Physiological versus pathological left ventricular hypertrophy

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Abstract

Athletes commonly develop what is regarded as a benign increase in cardiac mass in response to physical training. However, prolonged training may lead to a degree of cardiac remodeling that mimics hypertrophic cardiomyopathy (HCM). Left ventricular hypertrophy (LVH) can be defined echocardiographically as a left ventricular wall thickness (LVWT) of greater than 12mm. A LVWT of 12-16mm represents a "grey zone" of overlap between physiological LVH and mild HCM. In this situation, an enlarged left ventricular (LV) cavity size (>56mm) in the absence of symptoms is highly suggestive of physiological LVH. Other markers that favor physiological LVH include normal LV diastolic function, a concentric pattern of hypertrophy, left atrial size <50mm and absence of LV outflow tract obstruction. Where diagnostic doubt remains, Holter monitoring, cardiopulmonary exercise testing, cardiac magnetic resonance imaging or trial of detraining can be considered. The correct diagnosis is essential as HCM increases an athlete's risk of sudden cardiac death and may result in disqualification from professional sport.

Keywords: left ventricular hypertrophy; hypertrophic cardiomyopathy; athlete's heart; echocardiography.

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Basic Article

Introduction

Athletes commonly develop what is generally regarded as a benign increase in cardiac mass with associated circulatory and morphological changes in response to physical training. However, prolonged conditioning may eventually result in a degree of cardiac remodeling that mimics certain pathological conditions including hypertrophic cardiomyopathy (HCM).

Echocardiography is fundamental in the assessment of left ventricular hypertrophy (LVH), which is defined as a left ventricular wall thickness (LVWT) greater than 12mm [1,2]. A meta-analysis of almost 1000 echocardiographic studies of highly trained male athletes demonstrated that athletes exhibited a 15–20% increase in septal and left ventricle (LV) posterior wall thickness [3]. A small proportion of athletes may have a LVWT comparable to or overlapping with mild forms of HCM.

The differentiation between HCM and physiological LVH is crucial as HCM accounts for one third of all exercise-related sudden cardiac deaths (SCD) in trained athletes under the age of 35 years [4]. African-Americans account for a disproportionate number of sudden cardiac deaths due to previously undiagnosed HCM [5].

Pathophysiology

Cardiovascular adaptations to training depend upon the form of exercise undertaken. The initial response to isotonic (endurance) training, such as long-distance running and swimming, includes increased maximum oxygen consumption, cardiac output and systolic blood pressure, with an associated decrease in peripheral vascular resistance [6]. Long-term effects include increased maximal oxygen uptake due to increased cardiac output and arteriovenous oxygen difference. The net effect is a volume loaded left ventricle with an increased cardiac output in order to generate a sufficiently large stroke volume.

In contrast, isometric (strength) training, such as wrestling and weight training, causes only mildly increased oxygen consumption and cardiac output in the acute phase, with significant increase in blood pressure, peripheral vascular resistance and heart rate [6]. Long-term, there is no significant increase in oxygen uptake and the net effect is a pressure loaded left ventricle.

Sports such as cycling, rowing and football are examples of combined isotonic and isometric exercise and therefore athletes participating in these sports show a combination of the above responses to varying degrees.

HCM is the commonest genetic heart muscle disease. It is caused by gene mutations encoding proteins within the cardiac sarcomere. Affected individuals exhibit a broad range of phenotypes but typically show a hypertrophied, non-dilated LV in the absence of other causes. LVWT and the extent of LVH may vary from mildly elevated (13–15mm) to massive (>50mm) [7].

At a cellular level, HCM is associated with myocyte disarray, myocardial fibrosis and extravascular collagen deposits. The ventricle is stiff with impaired myocardial relaxation due to abnormal sarcoplasmic calcium kinetics [3]. This results in impaired LV filling and echocardiographic evidence of diastolic dysfunction.

The prevalence of HCM in the general population is 0.2% [8]. The estimated prevalence in athletes is 0.07% based on the Italian pre-participation screening program involving over 34,000 athletes [9]. At least 10% of adolescent patients with HCM may be at unacceptably high risk of sudden cardiac death [10].

The assessment of patients with LVH

History and examination

Patients with HCM may report a family history of sudden cardiac death, an important marker of increased risk in this patient group. Persons with athletic hypertrophy are much less likely to give such a history. There are no specific physical findings distinguishing an athlete with pathological from non-pathological hypertrophy.

12-lead ECG

Approximately 40% of trained athletes have an abnormal resting ECG [6]. The most commonly reported alterations are early repolarization patterns, increased QRS voltages, diffuse T-wave inversion, and deep Q waves. T-wave inversion beyond lead V2 raises the possibility of pathological LVH although there is evidence to suggest that T-wave inversion in V1–V4 should be considered a normal variant in African-American athletes [10].

ECG changes that may suggest HCM rather than physiological LVH include left bundle branch block (LBBB) and ST depression or deep T wave inversion (>0.2mV) in two contiguous leads [7].

Echocardiography

Many large studies have been performed assessing the echocardiographic features of the hearts of trained athletes.

It has been shown that athletes have a significantly greater maximal LVWT, end-diastolic cavity size and LV mass compared to non-athletic controls [11]. Of 720 adolescent athletes, 5% had LVWT greater than upper limit of normal (normal 9-12mm depending upon age and gender). All of these athletes had concentric LVH with greater than predicted LV end-diastolic cavity size and normal mitral inflow velocity patterns [11].

Ethnicity and gender may have an impact on LVWT measurements in athletes. A study of 300 black male athletes and 300 white males athletes showed a prevalence of LVH (LVWT >12mm) of 18% in black athletes compared to 4% in white athletes [3]. Athletes with LVH tend to be males aged over 16 years. A study of over 1000 female Italian athletes had a largest recorded LVWT of 12mm [12].

There exists a so-called “grey-zone” of overlap between physiological LVH and mild HCM in terms of LVWT. This “grey zone” of 12–16mm is present in 2%

of highly trained athletes [7,13] and clearly presents a diagnostic dilemma. In this situation, LV cavity size is the single most important discriminator between physiological LVH and HCM with an enlarged cavity size in the absence of symptoms being highly suggestive of physiological LVH [3]. LV dilatation is recognized in HCM but this is usually a manifestation of end-stage disease associated with New York Heart Association functional class III or IV [14]. Where the LV cavity size is not enlarged, a number of features can be used to differentiate HCM from physiological LVH (Table 1).

HCM is associated with diastolic dysfunction. Echocardiographically, this may manifest as reversed E:A ratio, prolonged E deceleration time (>240ms), low early diastolic velocities (*E'*<9cm/s) or reversed S/D ratio on pulmonary vein Doppler. Additionally, *E/E'*>12 is a hallmark of HCM, and is indicative of raised left atrial filling pressures. Most trained athletes have a *E/E'*<8 [3]. Left atrial size is often mildly increased in athletes, with up to 50mm in men and 45mm in women rarely being associated with pathological conditions [15]. A left atrial size greater than 50mm in adult athletes raises the possibility of pathological LVH.

Physiological LVH produces a concentric pattern of hypertrophy with a septum to posterior wall ratio of less than 1.5:1 [15] (Fig. 1). Asymmetrical septal hypertrophy, defined as a septum to posterior wall ratio of 2:1 or greater, is diagnostic of HCM (Fig. 2). LV outflow tract obstruction caused by systolic anterior motion of

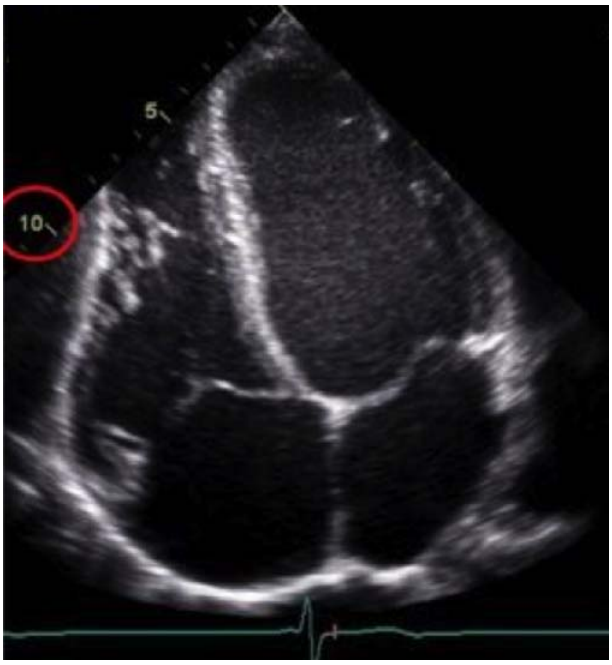

Fig. 1 *Athletes heart with dilated LV cavity and overall increased LV mass.*

	Features suggestive of athlete's heart	**Features suggestive HCM**
History	No family history of HCM/SCD	Positive family history HCM/SCD
ECG	ST changes and T wave inversion isolated to V1 and V2	ST depression or T wave inversion in 2 contiguous leads (except V1 and V2), LBBB
Echo LV wall thickness	<12mm	>16mm
Echo LV cavity	>56mm	<56mm
Echo diastolic function	*E/E'* < 8	*E/E'* > 12
	E'>9cm/s	*E'*<9cm/s
	Normal E:A ratio	Reversed E:A ratio
	E deceleration time<240ms	E deceleration time>240ms
Echo LA size	<50mm	>50mm
Echo LVOT velocity	Normal	Obstruction due to systolic anterior motion of AMVL
CPEX	Peak O_2>50ml/kg/min	Peak O_2<50ml/kg/min
Holter	No NSVT	NSVT
CMR	No post-gadolinium enhancement, Uniform hypertrophy	Post-gadolinium enhancement, Asymmetrical hypertrophy
Impact of deconditioning	2-5mm reduction in LVWT	No change

Table 1 *Features that help distinguish a normal athletes heart from a cardiomyopathy.* HCM *hypertrophic cardiomyopathy,* SCD *sudden cardiac deaths,* LBBB *left bundle branch block,* AMVL *anterior mitral valve leaflet,* NSVT *non-sustained ventricular tachycardia,* LVWT *left ventricular wall thickness.*

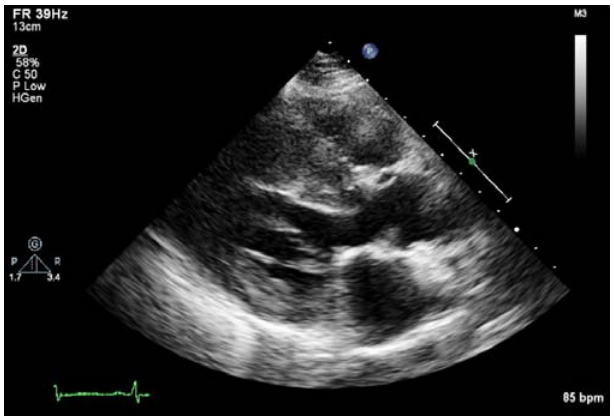

Fig. 2 Hypertrophic cardiomyopathy (HCM) with asymmetrical hypertrophy and reduced LV cavity size.

the anterior mitral valve leaflet (AMVL) is also suggestive of HCM [13].

Further tests may be considered in situations where the diagnosis remains unclear following clinical assessment, ECG and echocardiography (Fig. 3).

Holter monitoring

Holter may be useful to identify episodes of non-sustained ventricular tachycardia (NSVT) that may suggest a pathological cause for LVH.

Cardiopulmonary exercise testing (CPEX)

Most individuals with HCM have low peak oxygen consumption irrespective of symptom status [16]. This is in contrast to high peak oxygen consumption in those with physiological LVH. A peak oxygen consumption > 50 ml/kg/min favors physiological adaption [3]. Exercise testing is also useful in identifying abnormalities in exercise blood pressure response and exercise induced arrhythmias.

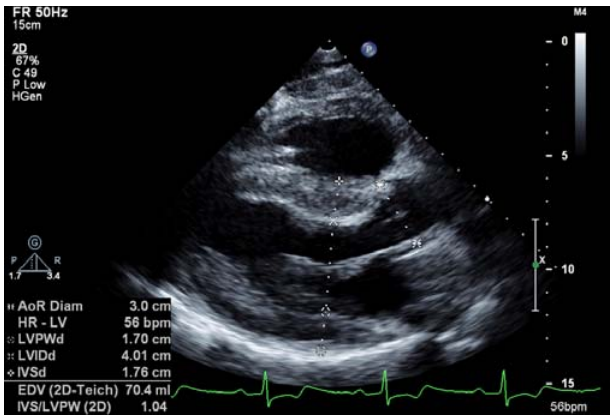

Fig. 3 Equivocal case of 23-year old with symmetrical left ventricular hypertrophy (LVH) and no family history of hypertrophic cardiomyopathy (HCM). However, LV cavity size is normal and there is also evidence of LV diastolic dysfunction.

Cardiac magnetic resonance imaging (MRI)

Cardiac MRI can be a useful adjunct to echocardiography in some cases. The superior image quality can identify segmental LV hypertrophy diagnostic of HCM. This may be present in the anterolateral free wall, posterior ventricular septum or the apex. In addition, the demonstration of delayed post-gadolinium enhancement is indicative of replacement fibrosis [17].

Physical deconditioning

Where the diagnosis remains unclear despite other tests, 3 months deconditioning with serial echocardiography or cardiac MRI may be useful. In physiological LVH, deconditioning would be expected to result in a reduction in wall thickness of 2–5mm. Whilst this option may confirm a diagnosis, it can have a quite significant impact on the athlete in terms of physical conditioning and inability to compete for this period, as well as psychological consequences. Understandably, many athletes are reluctant to pursue this option, and discussions regarding this should be handled sensitively.

Impact of diagnosis

The differentiation of physiological LVH from HCM is essential, as athletes with unequivocal or probable HCM should abstain from competitive sport and vigorous training. The identification of cardiovascular disease associated with sudden cardiac death may be basis for disqualification from a sport in order to minimize risk [18]. Additionally, inaccurate diagnosis of HCM may result is unnecessary withdrawal from sport, potentially resulting in both psychological distress and economic losses to the individual [7].

Many professional sporting bodies have adopted screening programs in an effort to identify those at risk of sudden cardiac death. These programs include 12-lead ECG and echocardiogram as a minimum, often with other additional tests. Some countries, such as Italy, have mandatory nationwide programs for professional athletes.

Summary

LVH is usually a normal physiological consequence of regular athletic training. However, a small proportion of

athletes demonstrate LVH which is in fact due to the presence of HCM, and which may put them at unacceptable risk of sudden cardiac death during competitive sport. The current mainstay of investigation is 12-lead ECG and echocardiography, with the use of additional tests where diagnostic doubt remains. Clearly, correct diagnosis is essential as the stakes are high and diagnosis of HCM usually results in disqualification from professional sport. A thorough and accurate assessment is essential to minimize the risk of serious cardiac events in this population group. Appropriate and effective imaging enables the differentiation of benign from pathological causes of LVH in the majority of cases. •

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