Participation in regular intensive exercise is associated with a modest increase in left ventricular wall thickness (LVWT) and cavity size. The magnitude of these physiological changes is predominantly determined by a variety of demographic factors which include age, gender, size, ethnicity, and sporting discipline. A small minority of male athletes participating in sporting disciplines involving intensive isotonic and isometric exercise may exhibit substantial increases in cardiac size that overlap with the phenotypic manifestation of the cardiomyopathies. The most challenging clinical dilemma incorporates the differentiation between physiological left ventricular hypertrophy (LVH) (athlete’s heart) and hypertrophic cardiomyopathy (HCM), which is recognized as the commonest cause of non-traumatic exercise related sudden cardiac death in young (<35 years old) athletes. This review aims to highlight the distribution and physiological upper limits of LVWT in athletes, determinants of LVH in athletes, and echocardiographic methods of differentiating athlete’s heart from HCM.

Introduction

Regular participation in intensive physical exercise is associated with central and peripheral cardiovascular adaptations that facilitate the generation of a large and sustained cardiac output and enhance the extraction of oxygen from exercising muscle for aerobic glycolysis, respectively. An increase in cardiac size is fundamental to the ability to generate a large stroke volume. Over the past three decades, the athlete’s heart has been the subject of several echocardiographic studies involving many thousands of athletes. Most studies have been cross sectional in design and focused on Caucasian athletes aged 18–35 years. These studies provide insight into the magnitude and determinants of cardiac size in athletes and are invaluable in aiding the differentiation of physiological left ventricular hypertrophy (LVH) (athlete’s heart) from hypertrophic cardiomyopathy (HCM), the leading cause of exercise related sudden cardiac death in young athletes.

This review will focus predominantly on LVH, defined as an increase in left ventricular wall thickness (LVWT) >12 mm, as opposed to left ventricular mass, to place it in context with day-to-day clinical application for cardiac physiologists and clinicians. The aim of the article is to highlight the distribution of LVWT measurements in athletes, provide information on the determinants and physiological upper limits LVH, and outline echocardiographic methods of differentiating physiological LVH (athlete’s heart) from HCM in an athlete with increased LVWT.

Left ventricular wall thickness measurements in athletes

Athletic training is associated with statistically significant increases in cardiac dimensions compared with sedentary individuals. A meta-analysis of almost 1000 M-mode echocardiographic studies in highly trained male athletes showed that athletes exhibited a 15–20% increase in septal and left ventricular posterior wall thickness, respectively. Most studies have been cross sectional in design and focused on Caucasian athletes aged 18–35 years. These studies provide insight into the magnitude and determinants of cardiac size in athletes and are invaluable in aiding the differentiation of physiological left ventricular hypertrophy (LVH) (athlete’s heart) from hypertrophic cardiomyopathy (HCM), the leading cause of exercise related sudden cardiac death in young athletes.

In terms of absolute values, however, the mean LVWT in athletes was between 10 and 11 mm and fell within the normally accepted range for sedentary individuals.

Subsequent two-dimensional echocardiographic studies in large cohorts of highly trained athletes have shown that the vast majority has an LVWT ≤12 mm and would not normally be considered to have LVH. However, a small minority of athletes exhibit substantial increases in the magnitude of LVWT measurements that overlap with those observed in patients with morphologically mild HCM. In an Italian study of 947 Italian Olympian athletes, 1.7% had an LVWT exceeding 12 mm. A more recent study of 3000 highly trained British athletes revealed that 1.5% of athletes exhibited an LVWT >12 mm² (Figure 1). The maximal value for LVWT in both studies was 16 mm suggesting that an athlete with a maximal LVWT >16 mm may be considered to have pathological LVH, although there have been isolated reports of LVH of up to 19 mm in some ultra-endurance athletes.
Determinants of left ventricular hypertrophy in athletes

The magnitude of LVH in an athlete is largely determined by demographic factors including age, gender, ethnicity, size, and type of sporting discipline in which that athlete participates. Athletes with LVH (maximal LVWT > 12 mm) are invariably males aged >16 years old. In a study of over 1000 female Italian athletes, the largest LVWT recorded was 12 mm. A more recent study of over 700 adolescent British athletes participating in a variety of ball, racket, and endurance sports showed that none of the athletes aged >16 years old exhibited an LVWT > 11 mm. In this study only three (0.4%) athletes had an LVWT ≥ 12 mm and all were aged ≥ 16 years old (Figure 2). The inability of female athletes to develop very marked increases in LVWT is likely to be related to lower circulating androgen levels. Adolescent athletes aged <16 years old are relatively physically immature and lack the ability to train at similar work loads to adult athletes. Furthermore, adolescent athletes have usually been participating in intensive exercise for a shorter duration.

The sporting discipline is an important determinant of LVH in athletes. Athletes participating ultra-endurance sport with a high isotonic and isometric component such as rowing, canoeing, swimming, cycling, and ultra-endurance running exhibit the greatest increases in LVWT. In the Italian study of 947 Olympian athletes, all 15 athletes (1.7%) with LVH participated in either rowing, canoeing, or cycling. Contrary to popular belief, athletes participating in pure isometric sports such as weight lifting or wrestling rarely exhibit an LVWT > 12 mm. Within any sporting discipline, the size of the athlete is an important determinant of measurement; a body surface area >2.0 m² increases the probability of identification of LVH.

There is emerging evidence that ethnicity may have an impact on LVWT measurements in athletes. An initial study of 260 black American inter-collegiate athletes showed that 13% of the athletes exhibited LVH, with LVWT measurements ranging from 13 to 18 mm. A more recent study, utilizing more modern echocardiographic technology with enhanced endocardial resolution, compared LVWT measurements in 300 black male athletes competing at regional or national level with 300 white male athletes of similar calibre. The two groups were of similar age and size and participated in football, rugby, tennis, boxing, sprinting, and athletics in equal proportions. The study revealed that 18% of black athletes exhibited LVH compared with just 4% of Caucasian athletes. Furthermore, 3% of black athletes had LVH > 14 mm compared with none of the Caucasian athletes (Figure 3). However, in concurrence with large studies in Caucasian athletes, none of the black athletes exhibited LVH > 16 mm. The black athletes had greater LVWT measurements compared with white athletes in every sporting discipline examined. The two groups of athletes did not differ in basal or peak exercise blood pressure measurements indicating that genetically mediated racial factors, rather than haemodynamic factors, contribute to the greater magnitude of LVH in response to the increased cardiac preload and after load associated with exercise.

Physiological left ventricular hypertrophy (athlete’s heart) or hypertrophic cardiomyopathy

A small minority of highly trained athletes exhibit substantial LVH, with values between 13 and 16 mm, which overlaps
with values observed in 10–15% of patients with morphologically mild HCM. Although the vast majority of individuals with HCM are unable to excel in sport due to the cardiac handicap, the disorder displays marked morphological and functional heterogeneity and some affected individuals are capable extraordinary athletic achievements.13

An athlete with LVH between 12 and 16 mm represents a grey zone between the extremes of physiological adaptation and mild expression of HCM. The differentiation between physiological LVH (athlete’s heart) and HCM is crucial, when one considers that HCM is the commonest cause of non-traumatic sudden death in sport among young athletes.6 An erroneous diagnosis has the potential for serious consequences. A false diagnosis of HCM mandates disqualification from most sporting disciplines to minimize the risk of sudden death14,15 and has profound physical, social, and psychological consequences. Conversely, an incorrect diagnosis of athlete’s heart may jeopardize a young life.

The differentiation between the two entities is usually straightforward but in some circumstances may be challenging for even the most able cardiologist. Systematic evaluation consisting of a detailed physical and family history, the demographics of the athlete, 12-lead ECG, and echocardiography are mandatory first-line investigations. Subsequent investigation with cardiopulmonary exercise testing, cardiac magnetic resonance imaging (MRI), assessment following detraining and screening for causal genetic mutations for HCM may be necessary in equivocal cases (Table 1).

**History and demographics**

The presence of angina, breathlessness that is disproportionate to the amount of exercise being performed, palpitations, dizziness, or syncope during exertion in an athlete with LVH are ominous symptoms and highly suggestive of pathology rather than physiology. A family history of HCM in a first-degree relative in an athlete with LVH should raise the suspicion of HCM, because the disorder is inherited as an autosomal dominant trait.16 The demographics of an athlete are pertinent when attempting to differentiate athlete’s heart from HCM. The identification of LVH in a female athlete are pertinent when attempting to differentiate athlete’s heart from HCM. The identification of LVH in a female athlete, any adolescent athlete aged <16 years old or any athlete participating in low intensity endurance sports is highly indicative of HCM, since all studies in the past three decades have confirmed LVH in adult male athletes participating in highly intensity endurance sports.1–5

**Echocardiography**

Echocardiography is pivotal in the differentiation between physiological LVH and HCM in a highly trained athlete. Information relating to the magnitude and distribution of LVH, left ventricular cavity size, associated left ventricular outflow obstruction, and indices of diastolic function is essential to resolve the diagnostic predicament.

On the basis of the large cohort studies, the physiological upper limit for LVH in a highly trained athlete is 16 mm.1,4,7 Therefore, LVH >16 mm should be considered pathological unless co-existing echocardiographic features or subsequent investigations indicate otherwise. Physiological LVH is homogeneous and symmetrical; athletes rarely exhibit differences of >2 mm between adjacent left ventricular myocardial segments and the ratio of the inter-ventricular wall thickness to the left ventricular posterior wall thickness in end-diastole is <1.5:1.17 In contrast, almost any pattern of hypertrophy is possible in HCM and contiguous portions of the left ventricle vary in the magnitude of LVH. Most individuals (60%) with HCM demonstrate asymmetrical septal hypertrophy and 10% reveal hypertrophy confined to the left ventricular apex.18

The left ventricular cavity size is the single most important discriminator between physiological LVH and HCM. Almost all athletes with physiological LVH have concomitant enlargement of the left ventricular cavity (Figure 4). Typical values of left ventricular cavity size in athletes with LVH range between 55 and 65 mm,15 although in our experience ~10% of athletes with LVH exhibit normal left ventricular cavity size.20 HCM is characterized by disparity between the magnitude of LVH and the left ventricular cavity size; LVH occurs at the expense of left ventricular cavity size. Most individuals with HCM have a small left ventricular cavity (<45 mm). In contrast with athletes, a dilated ventricle in HCM patients is a marker of end stage disease due to progressive myocardial fibrosis and is associated with impaired systolic function and significant functional limitation.21

**Table 1 Clinical features indicative of pathological left ventricular hypertrophy in the assessment of an athlete with a left ventricular wall thickness between 13 and 16 mm**

| Symptoms | Unexplained syncope—particularly during exercise
| Palpitations
| Shortness of breath disproportionate to the exercise performed
| Dizziness
| Chest pain
| Family history |
| Demographics |
| HCM in a first-degree relative
| Age <16 years old
| Female sex
| Participation in purely isometric sport
| Small body surface area
| Echocardiography |
| Left ventricular wall thickness >16 mm
| Asymmetrical septal hypertrophy
| Small left ventricular cavity diameter in end-diastole
| Presence of systolic anterior motion of the mitral valve leaflet and associated left ventricular outflow obstruction
| Abnormal indices of diastolic function
| Pathological Q-waves
| ST segment depression
| Left bundle branch block
| T-wave inversions in the lateral/inferior leads
| Cardiopulmonary exercise testing |
| Peak VO2 max <50mL/kg/min or <120% of predicted maximum
| Cardiac MRI |
| Demonstration of apical hypertrophy
| Demonstration of significant myocardial fibrosis with gadolinium enhancement
| Detraining |
| Failure of regression of left ventricular hypertrophy

Figure 4 Typical
Approximately 25% of individuals with HCM exhibit basal, dynamic left ventricular outflow tract obstruction and up to 70% develop obstruction with exercise due to systolic anterior motion of the anterior mitral valve leaflet against the inter-ventricular septum. The phenomenon is attributed to several factors including asymmetric septal hypertrophy, a narrow left ventricular outflow tract, anteriorly displaced papillary muscles, redundant mitral valve leaflets, and hyperdynamic systolic function. The demonstration of systolic anterior motion of mitral valve leaflets and associated left ventricular outflow obstruction at rest or immediately after exercise in an athlete with LVH is considered consistent with the diagnosis of HCM.

Assessment of indices of diastolic function utilizing conventional mitral valve inflow Doppler measurements and pulmonary vein Doppler are normal in athletes who have a compliant left ventricle that is capable of filling sufficiently to maintain a high stroke volume even at almost maximal rates. In contrast, individuals with HCM have LVH associated with increased muscle stiffness due to myocyte disarray and myocardial fibrosis as well as impaired sarcoplasmic calcium kinetics resulting in impaired myocardial relaxation. Consequently early (rapid), passive left ventricular filling is impaired as evidenced by the demonstration of a reversed E:A ratio, prolonged E-deceleration time (>240 ms), or isovolumic relaxation times (>90 ms), reversed S/D ratio during pulmonary vein Doppler.

Recent studies utilizing colour coded and pulsed-tissue Doppler echocardiography have provided more sensitive and specific methods of differentiating physiological LVH from morphologically mild HCM. Measurement of myocardial velocity gradients from digitized M-mode colour Doppler reveals that individuals with HCM exhibit impaired myocardial filling during the rapid filling phase of diastole and display reduced left ventricular posterior wall myocardial velocity gradients compared with athletes. Indeed, a small study comparing 25 individuals with HCM and 21 athletes with physiological LVH indicates that a myocardial velocity gradient of $<7 \text{s}^{-1}$ measured in early diastole, may be regarded as a sensitive and specific method of differentiating individuals with HCM from athletes with physiological LVH.

Assessment of longitudinal cardiac function with pulsed-tissue Doppler at the level of the mitral valve annulus has demonstrated that individuals with morphologically mild HCM, including those with normal mitral valve inflow Doppler measurements, exhibit lower early diastolic velocities ($E_a$ or $E$) compared with athletes. An $E$ of $<9 \text{cm/s}$ favours pathological LVH with a sensitivity approaching 90%. The $E/E'$ ratio may also be useful in differentiating physiological LVH from HCM. A $E/E'$ >12 is indicative of high left atrial filling pressures, a recognized pathophysiological hallmark of HCM, however most trained athletes exhibit a $E/E'$ <8.

Our experience of differentiating physiological LVH from HCM suggests that although small studies comparing athletes with physiological LVH and those with morphologically mild LVH have derived numerical parameters of diastolic function...
that facilitate the differentiation between the two entities, none of the aforementioned indices of diastolic function can be reliably utilized to confirm or refute the diagnosis of HCM in an athlete with LVH in every case.

Measurement of systolic function using conventional methods based on the percentage change of left ventricular volume between systole and diastole has always suggested that individuals with HCM have a high systolic ejection fraction. However, in the presence of small left ventricular cavity size, modest changes in the absolute volume of the left ventricle between systole and diastole results in a significantly higher calculated percentage change. The disorder is characterized by asymmetrical abnormalities of myocardial architecture as well as patchy myocardial fibrosis; therefore abnormal systolic function should be expected. Indeed pulsed-tissue Doppler studies have shown that many individuals with HCM exhibit impaired longitudinal systolic function. The identification of a mitral valve annular peak systolic velocity of $<9$ cm/s in an athlete with LVH should raise the suspicion of underlying pathology.30

Measurement of myocardial deformation (strain imaging), by either colour coded tissue Doppler or more recently two-dimensional speckle tracking, has improved our ability to quantify regional myocardial function. A recent study31 demonstrated that in patients with HCM strain and strain rate are abnormal even in the absence of myocardial fibrosis on cardiac MRI. Conversely, studies in athletes with LVH reveal normal circumferential, radial, and longitudinal profiles32,33 raising the possibility that myocardial strain imaging is yet another echocardiographic modality that may facilitate the differentiation between athlete’s heart and HCM (Figure 5).

Role of 12-lead ECG, cardiopulmonary exercise stress testing, and cardiac magnetic resonance imaging

The cause of LVH in an athlete may remain equivocal despite thorough echocardiographic evaluation. Enormous advances in the molecular genetics of HCM in the past two decades raise the potential role of genetic testing to resolve the diagnostic dilemma. Unfortunately, the condition exhibits marked genetic heterogeneity with over 200 mutations in 12 different genetic loci and is time consuming, labour-intensive, and expensive.16 The results of genetic testing are not available to the athlete in a timely fashion and the diagnostic yield is only 60–70%, therefore a negative gene test does not exclude HCM.34 In the current era, differentiation between physiological LVH and HCM continues to rely on non-invasive clinical investigations aimed at identifying the broader phenotype of HCM. Information obtained from a 12-lead ECG, cardiopulmonary exercise testing, and cardiac MRI provides invaluable adjunctive information (Table 1). With respect to the 12-lead ECG, although both physiological LVH and HCM are associated with large QRS complexes in left ventricular leads, the additional presence of ST segment depression, deep (more than $-0.2$ mV) T-wave inversions in the lateral or inferior leads, pathological Q-waves, and left bundle branch block are highly indicative of HCM.35,36 The identification of deep T-wave inversions in the anterior and/or lateral leads is a recognized feature of apical HCM37 and should prompt detailed assessment of the left ventricular apex at echocardiography, employing the use of a contrast agent to define the endocardial borders if necessary.38 In this regard, additional imaging with cardiac magnetic resonance will provide better definition of the left ventricular apex and also prove useful in the demonstration of LVH affecting the antero-lateral free wall (which may not be visualized clearly at echocardiography).39 Gadolinium enhanced magnetic resonance may identify myocardial fibrosis in the left ventricle in some affected individuals with HCM.41

The measurement of peak oxygen consumption during an exercise test is a useful method of differentiating physiological LVH from HCM. Athletes, participating in endurance sports have large peak oxygen consumption. A peak oxygen consumption of $>50$ mL/kg/min (or $>120\%$ of that predicted for age) in an athlete with mild LVH favours physiological adaptation.40 In contrast, most individuals with HCM have a sub-normal peak oxygen consumption irrespective of the magnitude of LVH and functional capacity, since the combination of impaired myocardial relaxation associated with a small left ventricular cavity, exercise related myocardial ischaemia, and dynamic left ventricular outflow obstruction is not conducive to the generation of...
large and sustained increase in stroke volume (and therefore cardiac output).

By virtue of the diversity of the morphological and functional manifestations of HCM, there is no single investigation that will identify all athletes with HCM and diagnostic uncertainty may persist despite a plethora of cardiac investigations. In these circumstances, it is our practice to attempt to persuade the athlete to detrain for 3 months followed by echocardiographic reassessment to ensure an accurate diagnosis, on the understanding that physiological LVH should regress completely back to normal, whereas pathological LVH will persist, albeit to a lesser extent. The detraining process is understandably associated with anxiety, and costs fitness and future team selection; however, it could be argued that it is a relatively small price to pay given the risks involved with on-going participation in strenuous exercise in an individual with HCM.

Conclusion
Most athletes exhibit modest increases in LVWT that fall within the normally accepted range for the general population. However, a small proportion of large adult male athletes usually participating in sports with a high isotonic and isometric component develop substantial LVH in the range between 13 and 16 mm which overlaps with measurements observed in morphologically mild HCM. The differentiation between physiological LVH and HCM is essential but can prove clinically challenging. Echocardiography permits detailed assessment of left ventricular structure and function and is fundamental to resolving the diagnostic dilemma. Additional investigations aimed at identifying the broad phenotype of HCM may be necessary to facilitate the differentiation between physiological LVH (athlete’s heart) and HCM.

Funding
J. R. is funded by a junior cardiac research fellow grant by the charitable organisation, Cardiac Risk in the Young (CRY).

Conflict of interest: none declared.

References


