCM or IDCM.

Left atrial size and sport practice: implications for normal ranges

Left atrial (LA) enlargement (*Figure 5*) is common in large cohorts of athletes,[76,77] because of LA pressure increase during exercise. Whether increased LA size could be one potential determinant of atrial fibrillation in athletes remains controversial.[78–80]

By using standardized methods, echocardiography allows identification of LA enlargement.[81] The 2D LA volume method (area-length method or modified Simpson) is preferable to the linear LA antero-posterior diameter. LA size should be indexed for the body surface area (LA volume index = LAVi).[82,83] Current ASE/EAE recommendations on LV diastolic function indicate a cut-off point of $\geq$34 mL/m^2 of 2D LAVi for establishing LA enlargement.[84] Demographic and anthropometric factors (e.g., ethnicity) are recognized determinants of LAVi, whereas the role of ageing remains debated.[85,86] Data from the large sample size ($n = 734$) of the NORRE study point out that age and gender do not influence 2D LAVi in normal subjects.[87]

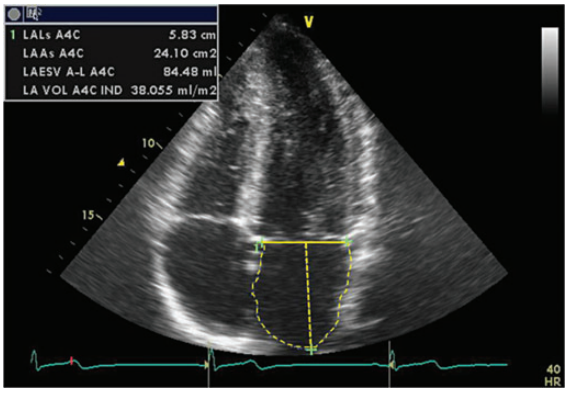

Figure 5: Left atrial dilation in an endurance athlete (rower). The current ASE/EAE recommendations on LV diastolic function indicates a cut-off point $\geq$34 mL/m^2 to define LA enlargement (see Nagueh SF *et al.*[83]). Accordingly, LA volume index = 38.055 mL/m^2 of this rower is consistent with LA enlargement. However, the development of athlete-specific normalcy criteria, ideally partitioned according to gender and sport activity, could help avoid labelling such left atrial dilation as pathological. LALs 4Ac, LA longitudinal diameter in apical four-chamber view; LAAs A4c, LA area; LAESV A-L A4C, LA end-systolic volume; LA Vol IND, LA volume index.

Prevalence of LA enlargement in competitive athletes were firstly reported by Pelliccia *et al.* who found a mild increase of LA antero-posterior diameter ($\geq$40 mm) in 18% of athletes, a marked dilatation ($\geq$45 mm) in 2%, and a close association between LA diameter and LV cavity dimension.[76] LA enlargement appeared to be influenced by the type of sport (greatest impact of sports which combines endurance and strength training). Upper limits of LA diameters (45 mm in women, 50 mm in men) were defined in athletes. *Figure 6* summarizes the data from two different studies that can be used to justify different normal ranges for LA size in athletes than in the normal population. The first study provided reference values and relative impact of different sport activities and found LA enlargement (LAVi $\geq$34 mL/m^2) in 3.2% of the athletes.[77] The key independent determinants of LAVi were training type and duration and LV end-diastolic volume. The second study compared prospectively LAVi determinants in healthy sedentary individuals and competitive athletes over a wide age range[87]: LAVi above 34 mL/m^2 was found in some healthy controls but it was evident in 67% of athletes. Of note, the ECG findings of isolated axis deviation or LA enlargement in 579 of 2533 athletes (22.9%) does not predict major structural or functional abnormalities at the echocardiographic evaluation.[88] The utilization of specific normal ranges (e.g. 95th percentile) of echocardiographic measured LAVi, ideally categorized by type of sport activity, could therefore help to avoid calling the findings of larger LA size in athletes as abnormal.

STE-derived LA strain has been used to assess LA function, which is enhanced in athletes[89] and impaired in HCM patients.[90] However, it would be premature to currently recommend its clinical use for the assessment of the athlete's heart. Since echocardiography shows a trend to underestimate LA volumes, CMR can be an attractive alternative imaging modality.[82,91] A very recent study demonstrated that both LA and right atrial (RA) volumes, despite being larger in athletes, did not differ from controls after normalization for total heart volume. Of interest, LA volumes were marginally lower in female athletes.[92]

Expert consensus key points:

- Upper limits of LA antero-posterior diameter (45 mm in women, 50 mm in men) have been defined in athletes.
- Although LAVi is preferred over LA antero-posterior diameter as measure of LA size, currently normal ranges have not been defined for LAVi in athletes. The normal range for sedentary healthy controls (34 mL/m^2) leads to frequent misclassification of dilated LA cavities in athletes.
- There is a need to develop normal ranges for LAVi in athletes and these should ideally be specific for gender and type of sport.
- Since echocardiography shows a trend to underestimate LA volumes, CMR can be an attractive alternative imaging modality and has confirmed less pronounced LA remodelling in female than in male athletes.

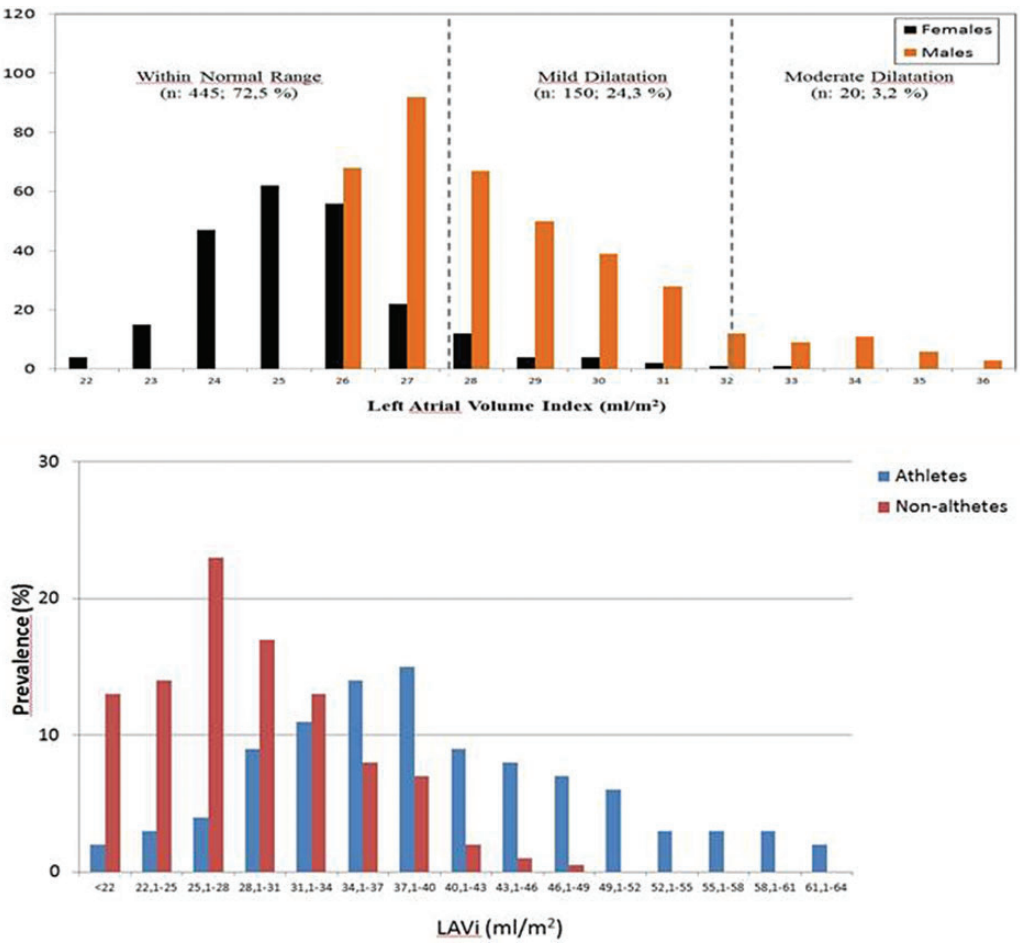

Figure 6: Distribution of LA volume index in athletes. In the upper panel distribution of LAVi in a population of 615 athletes (D'Andrea *et al.*[77]). In the lower panel distribution of LAVi in 158 athletes in comparison with 260 non-athletes (Nistri *et al.*[86]). Combined together these two studies demonstrate that LAVi measurements should be considered in conjunction with the athletic state of individual subjects.

RV chambers and function

Training activity has a well-known impact on the right heart chambers, which react to increased blood volume with both RV and RA dilation (*Figure 7*). Mild functional tricuspid regurgitation and dilation of the inferior vena cava, but with preserved respiratory reactivity (*Figure 7*), are also common. Once more than mild tricuspid regurgitation is present, a structural heart disease should be sought for an athlete. While the potential for concentric RV remodelling in athletes is less clear, eccentric RV remodelling is common in athletes.[93] The upper limits of RV and RA dimensions were derived from a cohort of 650 elite athletes using echocardiography. RV and RA dimensions appeared to be greater in elite endurance-trained athletes than in age- and sex-matched strength-trained athletes and sedentary controls.[94] Another echocardiographic study demonstrated a trend towards thicker RV free walls and larger RV cavities in 127 male elite endurance athletes.[95] Also, the inferior vena cava appeared to be dilated (average value = 26 mm, upper limit = 40 mm) in a study involving 58 endurance athletes.[96] Other reports confirmed these observations using CMR and suggested a balanced RV and LV enlargement with a similar balanced increase in RV and LV mass.[97,98] Controversial findings are available on the impact of strength training on the right ventricle. RV dilation coupled with enhanced systolic and diastolic function was observed in 40 endurance athletes but not in 24 strength-trained athletes, these results being possibly due to underpowered sample size of the second group of athletes.[99] In a recent systematic meta-analysis study of training mode, RV dilatation was greater in the endurance group than in controls but regression models demonstrated positive and significant associations between body surface area and RV parameters.[100] These results highlight the need of indexing RV parameters for the body surface area in athletes.

Standard echocardiography is the initial imaging modality of choice for RV assessment in athletes.[101] Normal values of RV wall thickness are <0.5 cm, as measured from the sub-costal or parasternal long-axis views.[81] Using M-mode or 2D imaging, RV-free wall thickness should be measured at end-diastole at the level of the tricuspid valve chords. The combination of multiple views permits to obtain more information with an entire assessment of the areas of increased wall thickness.[81] RV enlargement should be identified by measuring at least the RV basal diameter and RV base to apex diameter in the apical

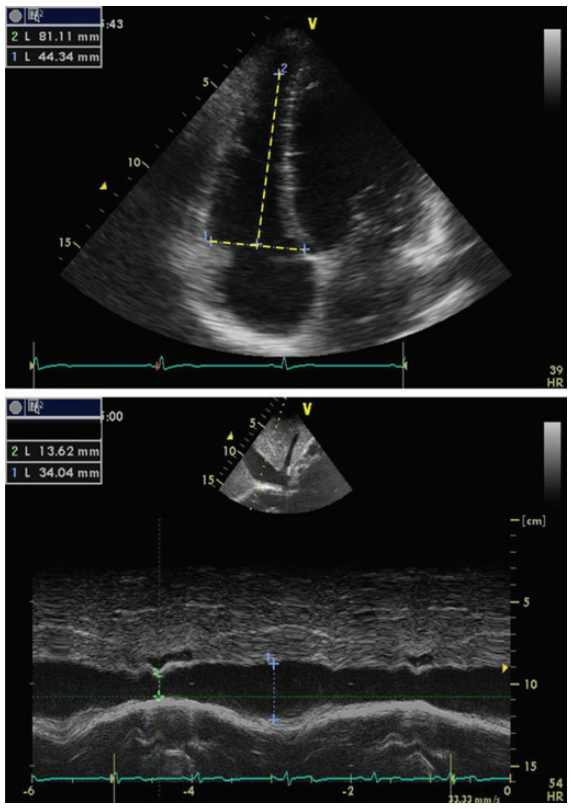

Figure 7: Right ventricular enlargement and inferior vena cava dilation in an endurance athlete**.** Upper panel: The apical four-chamber view shows increase of both RV basal diameter (1 = 33.34 mm) and of RV base-to-apex length diameter 2 = 81.11 mm). References normal values (RV basal diameter = 20–28 mm, RV base-to-apex length diameter = 71–79 mm) from Lang *et al.*[81]). Lower panel: M-mode recording inferior vena cava. 1 Maximal diameter = 34.04 mm, 2 minimal diameter = 13.62 mm. In athletes, inferior vena cava dilation is typically associated with extremely good respiratory reactivity.

four-chamber view.[81] Typical RV features of the athlete's heart (particularly in endurance athletes such as cycling, rowing, and canoeing)[1] can resemble those found in ARVC, which can be suspected in athletes with palpitations and/or arrhythmias. In ARVC the enlargement of RV cavity involves both inflow and outflow and may be associated with regional RV wall segmental morphological (thinning, bulging, and aneurysms) and functional (regional wall motion) abnormalities.[102–104] While in ARVC the left ventricle may also be affected (i.e. regional wall motion abnormalities or LV dilatation), in athletes RV cavity enlargement involves particularly RV inflow tract, is almost always associated with LV enlargement ('balanced enlargement') but RV systolic function—which can be echocardiographically detected by tricuspid annular plane systolic excursion, TAPSE is typically normal or even supranormal. *Table 3* summarizes RV key parameters, which should be measured by the standard echo Doppler examination in the athletes.

Among the advanced ultrasound technologies, 3D echocardiography showed greater RV end-diastolic volumes and RV EF in 430 elite endurance-trained athletes compared with 250 sedentary controls.[105] By combining 3D echo and 2D STE of the right ventricle, it appears that RV preload exerts its maximal influence on the lateral longitudinal fibres (RV lateral longitudinal strain). This may contribute to RV supranormal function in the athlete's heart, as the findings had been adjusted for potential confounders.[106]

In subjects with suboptimal echocardiographic images, CMR is the reference standard for the assessment RV myocardial thickness and chamber volumes, and offers high spatial and temporal resolution.[107–110] CMR is also able to identify RV myocardial muscle bands, such as the crista supraventricularis, which can be incorrectly included in the measurements of maximal LV wall thickness on echocardiographic assessment.[110] If the diagnosis of AVRC is suspected in athletes, CMR should always be requested. Although the ARVC diagnostic criteria were not developed for the subgroup of athletes, they highlight the importance of RV wall motion abnormalities, RV size, and function.[111,112] CMR evidence for fibro-fatty myocardial replacement in both RV and LV is not currently considered a diagnostic criterion for ARVC.[111,112] It also needs to be considered that cardiac imaging, whether by echocardiography or CMR, cannot confirm or exclude a diagnosis of ARVC on its own and clinical features need to be considered. A possible effect of exercise in accelerating the development of ARVC in athletes who are genetically predisposed should also be taken into account.[113,114]

EACVI expert consensus key points:

- Standard echocardiography is the first line cardiac imaging exam for differentiating RV remodelling in athlete's heart from pathologic right ventricles.
- Eccentric RV remodelling is common in athletes while the occurrence of concentric RV remodelling is unclear.
- A differential diagnosis of ARVC in athletes should be investigated with echocardiography and CMR. Neither imaging modality may confirm or exclude the diagnosis of ARVC, which remains a clinical diagnosis. RV dilatation and reduction in RV systolic function in the absence of LV remodelling should raise suspicion that this cannot be solely due to exercise training.

The detection of myocardial ischaemia and delineation of coronary anatomy in athletes

Cardiovascular disease is reported as one of the main causes of SCD in athletes, due to CAD in older or congenital coronary artery anomalies in younger athletes. At present, there is a broad range of screening recommendations for the diagnosis of myocardial ischaemia in athletes with important variations between countries, type of sport and competition level.[115] In 2007, the AHA suggested that a medical supervised exercise ECG testing should be performed only in competitive male athletes older than 40 years (or women older than 55 years) and at least two additional cardiovascular risk factors or in persons with a markedly abnormal single risk factor.[116] In 2011, the sections of Exercise Physiology and Sports Cardiology of the European Association of Cardiovascular Prevention and Rehabilitation stated that maximal exercise testing should be restricted to high-risk persons with at least moderate

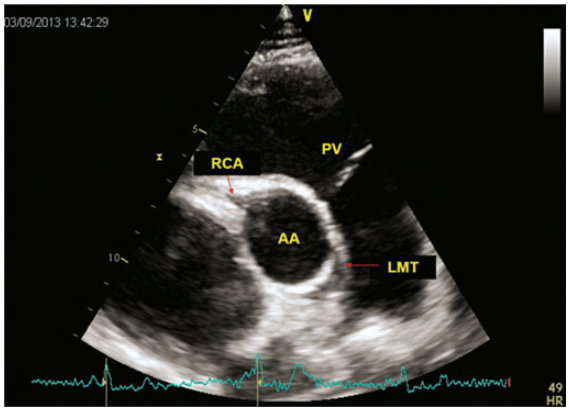

Figure 8: Echocardiographic assessment of coronary origin in an elite basketball player (red arrows), in a modified parasternal short-axis view. This kind of imaging requires an experienced operator and good image quality to confidently identify the ostia and proximal course of the coronary circulation. RCA, right coronary artery; LMT, left main trunk; PV, pulmonary valve; AA, ascending aorta.

intensity activity.[117] While much recent debate has focused on the efficacy of screening with ECG, current evidence suggests that the incremental cost-effectiveness ratio of cardiac imaging modalities is too high (above country-specific willingness-to-pay thresholds) in the context of a low prevalence of disease to justify their large use as primary screening modalities in athletes.[118]

Echocardiography

Systematic and accurate exploration of proximal coronary arteries may be useful in identifying athletes with anomalous coronary origin. Coronary ostia can be visualized in 90–92% of athletes using echocardiography (*Figure 8*) and identification of anomalous ostia is highly specific.[119] However, the sensitivity of echocardiography in detecting congenital coronary anomalies has never been reported.

Stress echocardiography

Exercise stress echocardiography is a low cost, widely available, feasible, and safe technique, better accepted than pharmacological stress echocardiography by athletes. It gives information about cardiac function, reserve, exercise capacity, and arrhythmias. CAD may be diagnosed by exercise stress echocardiography with moderate sensitivity and specificity (about 76 and 88%, respectively), comparing favourably with other stress-testing methods.[120,121] However, in athletes with anomalous implantation of coronary artery, the exercise stress echo can be normal (absence of inducible ischaemia), but this does not change the risk of SCD in such patients. Exercise stress echo is also of particular interest in atheletes with EF <45–50% at rest to test if there is contractile reserve (=EF increase) during exercise. A considerable EF increase suggests low EF at rest to be related to low preload, and not to LV systolic dysfunction.

Using adenosine stress echocardiography in endurance athletes, a supernormal coronary flow reserve (5.9 ± 1.0 vs. 3.7 ± 0.7 in controls, $P < 0.01$) in the distal left anterior descending coronary artery was observed. The hyperaemic flow velocities were higher, whereas resting flow velocities were lower than in controls.[122]

Cardiac nuclear imaging

Very limited data exist on the use of myocardial perfusion imaging (MPI) in asymptomatic athletes. Non-attenuation-corrected ^{99}mTc-sestamibi SPECT imaging was used to evaluate 18 young male elite athletes and myocardial perfusion defects were observed in areas with LVH, reducing the specificity of SPECT in the athlete's setting.[123] In another study, resting thallium-201 myocardial perfusion defects were common in young male endurance athletes but were not associated with echocardiographically detected LV wall motion abnormalities.[124] Using positron emission tomography (PET) and measuring myocardial blood flow, oxygen consumption and free fatty acid uptake with [^{15}O]H_2O, [^{15}O]O_2, and [^{18}F]FTHA during euglycaemic hyperinsulinaemia,[125] myocardial oxygen consumption, and blood flow per unit mass of the myocardium were found to be reduced in endurance athletes compared with sedentary subjects. This can be explained by reduced energy requirements due to anatomical and physiological changes of the athlete's heart as an adaptation to endurance training. Myocardial fatty acid uptake was not significantly changed during insulin stimulation. By assessing myocardial metabolism using [^{18}F]FDG PET,[126] the rate of glucose uptake per unit mass of the myocardium was similarly decreased in endurance athletes and weightlifters with an increased LV mass compared with sedentary men (*Figure 9*). Prolonged exercise training may also alter the cardiac sympathetic function, which can be detected by MIBG imaging. One study examined the ratio of heart/mediastinum count (H/M) and the washout rates of ^{123}I-MIBG in athletes and normal controls. There was a significant decrease in ^{123}I-MIBG myocardial uptake in athletes, as well as an increased washout rate.[127] Another study showed severely reduced myocardial MIBG uptake of the inferior region in athletes with sinus bradycardia, suggesting selective inferior myocardial wall sympathetic denervation, which may be related to increased vagal tone and athlete's bradycardia.[128] The magnitude to which this is a physiological or pathological change and whether it could have prognostic implications needs to be clarified. Taken together all these studies show that cardiac nuclear imaging in the athlete's setting is more suitable for research purposes than for a clinical application and should not be recommended as a first line test in competitive athletes.

Coronary cardiac tomography

Although coronary anomalies as well as myocardial bridging are frequent findings in routine coronary cardiac tomography (CCT), the exact prevalence is unknown, ranging for myocardial bridging from 15 to 85% at autopsy and 0.5 to 16% at coronary angiography.[129] CCT offers the opportunity to evaluate coronary arteries non-invasively (*Figure 10*) and, by using latest generations scanners, also with a very low radiation dose.[130] Moreover, subclinical CAD can be detected also by calcium scanning.[130] Owing to the high accuracy of CCT—especially in terms of ruling out significant CAD—it could provide valuable information also in the athletes setting. Considering that especially endurance athletes have favourable lipid values and a low-cardiovascular risk according to standard risk calculators, the 'true' cardiovascular risk might be underestimated. Moreover, the association between premature CAD and endurance training, e.g. marathon running, is discussed controversially. Möhlenkamp *et al.*[131] reported higher calcium scores in athletes including 108 marathon runners compared with age- and risk-factor-matched

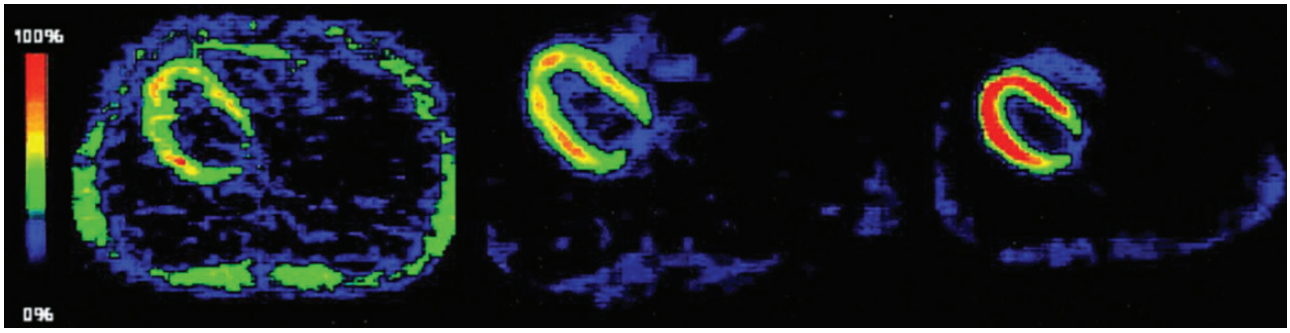

Figure 9: PET [^{18}F]FDG uptake in athletes. Examples of PET images showing similarly decreased [^{18}F]FDG uptake in endurance athletes and weight lifters compared with sedentary men (modified with permission, Takala *et al.*[126]).

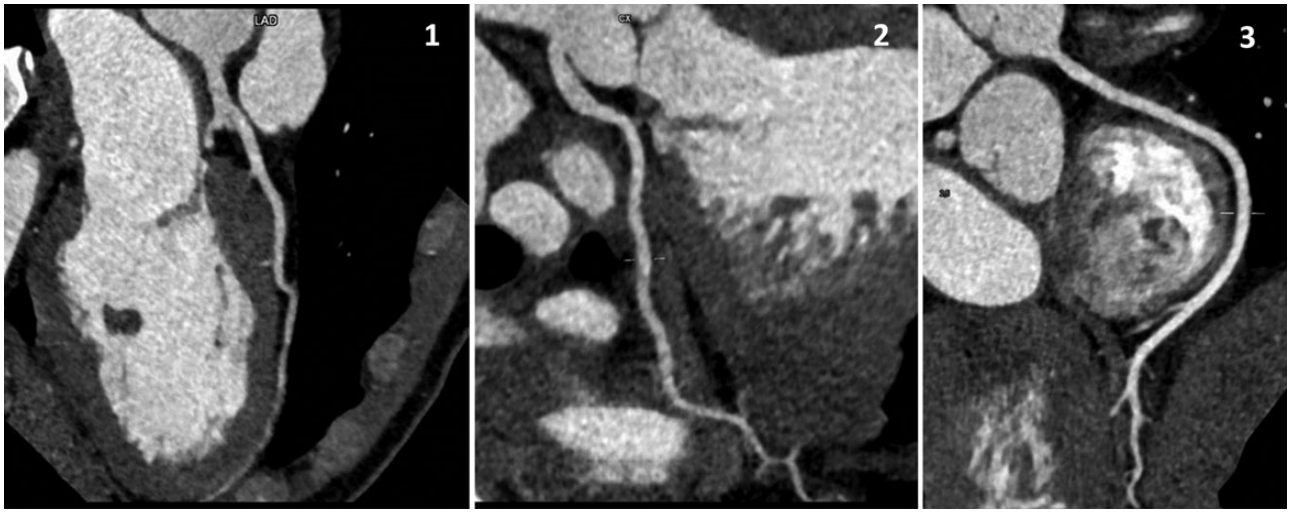

Figure 10: Image example of CCT. Non-invasive coronary angiography with not significant coronary artery stenosis. 1 LAD, 2 LCx, 3 RCA.

controls. This observation is of major importance as coronary calcification is an independent risk factor for all-cause mortality and cardiovascular events in the general population. Whether these observations can be generalized to athletes remains open to speculation. However, at present CCT should not be recommended as a first line imaging test in competitive athletes.[132]

Perfusion CMR imaging

Stress perfusion CMR imaging can help in the diagnosis of CAD in athletes as in the general population. Stress CMR has become a routine clinical test in many institutions, although it remains less available than stress echocardiography and cardiac nuclear imaging.[133] Current ESC guidelines recommend stress CMR alongside other tests as a gate keeper to invasive angiography in patients with suspected CAD and intermediate pre-test probability.[134] However, only very few studies were performed using stress perfusion CMR in athletes or in patients with HCM. In one of these, which compared 35 patients with HCM and 14 healthy controls, vasodilator stress myocardial perfusion was significantly reduced and correlated with the degree of hypertrophy (as an expression of coronary microvascular dysfunction) in HCM patients.[135] In cohorts of patients with overt HCM, HCM mutation carriers, athlete's heart with physiological LVH and normal controls, myocardial perfusion reserve by CMR was impaired only in overt HCM, but normal in athletes with LVH.[136] Thus, if diagnostic uncertainty prevails in an athlete with LVH, perfusion CMR could provide additional information to facilitate the differential diagnosis. CMR may also play an important role in depicting proximal coronary artery anomalies in athletes using coronary magnetic resonance angiography (MRA). Three-hundred-sixty healthy men and women (207 athletes and 153 non-athletes) were assessed with the standard CMR and an additional coronary MRA within a maximum of 10 min scan time: among 335 individuals with technically adequate CMR studies, four showed a malignant variant of the right coronary artery. The authors concluded that a 10 min coronary MRA is able to depict coronary origins and their proximal course. Therefore, this technique may be used as a non-invasive tool to exclude coronary artery anomalies in asymptomatic athletes under 35 years of age, as they have low risk of CAD.[137]

Table 4 *Average and upper limits of the main echocardiographic LV parameters in elite athletes (*sample sizes≥400)

Athlete's left heart morphologic and functional parameters						Upper limit
Authors	**Journal**	**Number of athletes**	**Type of sport**	**Parameter**	**Average value**	
Pelliccia *et al.*[1]	*Ann Intern Med* 1999;130:23–31	1309	Endurance/strength	LV end-diastolic diameter (adult male) (mm)	55	70
Whyte *et al.*[167]	*Eur J Appl Physiol* 2004;92:592–597	442	Endurance/strength	LV end-diastolic diameter (adult female) (mm)	49	66
Pelliccia *et al.*[168]	*JAMA* 1996;276:211–215	600	Endurance/strength			
Makan *et al.*[170]	*Heart* 2005;91:495–499	900	Endurance	LV end-diastolic diameter (adolescent) (mm)	51	60
Spirito *et al.*[31]	*Am J Cardiol* 1994;74:802–806	947	Endurance/strength	LV wall end-diastolic thickness (adult male) (mm)	10	16
Rawlins *et al.*[169]	*Circulation* 2010; 121:1078–1085	440	Endurance /strength	LV wall end-diastolic thickness (adult female) (mm)	9.5	13
Sharma *et al.*[6]	*J Am Coll Cardiol* 2002;40:1431–1436	720	Endurance/strength	LV wall end-diastolic thickness (adolescent) (mm)	9.5	12
Basavarajaiah *et al.*[166]	J Am Coll Cardiol 2008;51:2256–62	300	Endurance/strength	LV wall end-diastolic thickness (black athlete) (mm)	11.5	16
Pelliccia *et al.*[76]	*J Am Coll Cardiol* 2005;46:690-696	1777	Endurance/strength	LA diameter (male) (mm)	37	50
				LA diameter (female) (mm)	32	45
D'Andrea *et al.*[77]	*Am Heart J* 2010;159:1155–1161	650	Endurance/strength	LA volume index (male) (ml/m^2)	28	36
				LA volume index (female) (mL/m^2)	26.5	33
D'Andrea *et al.*[52]	*J Am Soc Echocardiogr* 2010;23:1281–1288	650	Endurance /strength	IVS Tissue Doppler s′ (cm/s)	13	18
				IVS Tissue Doppler e′ (cm/s)	24	21
				LV Tissue Doppler s′ (cm/s)	15	20
				LV Tissue Doppler e′ (cm/s)	16	22
				LV Tissue Doppler e′/a′ (cm/s)	1.45	1.7

EACVI expert consensus key points:

- Albeit debated, ECG screening remains the first line test for the diagnosis of heart disease in athletes.
- The incremental cost-effectiveness ratio of cardiac imaging modalities is too high in the context of low prevalence to justify their primary use for CAD diagnosis in asymptomatic athletes.
- Systematic and accurate exploration of proximal coronary arteries by echocardiography may be useful in identifying athletes with anomalous coronary origin, but the sensitivity of echocardiography in detecting congenital coronary anomalies has never been reported.
- Pharmacological stress echocardiography is rarely performed in athletes, whereas exercise stress echocardiography, a low cost, widely available, feasible, and safe technique, is very well accepted also by elite athletes.
- In symptomatic athletes in whom coronary anomalies or CAD may be suspected, it is reasonable to consider CCT and/or CMR, as well as attenuation-corrected SPECT MPI and PET MPI.

Intense exercise: good or dangerous?

The positive effect of training exercise on LV contractile reserve is recognized: preload is increased in endurance athletes, while afterload is increased through higher systemic resistance during physical effort in strength-trained athletes.[37] However, intense endurance exercise may not always be healthy. In some studies a transient reduction in cardiac function of unknown clinical relevance has been observed in endurance athletes. Immediately following exercise, acute increases in troponin and B-type natriuretic peptide were reported, especially when using high-sensitivity assays.[138,139] Echocardiographic studies showed that 'cardiac fatigue' could occur during prolonged exercise. Marginal decrease of global and regional LV systolic function (decrease of EF), alterations of LV diastolic function, and appearance of regional wall motion abnormalities were in fact documented in marathon runners.[140–143] Preload can be altered during exercise through dehydration, redistribution of blood flow, and increased HR, whereas afterload may be affected by changes in vascular resistance. Reductions of pulsed tissue Doppler-derived e′ velocity of both septal and lateral annulus as well as of Tissue Doppler indices of RV function were also reported after marathon completion.[144,145] By using STE, a decrease of longitudinal, circumferential and radial strains and also a reduction and delay of peak twisting was documented after ultralong duration exercise in triathletes.[146] Of note, while LV systolic dysfunction returned to normal within 48 h of the event, LV and RV diastolic abnormalities persisted up to 1 month after the marathon participation. Exercise-induced symptoms and/or ischaemic-like ECG signs were found to be often associated with a significant intraventricular gradient (>50 mmHg during/after exercise) in the absence of wall motion abnormalities in athletes.[147] These findings do not automatically imply permanent myocardial injury and may reflect temporary episodes of micro-injury followed by complete recovery. It has been speculated that this repair process may even strengthen the muscle to better tolerate subsequent loads of equal or greater intensity. In a study performed using PET imaging athletes had increased myocardial perfusion and improved adenosine-induced myocardial blood

Table 5 *Average and upper limits of the main echocardiographic RV parameters in elite athletes (*sample sizes ≥400)

Athlete's right heart morphologic and functional parameters						
Authors	**Journal**	**Number of athletes**	**Type of sport**	**Parameter**	**Average value**	**Upper limit**
D'Andrea *et al.*[94]	*Int J Cardiol* 2013;164:48–57	650	Endurance/power	RV end-diastolic diameter (basal) (RVD1) (mm) (male)	43.5	55
				RV end-diastolic diameter (basal) (RVD1) (mm) (female)	39	49
				RV end-diastolic diameter (middle ventricle) (RVD2) (mm) (male)	34	47
				RV end-diastolic diameter (middle ventricle) (RVD2) (mm) (female)	32	43
				RV end-diastolic diameter (base-to-apex) (RVD3) (mm) (male)	89	109
				RV end-diastolic diameter (base-to-apex) (RVD3) (mm) (female)	82	100
Zaidi *et al.*[173]	*Circulation* 2013;127:1783–92	675		RV proximal outflow tract diameter (RVOT1) (mm) (male)	32	43
				RV proximal outflow tract diameter (RVOT1) (mm) (female)	30	40
				RV distal outflow tract diameter (RVOT2) (mm) (male)	23.5	32
				RV distal outflow tract diameter (RVOT2) (mm) (female)	21.5	29
Zaidi *et al.*[173]	*Circulation* 2013;127:1783–92	675	Endurance	RA area (cm^2/m^2) (male)	19.5	28
				RA area (cm^2/m^2) (female)	15.5	24
D'Andrea *et al.*[152]	*Chest* 2011; 139(4):788–94	650	Endurance/power	Pulmonary artery systolic pressure (mmHg)	24	40
D'Andrea *et al.*[94]	*Int J Cardiol* 2013;164:48–57	650	Endurance/power	TAPSE (cm)	2.1	2.6
				RV area change (%)	48.5	54

flow reserve following a marathon run.[148] However, LGE was observed by CMR in 12% of marathon runners and its presence was correlated with the number of marathons previously performed, suggesting that intense sport activity could induce myocardial scarring.[131]

The right ventricle appears to be particularly vulnerable to the effects of intense endurance exercise.[146,149–154] RV dilation following an ultra-endurance triathlon without changes of LV dimensions was observed by M-mode,[143] 2D echo[148–150] and STE (reduction of longitudinal strain ~15% relative to baseline values).[152–154] The upper physiological limit of pulmonary arterial systolic pressure in endurance athletes may reach 40 mmHg at rest, in line with the greater increase in SV,[155] and pulmonary arterial pressure increase during exercise is more pronounced in athletes than in non-athletes.[156] Obviously, pulmonary arterial pressure can increase during effort. Repeated observations of RV dysfunction following prolonged intense exercise would suggest that there is some point in time in which the physiological demands of exercise can no longer be sustained by RV metabolic reserves. It remains to be determined whether recovery from repeated bouts of exercise-induced RV dysfunction is complete in all athletes.

EACVI expert consensus key points:

- Transient 'cardiac fatigue' can occur during prolonged exercise.
- Marginal decreases of global and regional LV systolic function (decrease of EF), alterations of LV diastolic function, and appearance of regional wall motion abnormalities have been documented in endurance athletes.
- RV dilation following an ultra-endurance triathlon without changes of LV dimensions has been observed and pulmonary arterial pressure is more pronounced during intensive exercise in athletes.

A proposal for multimodality imaging for distinguishing athlete's heart from cardiac disease

Considerations regarding pre-participation screening for the prevention of SCD in athletes

Strategies for the prevention of SCD are endorsed by sport governing bodies but mandatory pre-participation screening remains rare.[157] The goal of pre-participation screening of competitive athletes is the early identification of those with potentially fatal cardiovascular abnormalities, thus reducing the individual risk of SCD during sport activity.[115,158] Comprehensive pre-participation screening protocol in competitive athletes was established in Italy, in which family history, physical examination, and 12-lead ECG at rest—very effective for detection of electrical abnormalities and also HCM

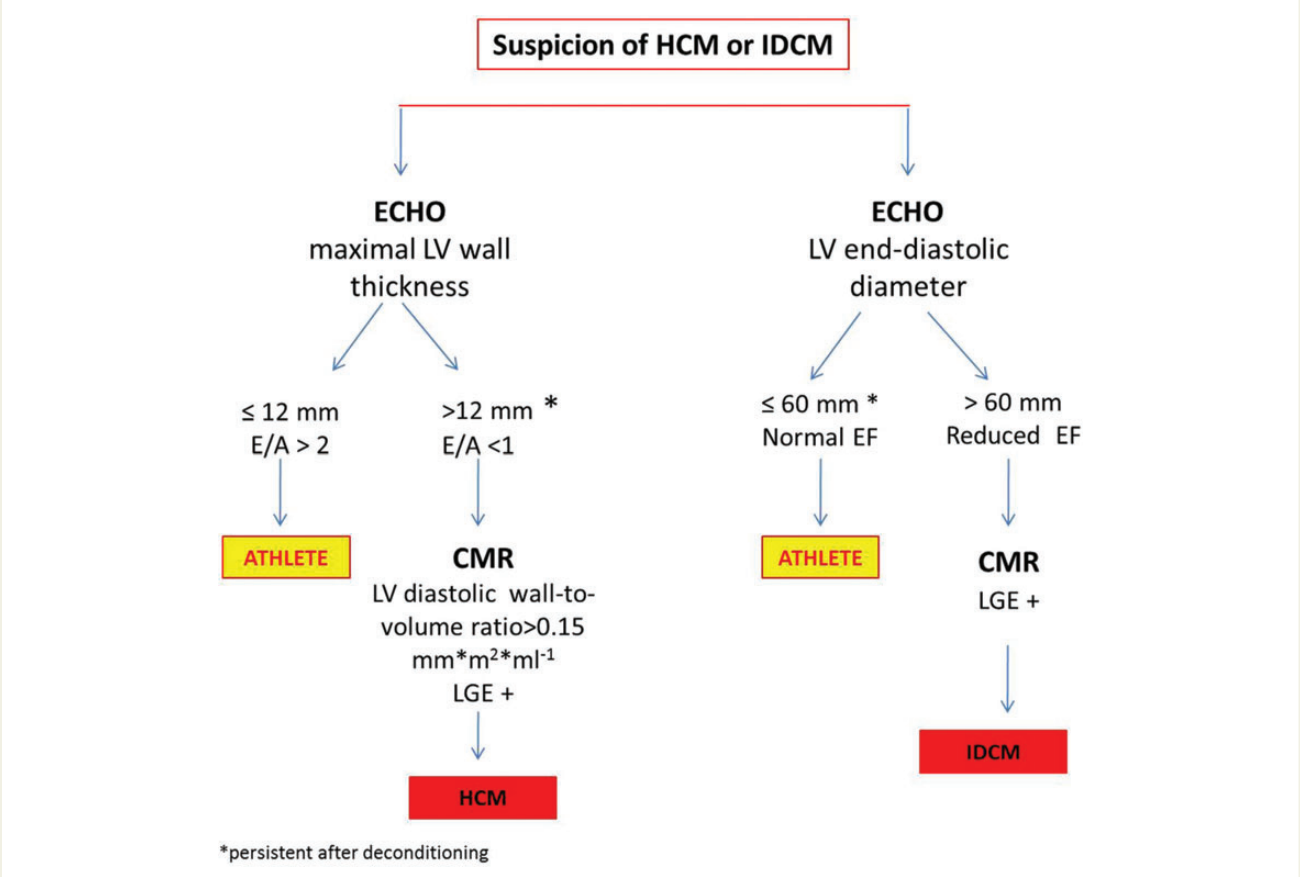

Figure 11: Proposed EACVI algorithm for differential diagnosis between athlete's heart and HCM or IDCM.

and ARVC in athletes[159–161]—are combined. With this protocol, near 90% reduction in the incidence rates of SCD from 3.6/100 000 per person-years to 0.4/100 000 per person-years was demonstrated in a secular trend study.[162] This is reflected in the ESC guidelines, which recommend the inclusion of a ECG at rest in pre-screening programmes.[115] In the same guidelines, conditions predisposing to SCD incorporate cardiac imaging (mainly echocardiography) in athletes with suspected or ascertained congenital and acquired heart diseases.[115] Conversely, the American Heart Association does not consider cardiac imaging and not support the routine use of the ECG in the athlete's setting.[116] Primary arguments against ECG use include the possibility of false-positive results, high-incremental cost-effectiveness ratio, and psychological implications for athletes and their families. Moreover, the interpretation of the athlete's ECG and recognition of normal variants according to age, ethnicity, gender, sports modality, or competitive level is often difficult and requires specific expertise. Furthermore, a recent study from Israel reported no change in SCD incidence rates in athletes following the implementation of screening programmes.[163] The role of pre-participation screening remains therefore controversial. To date, the current evidence is not sufficient to justify the use of cardiac imaging as primary screening modality in the guidelines on athletes, but these concerns shall not be confused with the very useful application of imaging for the assessment of athletes with symptoms, abnormal ECG or positive family history.[164]

The potential role of multimodality imaging

The multi-modality imaging approach of the athlete's heart has an important potential in order to differentiate it from serious cardiac diseases, which may mimic physiologic changes due to intensive training.[165] Before cardiac imaging can be utilized in pre-participation screening, specific reference values of the various cardiac structural and functional parameters in athletes are needed. *Table 4* [1,6,28,52,76,77,166–172] and *Table 5* [93,155,173] show average values and upper limits of the main echocardiographic LV and RV parameters, respectively, established in studies with large sample size in competitive (endurance and strength-trained) athletes. Efforts should be made to collect normal values of some missing parameters and also presenting them according to race, gender, and different sport disciplines. LV wall thickness is a key parameter since it can contribute to the distinction between athlete's LVH and HCM. LV end-diastolic diameter is another hinge parameter.

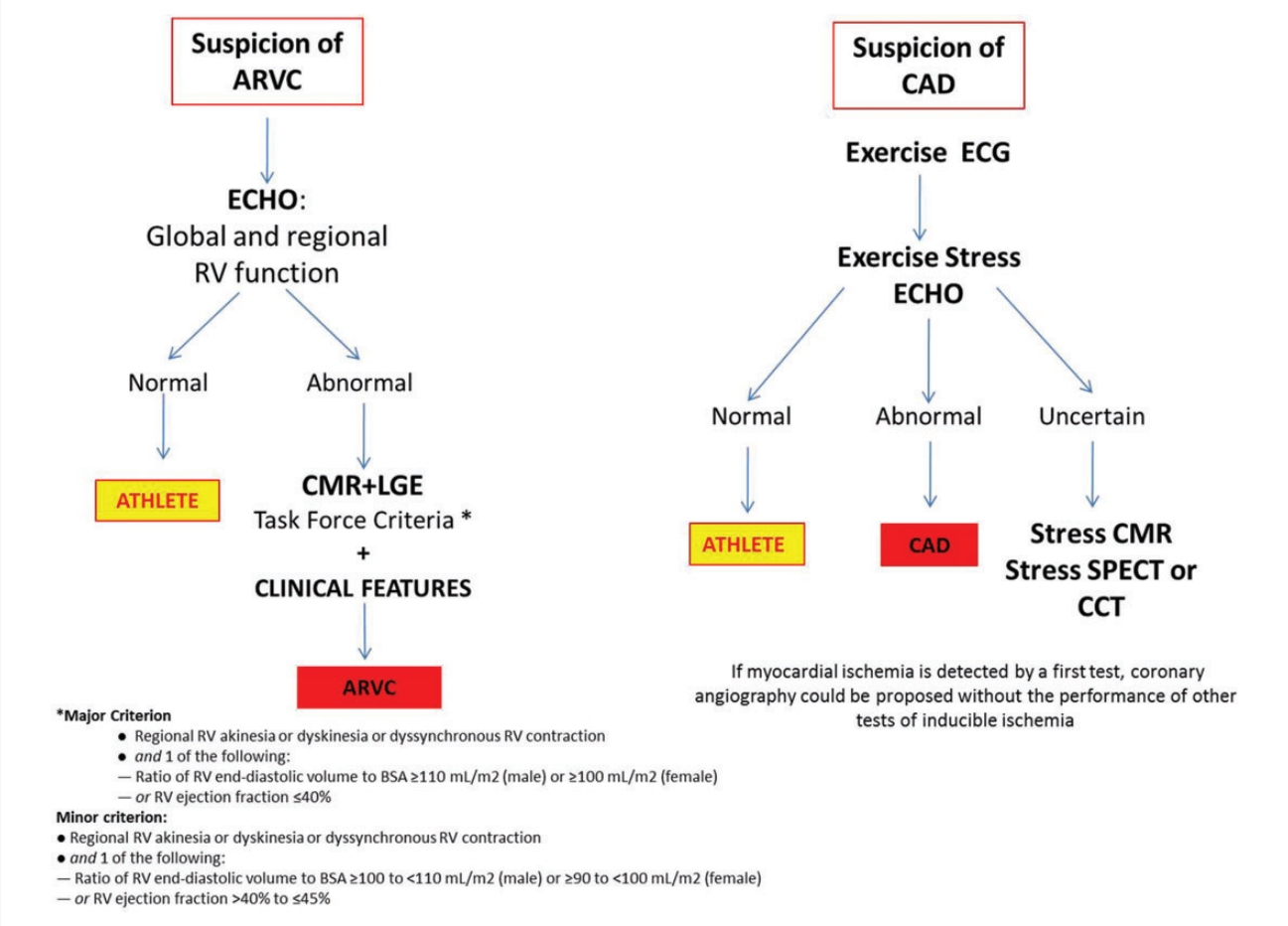

Figure 12: Proposed EACVI algorithm for differential diagnosis between athlete's heart and ARVC and diagnosis of CAD in athletes.

Patients with HCM show also early impairment of LV diastolic function, whereas athletes have supranormal diastolic function.

Figures 11 summarizes multi-modality imaging algorithms which can be applied to athletes when a suspicion of HCM and IDCM is evident, whereas *Figure 12* depicts cardiac imaging algorithms for diagnosis of ARVC or CAD. Obviously, these algorithms cannot be applied categorically. For instance, a reduction of LV wall thickness may be observed in physiological LVH but also in athletes with HCM, reflecting the complex interaction between genetic and environmental factors. Whenever, after echocardiography has been performed, uncertainty remains concerning differential diagnosis of athlete's heart, measurements of key parameters by CMR and tissue characterization by LGE CMR should be done in order to establish a definite diagnosis. Since all cut-off values of HCM or athlete's heart were derived from echocardiographic studies, the echo measurement could not be regarded as holding the same significance by CMR. In accordance with 2013 ESC guidelines on the management of stable CAD,[174] the work-up of athletes with suspected CAD should start with exercise ECG testing as the first step. When performing cardiac imaging tests, the presumably young age of the athletes and therefore the lower pre-test probability of CAD and the need to avoid exposure to radiation and increase the inherent cancer risk should be taken into account. In athletes with inconclusive results of maximal exercise ECG, it is reasonable to consider physical stress echocardiography as the first cardiac imaging choice and pharmacological stress echocardiography, CMR, nuclear cardiology, and/or CCT in selected cases. If myocardial ischaemia is detected by a first test, it is reasonable to propose invasive coronary angiography without the performance of CCT, to avoid cumulative tests and sometimes irradiation, if myocardial SPECT has been performed first for example.

EACVI expert consensus key points:

- The goal of pre-participation screening of competitive athletes is to identify those who have cardiovascular abnormalities, thus reducing the risk of SCD during sport activity.
- ESC guidelines recommend pre-screening including ECG at rest, but the American Heart Association does not recommend this.
- ESC guidelines propose echocardiography and, possibly, other non-invasive cardiac imaging, in athletes with suspected or ascertained congenital heart disease, heart valve disease, cardiomyopathies, and myocarditis.
- Normal ranges for all relevant cardiac parameters and for each imaging technique are needed, by categorizing the majority of parameters by gender and type of sport.
- CMR may help to differentiate athlete's heart from other forms of LVH and LV dilatation through demonstration of non-ischaemic patterns of LGE, which would not be seen in exercise-related remodelling.
- In athletes with suspected CAD, cardiac imaging provocative tests should be performed when the results of exercise ECG appear uncertain. Among provocative tests, physical exercise echocardiography may be the first choice. The use of CCT and nuclear cardiology techniques should be restricted to athletes with unclear stress echocardiography.

Future perspective

Cardiac imaging is important in identifying cardiovascular disease in athletes, but the final diagnosis has to be based on multiple factors including medical history, sports history, training load, symptoms, age, gender, ECG (resting and exercise), or genetic analysis. The controversy of using echocardiography in the pre-participation screening of competitive athletes is likely to remain as it is mainly around the high-incremental cost-effectiveness ratio and the impact of false-positive results on athletes and family. Although studies are still limited, cardiac ultrasound using pocket size imaging devices might offer a cheap but valid possibility of first-line imaging assessment[175] also in athletes. Whenever needed, more advanced cardiac imaging techniques, such as CCT, CMR, and nuclear imaging may add incremental diagnostic and prognostic information. CMR LGE, CMR T1 mapping, low-dose CCT, and new PET tracers offer the greatest potential.

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References

1. Pelliccia A, Culasso F, Di Paolo FM, Maron BJ. Physiologic left ventricular cavity dilatation in elite athletes. *Ann Intern Med* 1999;**130**:23–31.
2. 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;**32**: 295–301.
3. Abergel E, Chatellier G, Hagege AA, Oblak A, Linhart A, Ducardonnet A *et al.* Serial left ventricular adaptations in world-class professional cyclists: implications for disease screening and follow-up. *J Am Coll Cardiol* 2004;**44**:144–9.
4. Wolfe LA, Cunningham DA, Davis GM, Rosenfeld H. Relationship between maximal oxygen uptake and left ventricular function in exercise. *J Appl Physiol Respir Environ Exerc Physiol* 1978;**44**:44–9.
5. Morganroth J, Maron BJ, Henry WL, Epstein SE. Comparative left ventricular dimensions in trained athletes. *Ann Intern Med* 1975;**82**:521–4.
6. Sharma S, Maron BJ, Whyte G, Firoozi 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**: 1431–6.
7. Pluim BM, Zwiinderman AH, van der Laarse A, van der Wal EE. The athlete's heart. A meta-analysis of cardiac structure and function. *Circulation* 2000;**101**:336–44.
8. Gilbert CA, Nutter DO, Felner JM, Perkins JV, Heymsfield SB, Schlant RC. Echocardiographic study of cardiac dimensions and function in the endurance-trained athlete. *Am J Cardiol* 1977;**40**:528–33.
9. Caso P, D'Andrea A, Galderisi M, Liccardo B, Severino S, De Simone L *et al.* Pulsed Doppler tissue imaging in endurance athletes: relation between left ventricular preload and myocardial regional diastolic function. *Am J Cardiol* 2000;**85**:1131–6.
10. 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**:1856–63.
11. Blair SN, Kohl HW III, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. *JAMA* 1989;**262**:2395–401.
12. Teramoto M, Bungum TJ. Mortality and longevity of elite athletes. *J Sci Med Sport* 2010;**13**:410–6.
13. Marijon E, Tafflet M, Antero-Jacquemin J, El Helou N, Berthelot G, Celermajer DS *et al.* Mortality of French participants in the Tour de France (1947–2012). *Eur Heart J* 2013;**34**:3045–50.
14. 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**: 1959–63.
15. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. *Circulation* 2009;**119**:1085–92.
16. Maron BJ, Haas TS, Doerer JJ, Thompson PD, Hodges JS. Comparison of U.S. and Italian experiences with sudden cardiac deaths in young competitive athletes and implications for pre-participation screening strategies. *Am J Cardiol* 2009;**104**: 276–80.
17. Maron BJ. Sudden death in young athletes. *N Engl J Med* 2003;**349**:1064–75.

18. Chandra N, Bastiaenen R, Papadakis M, Sharma S. Sudden cardiac death in young athletes: practical challenges and diagnostic dilemmas. *J Am Coll Cardiol* 2013;**61**: 1027–40.
19. Terry GC, Kyle JM, Ellis JM Jr, Cantwell J, Courson R, Medlin R. Sudden cardiac arrest in athletic medicine. *J Athl Train* 2001;**36**:205–9.
20. Deligiannis A, Björnstad H, Carre F, Heidbüchel H, Kouidi E, Panhuyzen-Goedkoop NM *et al.*, ESC Study Group of Sports Cardiology. ESC study group of sports cardiology position paper on adverse cardiovascular effects of doping in athletes. *Eur J Cardiovasc Prev Rehabil* 2006;**13**:687–94.
21. Pluim BM, Katwinski PJ, Montgomery HE. Cardiac effects of anabolic steroids. *Heart* 2004;**90**:473–5.
22. Nottin S, Nguyen LD, Terbah M, Obert P. Cardiovascular effects of androgenic anabolic steroids in male body builders determined by tissue Doppler imaging. *Am J Cardiol* 2006;**97**:912–5.
23. Baggish AL, Weiner RB, Kanayama G, Hudson JI, Picard MH, Hutter AM Jr *et al.* Long-term anabolic-androgenic steroid use is associated with left ventricular dysfunction. *Circ Heart Fail* 2010;**3**:472–6.
24. Luijkx T, Velthuis BK, Backx FJ, Buckens CF, Prakken NH, Rienks R *et al.* Anabolic androgenic steroid use is associated with ventricular dysfunction on cardiac MRI in strength trained athletes. *Int J Cardiol* 2013;**167**:664–8.
25. D'Andrea A, Caso P, Salerno G, Scarafile R, De Corato G, Mita C *et al.* Left ventricular early myocardial dysfunction after chronic misuse of anabolic androgenic steroids: a Doppler myocardial and strain imaging analysis. *Br J Sports Med* 2007;**41**: 149–55.
26. Angell PJ, Chester N, Green DJ. Anabolic steroid use and longitudinal, radial and circumferential cardiac motion. *Med Sci Sports Exerc* 2012;**44**:583–90.
27. Angell PJ, Chester N, Sculthorpe N, Whyte G, George K, Somauroo J. Performance enhancing drug abuse and cardiovascular risk in athletes: implications for the clinician. *Br J Sports Med* 2012;**46**(Suppl. I):I78–84.
28. Schwartz BG, Rezkalla S, Kloner RA. Cardiovascular effects of cocaine. *Circulation* 2010;**122**:2558–69.
29. Aquaro GD, Gabutti A, Meini M, Prontera C, Pasanisi E, Passino C *et al.* Silent myocardial damage in cocaine addicts. *Heart* 2011;**97**:2056–62.
30. Steding K, Engblom H, Buhre T, Carlsson M, Mosén H, Wohlfart B *et al.* Relation between cardiac dimensions and peak oxygen uptake. *J Cardiovasc Magnet Res* 2010;**12**:8.
31. Spirito P, Pelliccia A, Proschan MA, Granata M, Spataro A, Bellone P *et al.* Morphology of the 'athlete's heart' assessed by echocardiography in 947 elites athletes representing 27 sports. *Am J Cardiol* 1994;**74**:802–6.
32. Di Paolo FM, Schmied C, Zerguini YA, Junge A, Quattrini F, Culasso F *et al.* The athlete's heart in adolescent Africans: an electrocardiographic and echocardiographic study. *J Am Coll Cardiol* 2012;**59**:1029–236.
33. Maron BJ. Structural features of the athlete heart as defined by echocardiography. *J Am Coll Cardiol* 1986;**7**:190–203.
34. 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**: 125–8.
35. 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**:944–9.
36. Urhausen A, Albers T, Kindermann W. Are the cardiac effects of anabolic steroid abuse in strength athletes reversible? *Heart* 2004;**90**:496–501.
37. Fagard R, Van Den Broeke C, Amery A. Left ventricular dynamics during exercise in elite marathon runners. *J Am Coll Cardiol* 1989;**14**:112–8.
38. D'Andrea A, Limongelli G, Caso P, Sarubbi B, Della Pietra A, Brancaccio P *et al.* Association between left ventricular structure and cardiac performance during effort in two morphological forms of athlete's heart. *Int J Cardiol* 2002;**86**:177–84.
39. George KP, Warburton DE, Oxborough D, Scott JM, Esch BT, Williams K *et al.* Upper limits of physiological cardiac adaptation in ultramarathon runners. *J Am Coll Cardiol* 2011;**57**:754–5.
40. Florescu M, Stoicescu C, Magda S, Petcu I, Radu M, Palombo C *et al.* 'Supranormal' cardiac function in athletes related to better arterial and endothelial function. *Echocardiography* 2010;**27**:659–67.
41. Zoncu S, Pelliccia A, Mercuro G. Assessment of regional systolic and diastolic wall motion velocities in highly trained athletes by pulsed wave Doppler tissue imaging. *J Am Soc Echocardiogr* 2002;**15**:900–5.
42. Vinereanu D, Florescu N, Schulthorpe N, Tweddel 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**:53–8.
43. Fagard RH. Impact of different sports and training on cardiac structure and function. *Cardiology Clinics* 1997;**15**:397–412.
44. D'Andrea A, Caso P, Severino S, Galderisi M, Sarubbi B, Limongelli G *et al.* Effects of different training protocols on left ventricular myocardial function in competitive athletes: a Doppler tissue imaging study. *Ital Heart J* 2002;**3**:34–5.
45. Severino S, Caso P, Galderisi M, De Simone L, Petrocelli A, de Divitiis O *et al.* Use of pulsed Doppler Tissue Imaging to assess regional left ventricular diastolic dysfunction in hypertrophic cardiomyopathy. *Am J Cardiol* 1998;**82**:1394–8.
46. Cardim N, Gouveia Oliveira A, Longo S. Doppler tissue imaging: regional myocardial function in hypertrophic cardiomyopathy and in athlete's heart. *J Am Soc Echocadiogr* 2003;**16**:223–32.
47. Galderisi M, Caso P, Severino S, Petrocelli A, De Simone L, Izzo A *et al.* Myocardial diastolic impairment caused by left ventricular hypertrophy involves basal septum more than other walls: analysis by pulsed Doppler tissue imaging. *J Hypertens* 1999; **17**:685–93.
48. Matsumura Y, Elliott PM, Virdee MS, Virdee MS, Sorajja P, Doi Y *et al.* Left ventricular diastolic function assessed using Doppler tissue imaging in patients with hypertrophic cardiomyopathy: relation to symptoms and exercise capacity. *Heart* 2002;**87**:247–51.
49. Richand V, Lafitte S, Reant P, Serri K, Lafitte M, Brette S *et al.* 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**:128–32.
50. Nottin S, Doucende G, Schuster-Beck I, Dauzat m, Obert P. Alteration in left ventricular normal and shear strain evaluated by 2D-strain echocardiography in the athlete's heart. *J Physiol* 2008;**586**:4721–33.
51. Saghir M, Areces M, Makan M. Strain rate imaging differentiates hypertensive cardiac hypertrophy from physiologic cardiac hypertrophy (athlete's heart). *J Am Soc Echocardiogr* 2007;**20**:151–7.
52. D'Andrea A, Cocchia R, Riegler L, Scarafile R, Salerno G, Gravino R *et al.* Left ventricular myocardial velocities and deformation indexes in top-level athletes. *J Am Soc Echocardiogr* 2010;**23**:1281–8.
53. Galderisi M, Lomoriello VS, Santoro A, Esposito R, Olibet M, Raia R *et al.* 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**:1190–8.
54. Richand V, Lafitte S, Reant P, Serri K, Lafitte M, Brette S *et al.* 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**:128–32.
55. Vitarelli A, Capotosto L, Placanica G, Caranci F, Pergolini M, Zardo F *et al.* Comprehensive assessment of biventricular function and aortic stiffness in athletes with different forms of training by three-dimensional echocardiography and strain imaging. *Eur Heart J Cardiovasc Imaging* 2013;**14**:1010–20.
56. Pattynama PM, Lamb HJ, van der Velde EA, van der Wall EE, de Roos A. Left ventricular measurements with cine and spin-echo MR imaging: a study of reproducibility with variance component analysis. *Radiology* 1993;**187**:261–8.
57. Semelka RC, Tomei E, Wagner S, Mayo J, Caputo G, O'Sullivan M *et al.* Interstudy reproducibility of dimensional and functional measurements between cine magnetic resonance studies in the morphologically abnormal left ventricle. *Am Heart J* 1990;**119**:1367–73.
58. Rehr RB, Malloy CR, Filipchuk NG, Peshock RM. Left ventricular volumes measured by MR imaging. *Radiology* 1985;**156**:717–9.
59. Ceelen F, Hunter RJ, Boubertakh R, Sommer WH, Armbruster M, Schilling RJ *et al.* Effect of atrial fibrillation ablation on myocardial function: insights from cardiac magnetic resonance feature tracking analysis. *Int J Cardiovasc Imaging* 2013;**29**: 1807–17.
60. Augustine D, Lewandowski AJ, Lazdam M, Rai A, Francis J, Myerson S *et al.* Global and regional left ventricular myocardial deformation measures by magnetic resonance feature tracking in healthy volunteers: comparison with tagging and relevance of gender. J Cardiovasc Magn *Reson* 2013;**15**:8.
61. Kim RJ, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O *et al.* Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation* 1999;**100**:1992–2002.
62. Mahrholdt H, Wagner A, Judd RM, Sechtem U. Assessment of myocardial viability by cardiovascular magnetic resonance imaging. *Eur Heart J* 2002;**23**:602–19.
63. 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**:1461–74.
64. Moon JC, Messroghli DR, Kellman P, Piechnik SK, Robson MD, Ugander M *et al.* 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.
65. Petersen SE, Selvanayagam JB, Francis JM, Myerson SG, Wiesmann F, Robson MD *et al.* 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**:551–8.

66. Rickers C, Wilke NM, Jerosch-Herold M, Casey SA, Panse P, Panse N *et al.* Utility of cardiac magnetic resonance imaging in the diagnosis of hypertrophic cardiomyopathy. *Circulation* 2005;**112**:855–61.
67. Moon JC, Fisher NG, McKenna WJ, Pennell DJ. Detection of apical hypertrophic cardiomyopathy by cardiovascular magnetic resonance in patients with non-diagnostic echocardiography. *Heart* 2004;**90**:645–9.
68. Bruder O, Wagner A, Jensen CJ, Schneider S, Ong P, Kispert EM *et al.* Myocardial scar visualized by cardiovascular magnetic resonance imaging predicts major adverse events in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2010;**56**:875–87.
69. O'Hanlon R, Grasso A, Roughton M, Moon JC, Clark S, Wage R *et al.* Prognostic significance of myocardial fibrosis in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2010;**56**:867–74.
70. Petersen SE, Jerosch-Herold M, Hudsmith LE, Robson MD, Francis JM, Doll HA *et al.* Evidence for microvascular dysfunction in hypertrophic cardiomyopathy: new insights from multiparametric magnetic resonance imaging. *Circulation* 2007; **115**:2418–25.
71. Moon JC, McKenna WJ, McCrohon JA, Elliott PM, Smith GC, Pennell DJ. Toward clinical risk assessment in hypertrophic cardiomyopathy with gadolinium cardiovascular magnetic resonance. *J Am Coll Cardiol* 2003;**41**:1561–7.
72. McCrohon JA, Moon JC, Prasad SK, McKenna WJ, Lorenz CH, Coats AJ *et al.* Differentiation of heart failure related to dilated cardiomyopathy and coronary artery disease using gadolinium-enhanced cardiovascular magnetic resonance. *Circulation* 2003;**108**:54–9.
73. Mangold S, Kramer U, Franzen E, Erz G, Bretschneider C, Seeger A *et al.* Detection of cardiovascular disease in elite athletes using cardiac magnetic resonance imaging. *Rofo* 2013;**185**:1167–74.
74. 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**: 1596–601.
75. Assomull RG, Prasad SK, Lyne J, Smith G, Burman ED, Khan M *et al.* Cardiovascular magnetic resonance, fibrosis, and prognosis in dilated cardiomyopathy. *J Am Coll Cardiol* 2006;**48**:1977–85.
76. Pelliccia A, Maron BJ, Di Paolo FM, Biffi A, Quattrini FM, Pisicchio C *et al.* Prevalence and clinical significance of left atrial remodeling in competitive athletes. *J Am Coll Cardiol* 2005;**46**:690–6.
77. D'Andrea A, Riegler R, Cocchia R, Scarafile R, Salerno G, Gravino R *et al.* Left atrial volume index in highly trained athletes. *Am Heart J* 2010;**159**:1155–61.
78. Molina L, Mont L, Marrugat J, Berruezo A, Brugada J, Bruguera J *et al.* Long-term endurance sport practice increases the incidence of lone atrial fibrillation in men: a follow-up study. *Europace* 2008;**10**:618–23.
79. Mont L, Elosua R, Brugada J. Endurance sport practice as a risk factor for atrial fibrillation and atrial flutter. *Europace* 2009;**11**:11–7.
80. Mont L, Tamborero D, Elosua R, Molina I, Coll-Vinent B, Sitges M *et al.* GIRAFA (Grup Integrat de Recerca en Fibril-lació Auricular) investigators. Physical activity, height, and left atrial size are independent risk factors for lone atrial fibrillation in middle-aged healthy individuals. *Europace* 2008;**10**:15–20.
81. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA *et al.*; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjuction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *Eur J Echocardiogr* 2006;**7**:79–108.
82. Abhayaratna WP, Seward JB, Appleton CP, Douglas PS, Oh JK, Tajik AJ *et al.* Left atrial size: physiologic determinants and clinical applications. *J Am Coll Cardiol* 2006;**47**:2357–663.
83. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Eur J Echocardiogr* 2009;**10**:165–93.
84. Thomas L, Levett K, Boyd A, Leung DY, Schiller NB, Ross DL. Compensatory changes in atrial volumes with normal aging: is atrial enlargement inevitable? *J Am Coll Cardiol* 2002;**40**:1630–5.
85. Aurigemma GP, Gottdiener JS, Arnold AM, Chinali M, Hill JC, Kitzman D. Left atrial volume and geometry in healthy aging. The Cardiovascular Health study. *Circ Cardiovasc Imaging* 2009;**2**:282–9.
86. Nistri S, Galderisi M, Ballo P, Olivotto I, D'Andrea A, Pagliani L *et al.*, on behalf of the Working Group of Echocardiography of the Italian Society of Cardiology. Determinants of echocardiographic left atrial size: implications for normalcy. *Eur J Echocardiogr* 2011;**12**:826–33.
87. Kou S, Caballero L, Dulgheru R, Voilliot D, De Sousa C, Kacharava G *et al.* Echocardiographic reference ranges from normal cardiac chamber size: results from NORRE study. *Eur Heart J Cardiovasc Imaging* 2014;**15**:680–90.
88. Gati S, Sheikh N, Ghani S, Zaidi A, Wilson M, Raju H *et al.* Should axis deviation or atrial enlargement be categorised as abnormal in young athletes? The athlete's electrocardiogram: time for re-appraisal of markers of pathology. *Eur Heart J* 2013;**34**: 3461–8.
89. D'Ascenzi F, Pelliccia A, Natali BM, Zacà V, Cameli M, Alvino F *et al.* Morphological and Functional adaptation of left and right atria induced by training in highly trained female athletes. *Circ Cardiovasc Imag* 2014;**7**:222–9.
90. Gabrielli L, Enríquez A, Córdova S, Yáñez F, Godoy I, Corbalán R. Assessment of left atrial function in hypertrophic cardiomyopathy and athlete's heart: a left atrial myocardial deformation study. *Echocardiography* 2012;**29**:943–9.
91. 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**:71–9.
92. Mosén H, Steding-Ehrenborg K. Atrial remodelling is less pronounced in female endurance-trained athletes compared with that in male athletes. *Scand Cardiovasc J* 2014;**48**:20–6.
93. Knutsen KM, Stugaard M, Michelsen S, Otterstad JE. M-mode echocardiographic findings in apparently healthy, nonathletic Norwegians aged 20–70 years. Influence of age, sex and body surface area. *J Intern Med* 1989;**225**:111–5.
94. D'Andrea A, Riegler L, Golia E, Cocchia R, Scarafile R, Salerno G *et al.* Range of right heart measurements in top-level athletes: the training impact. *Int J Cardiol* 2013;**164**: 48–57.
95. Hauser AM, Dressendorfer RH, Vos M, Hashimoto T, Gordon S, Timmis GC. Symmetric cardiac enlargement in highly trained endurance athletes: a two-dimensional echocardiographic study. *Am Heart J* 1985;**109**:1038–44.
96. Goldhammer E, Mesnick N, Abinader EG, Sagiv M. Dilated inferior vena cava: a common echocardiographic finding in highly trained elite athletes. *J Am Soc Echocardiogr* 1999;**12**:988–93.
97. 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**:1856–63.
98. Scharf M, Brem MH, Wilhelm M, Schoepf UJ, Uder M, Lell MM. Cardiac magnetic resonance assessment of left and right ventricular morphologic and functional adaptations in professional soccer players. *Am Heart J* 2010;**159**:911–8.
99. Baggish AL, Wang F, Weiner RB, Elinoff JM, Tournoux F, Boland A *et al.* Training-specific changes in cardiac structure and function: a prospective and longitudinal assessment of competitive athletes. *J Appl Physiol* 2008;**104**:1121–8.
100. Utomi V, Oxborough D, Whyte GP, Somauroo J, Sharma S, Shave R *et al.* 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**:1727–33.
101. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K *et al.* Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2010;**23**:685–713.
102. Sen-Chowdhry S, Lowe MD, Sporton SC, McKenna WJ. Arrhythmogenic right ventricular cardiomyopathy: clinical presentation, diagnosis, and management. *Am J Med* 2004;**117**:685–95-.
103. Zaidi A, Ghani S, Sheikh N, Gati S, Bastiaenen R, Madden B *et al.* Clinical significance of electrocardiographic right ventricular hypertrophy in athletes: comparison with arrhythmogenic right ventricular cardiomyopathy and pulmonary hypertension. *Eur Heart J* 2013;**34**:3649–56.
104. Sen-Chowdhry S, Prasad SK, McKenna WJ. Complementary role of echocardiography and cardiac magnetic resonance in the non-invasive evaluation of suspected arrhythmogenic right ventricular cardiomyopathy. *J Interv Card Electrophysiol* 2004; **11**:15–7.
105. D'Andrea A, Riegler L, Morra S, Scarafile R, Salerno G, Cocchia R *et al.* Right ventricular morphology and function in top-level athletes: a three-dimensional echocardiographic study. *J Am Soc Echocardiogr* 2012;**25**:1268–76.
106. Esposito R, Galderisi M, Schiano-Lomoriello V, Santoro A, De Palma D, Ippolito R *et al.* 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* 2013;**31**: 996–1004.
107. Nagueh SF, Bierig SM, Budoff MJ, Desai M, Dilsizian V, Eidem B *et al.* American Society of Echocardiography; American Society of Nuclear Cardiology; Society for Cardiovascular Magnetic Resonance; Society of Cardiovascular Computed Tomography. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with hypertrophic cardiomyopathy: endorsed by the American Society of Nuclear Cardiology, Society for Cardiovascular Magnetic Resonance, and Society of Cardiovascular Computed Tomography. *J Am Soc Echocardiogr* 2011;**24**:473–98.

108. Nishimura RA, Ommen SR, Rakowski H, Seidman CE, Towbin JA, Udelson JE. 2011 ACCF/AHA guidelines for the diagnosis and treatment of hypertrophic cardiomyopathy: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2011;**124**:2761–96.
109. Grothues F, Moon JC, Bellenger NG, Smith GS, Klein HU, Pennell DJ. Interstudy reproducibility of right ventricular volumes, function, and mass with cardiovascular magnetic resonance. *Am Heart J* 2004;**147**:218–23.
110. Maron MS. Clinical utility of cardiovascular magnetic resonance in hypertrophic cardiomyopathy. *J Cardiovasc Magn Reson* 2012;**1**:14:13.
111. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA *et al.* Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. *Circulation* 2010;**121**:1533–41.
112. Luijkx T, Velthuis BK, Prakken NH, Cox MG, Bots ML, Mali WP *et al.* 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**:885–91.
113. Kirchhof P, Fabritz L, Zwiener M, Witt H, Schäfers M, Zellerhoff S *et al.* Age- and training-dependent development of arrhythmogenic right ventricular cardiomyopathy in heterozygous plakoglobin-deficient mice. *Circulation* 2006;**114**:1799–806.
114. James CA, Bhonsale A, Tichnell C, Murray B, Russell SD, Tandri H *et al.* Exercise increases age-related penetrance and arrhythmic risk in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers. *J Am Coll Cardiol* 2013;**62**:1290–7.
115. Corrado D, Pelliccia A, Bjørnstad HH, Vanhees L, Biffi A, Borjesson M *et al.* Study Group of Sport 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. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. Consensus statement of the Study Group of Sport 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**:516–24.
116. Maron BJ, Thompson PD, Ackerman MJ, Balady G, Berger S, Cohen D *et al.*, American Heart Association Council on Nutrition, Physical Activity, and Metabolism. Recommendations and considerations related to pre-participation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation* 2007;**115**:1643–455.
117. Borjesson M, Urhausen A, Kouidi E, Dugmore D, Sharma S, Halle M *et al.* Cardiovascular evaluation of middle-aged/ senior individuals engaged in leisure-time sport activities: position stand from the sections of exercise physiology and sports cardiology of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2011;**18**:446–58.
118. La Gerche A, Baggish AL, Knuuti J, Prior DL, Sharma S, Heidbuchel H *et al.* Cardiac imaging and stress testing asymptomatic athletes to identify those at risk of sudden cardiac death. *JACC Cardiovasc Imaging* 2013;**6**:993–1007.
119. Zeppilli P, Dello Russo A, Santini C, Palmieri V, Natale L, Giordano A. In vivo detection of coronary artery anomalies in asymptomatic athletes by echocardiographic screening. *Chest* 1998;**114**:89–93.
120. Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. *Ann Intern Med* 1999;**130**:719–28.
121. D'Andrea A, Severino S, Caso P, Liccardo B, Forni A, Fusco A *et al.* Prognostic value of supine bicycle exercise stress echocardiography in patients with known or suspected coronary artery disease. *Eur J Echocardiogr* 2005;**6**:271–9.
122. Hildick-Smith DJ, Johnson PJ, Wisbey CR, Winter EM, Shapiro LM. Coronary flow reserve is supranormal in endurance athletes: an adenosine transthoracic echocardiographic study. *Heart* 2000;**84**:383–9.
123. Bartram P, Toft J, Hanel B, Ali S, Gustafsson F, Mortensen J *et al.* False-positive defects in technetium-99 m sestamibi myocardial single-photon emission tomography in healthy athletes with left ventricular hypertrophy. *Eur J Nucl Med* 1998; **25**:1308–12.
124. Andersson LG, Henriksen E, Damm S, Jonason T, Niklasson U, Wesslén L *et al.* Thallium-201 myocardial imaging at rest in male orienteers and other endurance athletes. *Ups J Med Sci* 2001;**106**:59–66.
125. Takala TO, Nuutila P, Katoh C, Luotolahti M, Bergman J, Mäki M *et al.* Myocardial blood flow, oxygen consumption, and fatty acid uptake in endurance athletes during insulin stimulation. *Am J Physiol* 1999;**277**:E585–90.
126. Takala TO, Nuutila P, Knuuti J, Luotolahti M, Yki-Jarvinen H. Insulin action on heart and skeletal muscle glucose uptake in weightlifters and endurance athletes. *Am J Physiol* 1999;**276**:E706–11.
127. Matsuo S, Nakamura Y, Takahashi M, Matsui T, Kusukawa J, Yoshida S *et al.* Cardiac sympathetic dysfunction in an athlete's heart detected by 123I-metaiodobenzylguanidine scintigraphy. Jpn Circ J 2001;**65**:371–4.
128. Estorch M, Serra-Grima R, Flotats A, Marí C, Bernà L, Catafau A *et al.* Myocardial sympathetic innervation in the athlete's sinus bradycardia: is there selective inferior myocardial wall denervation? *J Nucl Cardiol* 2000;**7**:354–8.
129. Leschka S, Koepfli P, Husmann L, Plass A, Vachenauer R, Gaemperli O *et al.* Myocardial bridging: depiction rate and morphology at CT coronary angiography—comparison with conventional coronary angiography. *Radiology* 2008;**246**:754–62.
130. Schroeder S, Achenbach S, Bengel F, Burgstahler C, Cademartiri F, de Feyter P. 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**:531–56.
131. Möhlenkamp S, Lehmann N, Breuckmann F, Bröcker-Preuss M, Nassenstein K, Halle M *et al.* Running the risk of coronary events: prevalence and prognostic relevance of coronary atherosclerosis in marathon runners. *Eur Heart J* 2008;**29**: 903–1910.
132. Thiene G, Corrado D, Schiavon M, Basso C. Screening of competitive athletes to prevent sudden death: implement programmes now. *Heart* 2013;**99**:304–6.
133. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A *et al.* 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.
134. Bruder O, Wagner A, Lombardi M, Schwitter J, van Rossum A, Pilz G *et al.* European Cardiovascular Magnetic Resonance (EuroCMR) registry–multinational results from 57 centers in 15 countries. *J Cardiovasc Magn Reson* 2013;**15**:9.
135. Petersen SE, Jerosch-Herold M, Hudsmith LE, Robson MD, Francis JM, Doll HA *et al.* Evidence for microvascular dysfunction in hypertrophic cardiomyopathy: new insights from multi-parametric magnetic resonance imaging. *Circulation* 2008; **115**:2418–25.
136. Karamitsos TD, Dass S, Suttie J, Sever E, Birks J, Holloway CJ *et al.* Blunted myocardial oxygenation response during vasodilator stress in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2013;**61**:1169–76.
137. Prakken NH, Cramer MJ, Olimulder MA, Agostoni P, Mali WP, Velthuis BK. Screening for proximal coronary artery anomalies with 3-dimensional MR coronary angiography. *Int J Cardiovasc Imaging* 2010;**26**:701–10.
138. Shave R, Baggish A, George K, Wood M, Scharhag J, Whyte G *et al.* Exercise-induced cardiac troponin elevation: evidence, mechanisms, and implications. *J Am Coll Cardiol* 2010;**56**:169–76.
139. Mousavi N, Czarnecki A, Kumar K, Fallah-Rad N, Lytwyn M, Han SY *et al.* Relation of biomarkers and cardiac magnetic resonance imaging after marathon running. *Am J Cardiol* 2009;**103**:1467–72.
140. Trivax JE, Franklin BA, Goldstein JA, Chinnaiyan KM, Gallagher MJ, de Jong AT *et al.* Acute cardiac effects of marathon running. *J Appl Physiol* 2010;**108**:1148–53.
141. Shave R, George K, Whyte G, Hart E, Middleton N. Post exercise changes in left ventricular function: the evidence so far. *Med Sci Sports Exerc* 2008;**40**:1393–9.
142. Neilan TG, Januzzi JL, Lee-Lewandrowski E, Ton-Nu TT, Yoerger DM, Jassal DS *et al.* Myocardial injury and ventricular dysfunction related to training levels among non elite participants in the Boston marathon. *Circulation* 2006;**114**: 2325–33.
143. Neilan TG, Yoerger DM, Douglas PS, Ton-Nu TT, Yoerger DM, Jassal DS *et al.* Persistent and reversible cardiac dysfunction among amateur marathon runners. *Eur Heart J* 2006;**27**:1079–84.
144. Cotrim C, Almeida AR, Miranda R, Almeida AG, Cotrim H, Picano E *et al.* Stress-induced intraventricular gradients in symptomatic athletes during upright exercise continuous wave Doppler echocardiography. *Am J Cardiol* 2010;**106**: 808–1812.
145. Nottin S, Doucende G, Schuster I, Tanguy S, Dauzat M, Obert P. Alteration in left ventricular strains and torsional mechanics after ultralong duration exercise in athletes. *Circ Cardiovasc Imaging* 2009;**2**:323–30.
146. Douglas PS, O'Toole ML, Hiller WD, Reichek N. Different effects of prolonged exercise on the right and left ventricles. *J Am Coll Cardiol* 1990;**15**:64–9.
147. La Gerche A, Connelly KA, Mooney DJ, MacIsaac AI, Prior DL. Biochemical and functional abnormalities of left and right ventricular function after ultra-endurance exercise. *Heart* 2008;**94**:860–6.
148. Kallioski KK, Laaksonen MS, Luotolahti M, Laine H, Takala TO, Nuutila P *et al.* Myocardial perfusion after marathon running. *Scand J Med Sci Sports* 2004;**14**: 208–14.
149. La Gerche A, Burns AT, Mooney DJ, Inder WJ, Taylor AJ, Bogaert J *et al.* Exercise-induced right ventricular dysfunction and structural remodelling in endurance athletes. *Eur Heart J* 2012;**33**:998–1006.
150. D'Andrea A, Caso P, Sarubbi B, Limongelli G, Liccardo B, Cice G *et al.* Right ventricular myocardial adaptation to different training protocols in top-level athletes. *Echocardiography* 2003;**20**:329–36.
151. La Gerche A, Heidbüchel H, Burns AT, Mooney DJ, Taylor AJ, Pfluger HB *et al.* Disproportionate exercise load and remodeling of the athlete's right ventricle. *Med Sci Sports Exerc* 2011;**43**:974–81.

152. D'Andrea A, Caso P, Bossone E, Scarafile R, Riegler L, Di Salvo G *et al.* Right ventricular myocardial involvement in either physiological or pathological left ventricular hypertrophy: an ultrasound speckle- tracking two-dimensional strain analysis. *Eur J Echocardiogr* 2010;**11**:492–500.
153. Oxborough D, Shave R, Warburton D, Williams K, Oxborough A, Charlesworth S. Dilatation and dysfunction of the right ventricle immediately after ultra-endurance exercise: exploratory insights from conventional two-dimensional and speckle tracking echocardiography. *Circ Cardiovasc Imaging* 2011;**4**:253–63.
154. La Gerche A, Burns AT, D'Hooge J, Macisaac AI, Heidbüchel 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**:53–262.
155. D'Andrea A, Naeije R, D'Alto M, Argiento P, Golia E, Cocchia R *et al.* Range in pulmonary artery systolic pressure among highly trained athletes. *Chest* 2011;**139**: 788–94.
156. Bossone E, Rubenfire M, Bach DS, Ricciardi M, Armstrong WF. Range of tricuspid regurgitation velocity at rest and during exercise in normal adult men: implications for the diagnosis of pulmonary hypertension. *J Am Coll Cardiol* 1999; **33**:1662–6.
157. Chandra N, Bastiaenen R, Papadakis M, Sharma S. Sudden cardiac death in young athletes: practical challenges and diagnostic dilemma. *J Am Coll Cardiol* 2013;**61**: 1027–40.
158. Chandra N, Papadakis M, Sharma S. Pre-participation screening of young competitive athletes for cardiovascular disorders. *Phys Sports Med* 2010;**38**:54–63.
159. Ljungqvist A, Jenoure PJ, Engebretsen L, Alonso JM, Bahr R, Clough AF *et al.* The International Olympic Committee (IOC) consensus statement on periodic atlhete evaluation of elite athletes, March 2009. *Clin J Sport Med* 2009;**19**:347–65.
160. Montgomery JV, Harris KM, Casey SA, Zenovich AG, Maron BJ. Relation of electrocardiographic patterns to phenotypic expression and clinical outcome in hypertrophic cardiomyopathy. *Am J Cardiol* 2005;**96**:270–5.
161. Marcus FI. Electrocardiographic features of inherited diseases that predispose to the development of cardiac arrhythmias, long QT syndrome, arrhythmogenic right ventricular cardiomyopathy/dysplasia, and Brugada syndrome. *J Electrocardiol* 2000;**33**:S1–S10.
162. Corrado D, Basso C, Pavei A, Michieli P, Schiavon M, Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA* 2006;**296**:1593–601.
163. Steinvil A, Chundadze T, Zeltser D, Rogowki O, Halkin A, Galily Y *et al.* Mandatory electrocardiographic screening of athletes to reduce their risk for sudden death. *J Am Coll Cardiol* 2011;**57**:1291–6.
164. La Gerche A, Baggish AL, Knuuti J, Prior DL, Sharma S, Heidbuchel H *et al.* Cardiac imaging and stress testing in asymptomatic athletes to identify those at risk of sudden cardiac death. JACC Cardiovasc *Imaging* 2013;**6**:993–1007.
165. La Gerche A, Taylor AJ, Prior DL. Athlete's Heart: the potential for multimodality imaging to address the critical remaining questions. *J Am Coll Cardiol Img* 2009;**2**: 350–63.
166. Basavarajaiah S, Wilson M, Whyte G, Shah A, McKenna W, Sharma S. Prevalence of hypertrophic cardiomyopathy in highly trained athletes: relevance to preparticipation screening. *J Am Coll Cardiol* 2008;**51**:1033–9.
167. Whyte GP, George K, Sharma S, Firoozi S, Stephens N, Senior R *et al.* The upper limit of physiological cardiac hypertrophy in elite male and female athletes: the British experience. *Eur J Appl Physiol* 2004;**92**:592–7.
168. 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**:211–2155.
169. Rawlins J, Carre F, Kervio G, Papadakis M, Chandra N, Edwards C *et al.* Ethnic differences in physiological cardiac adaptation to intense physical exercise in highly trained female athletes. *Circulation* 2010;**121**:1078–85.
170. Makan J, Sharma S, Firoozi S, Whyte G, Jackson PG, McKenna WJ. Physiological upper limits of ventricular cavity size in highly trained adolescent athletes. *Heart* 2005;**91**:495–9.
171. Pelliccia A, Di Paolo FM, De Blasiis E, Quattrini FM, Pisicchio C, Guerra E *et al.* Prevalence and clinical significance of aortic root dilation in highly trained competitive athletes. *Circulation* 2010;**122**:698–706.
172. D'Andrea A, Cocchia R, Riegler L, Scarafile R, Salerno G, Gravino R *et al.* Aortic root dimensions in elite athletes. *Am J Cardiol* 2010;**105**:1629–34.
173. Zaidi A, Ghani S, Sharma R, Oxborough D, Panoulas VF, Sheikh N *et al.* Physiological right ventricular adaptation in elite athletes of African and Afro-Caribbean origin. *Circulation* 2013;**127**:1783–92.
174. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budai A *et al.* 2013 ESC guidelines on the management of stable coronary artery disease. *Eur Heart J* 2013;**34**:2949–3003.
175. Sicari R, Galderisi M, Voigt JU, Habib G, Zamorano JL, Lancellotti P *et al.* The use of pocket size imaging devices: a position statement of the European association of Echocardiography. *Eur J Echocardiogr* 2011;**12**:85–7.