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Imaging in hypertensive heart disease

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Abstract

Hypertensive heart disease is the target organ response to arterial hypertension. Left ventricular hypertrophy represents an important predictor for cardiovascular events. Myocardial fibrosis, a common end point in hypertensive heart disease, has been linked to the development of left ventricular hypertrophy and diastolic dysfunction. Echocardiography is clinically useful in the detection of left ventricular hypertrophy and the assessment of diastolic function. Although echocardiography is more widely available, cardiac magnetic resonance has been demonstrated to be more reproducible for the estimation of left ventricular mass. Future developments in cardiac magnetic resonance techniques may facilitate the quantification of diffuse fibrosis that occurs in hypertensive heart disease. Thus, advances in cardiac imaging provide comprehensive, noninvasive tools for imaging left ventricular hypertrophy, diastolic dysfunction, myocardial fibrosis and ischemia observed in hypertensive heart disease. The objective of this article is to summarize the state-of-the-art and the future of multimodality imaging of hypertensive heart disease.

Keywords

cardiac magnetic resonance; diastolic function; echocardiography; hypertension; hypertensive heart disease; left ventricular hypertrophy; left ventricular mass; myocardial fibrosis

Hypertensive heart disease (HHD) is the target organ response to systemic arterial hypertension. Patients with longstanding hypertension are at increased risk for developing left ventricular hypertrophy (LVH) and diastolic dysfunction [1]. Arterial hypertension represents one of the most common risk factors for the development of heart failure, conferring approximately a twofold increased risk in men and a threefold risk in women relative to normotensive subjects [2]. This article summarizes the state-of-the-art and the future of multi-modality noninvasive imaging in HHD with a focus on imaging LVH, diastolic dysfunction, myocardial fibrosis and ischemia secondary to hypertension.

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Why is HHD important?

Left ventricular hypertrophy develops as an initially adaptive response of the normal heart to an increased afterload from a variety of reasons, systemic hypertension being the most common. Data from the Framingham Heart Study has established LVH as a risk factor for cardiovascular morbidity and mortality, independent of other cardiovascular risk factors, including blood pressure (BP) itself [4,5]. LVH regression during treatment [6] has translated to improvement in cardiovascular outcomes [7,8]. It is therefore important to identify patients with LVH, both for prognosis and for tighter BP control. Ventricular arrhythmias occur more frequently in hypertensive patients [9], with QT dispersion increasing directly with left ventricular mass (LVM) [10]. There is also a link between HHD and atrial fibrillation, whose likelihood increases by 40–50% in the presence of hypertension [11]. Increased susceptibility to ischemic heart disease rounds out the cardiovascular sequelae of HHD, with a sixfold higher risk of myocardial infarction in hypertensive patients than in normotensive individuals [2].

Imaging hypertensive LVH

LV mass

The identification of LVH in the hypertensive patient is important from a prognostic standpoint. It identifies the patient with hypertension who may require more aggressive BP control. In patients with essential hypertension and baseline LVH on ECG, lower LVM during antihypertensive treatment is associated with lower rates of clinical end points, independently of the effects of BP lowering and treatment modality [12].

The calculation of LVM on echo is based on a mathematical formula:

$$LVM = 0.8 \left(1.04 \left[(LVIDD + PWTD + IVSD)^3 - (LVIDD)^3 \right] \right) + 0.6g$$

as modified by Devereux *et al.* using the American Society of Echocardiography convention [13], where LVIDD is left ventricle internal dimension in diastole, PWTD is posterior wall thickness in diastole and IVSD is intraventricular septal thickness in diastole. This modified formula was validated on necropsy findings in 52 subjects [13]. **Table 1** shows previously published cut-off values for LVH and LVM evaluated by echocardiography and cardiac magnetic resonance (CMR).

Relative wall thickness

Relative wall thickness (RWT) is measured in clinical studies as:

$$\frac{(IVSD + PWTD)}{LVIDD}$$

The reference cut-off value for increased RWT derived from upper limits of normal samples is usually 0.45 [14]. RWT provides information regarding LV geometry independent of other calculations [15], precluding the requirement of most corrections. LV geometry as

evaluated by RWT may provide an independent stratification of LV systolic and diastolic functions in essential hypertension [15]. Measurements of LV mass and RWT are prognostically important in the hypertensive patients without LVH. In the Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) study, patients with inappropriately high but nonhypertrophic LV mass had a higher RWT and BMI. It was observed that inappropriately high LV mass was associated with relevant, often preclinical, manifestations of cardiac disease in the absence of traditionally defined echocardiographic LV hypertrophy and concentric geometry [16].

Geometric patterns of LV remodeling in hypertension

Different geometric forms of LVH have been adopted to classify the maladaptive responses of the LV in hypertension [14,17]. LV geometry is classified into four exclusive groups (**Figure 1**; [18]) on the basis of LVM and RWT: concentric LVH (increased mass and increased RWT), eccentric LVH (increased mass and normal RWT), concentric remodeling (normal mass and increased RWT) and normal geometry (normal mass and normal RWT). Concentric hypertrophy carries the highest risk and eccentric hypertrophy an intermediate risk, whereas concentric remodeling is associated with a smaller, albeit important risk [19,20].

Echocardiography to assess LVH in HHD

The prevalence of LVH on echocardiography in hypertensive patients has been reported to be approximately 40% [21,22]. Both M-mode (**Figure 2**) and 2D echocardiography are used in the measurement of LVM. M-mode echocardiography has the advantage of superior endocardial definition, as the high frame rate improves the spatial resolution. M-mode echocardiography was the first echo method to be validated and it is relatively simple and quick. The M-mode method measures the left ventricle (LV) in one dimension and assumes a prolate ellipsoid shape for the LV with a ratio of long:short axis lengths of 2:1. The M-mode method will detect all but the mildest degrees of LVH.

However, the accuracy and reproducibility of M-mode echocardiography at measuring LVM has been debated. There is a potential for variations in measured wall thickness, depending on the ultrasound beam angle to the LV wall and the assumption that the wall thickness is uniform throughout the LV. In addition, the assumed prolate ellipsoid shape of the LV is no longer valid in patients with LVH [23]. Furthermore, LVM as measured by M-mode echocardiography relies on linear measurements of wall thickness [12], which, when cubed, increase the standard deviation (SD) by a factor of 2–3. As elevated LVM is defined as mean +2 SD, M-mode echocardiography has the potential to underestimate the prevalence of LVH in hypertensive cohorts (**Table 1**) [24,25].

Two dimensional echocardiography (**Figure 3**) is thought to be more accurate and reproducible than the M-mode method [26], and is now more commonly used for LVM measurements. 2D echocardiography relies on mathematical formulae to estimate the LVM but there is no cube function in these formulae and hence measurement errors are not magnified. However, it still assumes a prolate ellipsoid shape of the LV and a uniform LV wall thickness.

3D echocardiography for LVH assessment

3D echocardiography has improved the intra- and inter-observer variability of the LVM measurements compared with M-mode and 2D echocardiography [27], with its accuracy reported to be close to that of CMR [28]. Quantification of LVM using real-time 3D echocardiography is highly reproducible and correlates well with CMR [29]. In contrast to M-mode and 2D echocardiography, 3D echocardiography does not rely on geometrical assumptions for calculating LVM [29]. The second-generation real-time 3D technology that offers second-generation matrix array probes with 3000 simultaneously active ultrasound elements has solved the acquisition difficulties, while advances in computer technology and analysis software have shortened the duration of postprocessing [30]. However, superior-quality 3D images are still dependent on optimal echo windows and up to a third of patients have suboptimal echo windows for this purpose.

CMR for LVH assessment

As discussed previously, the cubing of the measurements for LV wall thickness when using M-mode echocardiography amplifies any errors of such measurements, resulting in a significant variation of LVM estimates compared with direct measurement using techniques such as CMR [31,32]. CMR has been demonstrated to be more reproducible than either M-mode or 2D echocardiography measurements [32–34] for the estimation of LVM [35,36]. It provides a spatially defined 3D dataset at multiple levels throughout the heart, and hence the measurement of LVM does not require geometric assumptions about the shape of the LV. CMR has been validated in animal studies [37–39] and the excellent contrast between blood, and myocardial tissue and the high spatial resolution means that the endocardial and epicardial contours are easily defined. Presently, the methodology of choice for measuring LVM by CMR is steady-state free precession (SSFP) cine imaging (**Figure 4**). The absolute values of LVM measured by CMR tend to be lower than those for echocardiography (**Table 1**) because SSFP cine imaging allows the visualization of myocardial trabeculae and thus includes trabeculae in the LV volume measurement excluding it from the mass. Echocardiography, however, generally includes trabeculation in the measurement of LV mass. Although CMR has excellent reproducibility for measuring LVM and is widely perceived as the gold standard, its accuracy has not been validated against necropsy LV weight in humans.

Implications for clinical trials

Echocardiography has been successfully used in large clinical trials and has provided a wealth of knowledge in patients with hypertensive LVH [12,40]. Although 2D echocardiographic determination of LVM is useful in identifying patients with severe LVH, its high measurement variability impairs its value in the subgroup of hypertensive patients with milder concentric and/or eccentric LVH, and in those with concentric remodeling. Demonstration of LVM regression using M-mode or 2D echocardiographic methods requires relatively large cohorts of patients because of the relatively high observer and interstudy variability [41]. CMR or 3D echocardiography should be the techniques of choice in clinical trials investigating LVM regression where the accuracy of LVM measurements

will allow for the accurate detection of small degrees of change in LVM in smaller cohorts of patients, particularly when recruitment of large numbers of patients is not possible.

Cardiac magnetic resonance can also demonstrate parallel reductions in LV mass and chamber volume with normalization of LV ejection fraction during a relatively brief period of improved BP control with multiple agents that interrupt the hypertrophic stimuli from the RAAS. Particularly notable is the short duration of treatment required to detect such changes using a highly reproducible method such as CMR [42,43]. Echocardiographic studies of LVH regression have typically required longer treatment periods to demonstrate LVH regression as well as larger sample sizes. **Table 2** lists the advantages and disadvantages of the various methods currently available to assess LVH.

Assessment of intramyocardial function in HHD

Intramyocardial strain is a complex marker of the effect of hyper-trophy on myocardial mechanics. In hypertrophy, changes in gene expression, contractile protein kinetics, calcium handling and metabolism all occur and might contribute to reduced myocardial deformation, which initially may be adaptive. However, over the longer term it may affect global myocardial performance and prognosis. LV midwall shortening (MWS), an indirect measure of myocardial performance assessed by transthoracic echocardiography, is decreased in a subset of patients with hypertensive LVH [44]. These patients are at increased risk for cardiovascular events despite normal endocardial fractional shortening [45].

Echocardiographic calculation of MWS is a geometry-based index derived from linear measurements of the posterior and the septal walls, and consequently cannot distinguish between septal versus posterior wall function. Thus, whether depressed MWS represents global or regional intrinsic depression of LV myocardial function in pressure-overload hypertrophy is unknown. Previous experiments demonstrated that increased LV pressure could have dissimilar effects on regional LV wall stress because of different radii of curvature, resulting in regional mechanical heterogeneity caused by dissimilar afterload [46].

Cardiac magnetic resonance tissue tagging allows intramyocardial displacement and strain to be measured noninvasively by monitoring motion of identifiable material points distributed throughout the myocardium [47–49]. MWS is depressed in hypertensive LVH as demonstrated by CMR myocardial tagging [50]. The advent of Harmonic Phase imaging [51] has enabled the use of this technique in large epidemiologic studies such as the Multi-Ethnic Study of Atherosclerosis (MESA). In this cohort study designed to investigate the nature of atherosclerosis in asymptomatic individuals, a total of 1184 participants (aged 45–84 years) underwent tagged CMR. Regional LV function was quantified by analyzing peak systolic circumferential strain (Ecc). Higher diastolic BP (DBP) was associated with lower Ecc ($p = 0.002$). The study concluded that higher DBP and smoking are associated with decreased regional LV function in asymptomatic individuals [52]. The association between reduced regional LV function and higher DBP was substantially attenuated after controlling for LV mass, underscoring the importance of LVH in the development of regional LV dysfunction.

Diastolic dysfunction in HHD

Diastolic dysfunction is one of the earliest manifestations of HHD. It refers to abnormalities in the mechanical properties of the heart, such as decreased diastolic distensibility, slowed filling or relaxation of the LV – regardless of whether the LVEF is normal or abnormal, and whether the patient is symptomatic or asymptomatic [53,54]. Diastolic dysfunction is estimated to affect approximately 50% of hypertensive patients in the community [55] and correlates with the development of LVH [56,57]. Patients with longstanding hypertension are at increased risk for developing LVH-associated abnormalities of myocardial relaxation, which contribute to abnormal LV filling in diastole and elevated intracardiac filling pressures [57].

As discussed previously, the prediction of cardiovascular morbidity and mortality in hypertensive individuals may be independent of BP itself [58]. The abnormal compliance of the LV with increased filling pressures for a given volume and higher incidence of subendocardial ischemia with associated diastolic dysfunction are a few of the many postulated mechanisms for the deleterious effects of LVH.

Importance of imaging diastolic function in HHD

Adequate control of arterial pressure in hypertensive patients should favorably alter loading conditions in the short term, while, in the long term promote regression of hypertrophy. Diastolic dysfunction in HHD improves as LVH regresses [59]. Interestingly, abnormalities of diastolic function can also be detected by sensitive imaging techniques in the absence of LVH, thus suggesting that these abnormalities could precede or develop independently of LVH. The benefits of LVH regression in hypertensive individuals appear to be independent of and additive to the effects of BP lowering [12], suggesting that the improvement in diastolic dysfunction with LVH regression may play a role.

Echocardiography for diastolic dysfunction

Generally, in early hypertension there is delayed relaxation of the myocardium because of hypertrophy and mild degrees of stiffening, affecting the peak early filling (E-wave) and late diastolic filling (A-wave) velocities of the mitral valve inflow, manifested as a reduced E/A ratio. In severe, long-standing hypertension, the LV can develop systolic dysfunction as well. At this point, there may be evidence of more advanced diastolic dysfunction with a normal or high E/A ratio, representing pseudo-normal filling or a restrictive physiology.

Until recently, the most widely accepted and utilized method to assess LV diastolic function noninvasively has been assessment of transmitral inflow or pulmonary venous flows utilizing Doppler echocardiography [60,61]. Neither of these techniques evaluate LV relaxation directly. Instead, they measure the impact of altered LV diastolic properties by assessing diastolic flow velocities that result from pressure gradient changes at the mitral orifice, and systolic and diastolic flow velocities in the pulmonary veins, respectively. These conventional Doppler assessments are very much load-dependent, and as such can change dramatically due to small alterations in heart rate or ventricular preload [62,63].

Tissue Doppler imaging (TDI) is a relatively new technique that allows direct quantification of mitral annular velocities. TDI can measure early diastolic mitral annular velocity (Ea), and a late (atrial contraction) diastolic mitral annular velocity (Am) (**Figure 5**) [64]. Nagueh *et al.* and others have reported that, although transmitral Doppler E-wave velocity is altered by changes in preload or left atrial pressures [65], Ea at the lateral left ventricular base does not change significantly, and effects of preload can be corrected by a ratio of E/Ea [66].

Strain & strain rate

These measures provide a more detailed characterization of myocardial mechanics and may reveal subclinical abnormalities earlier in HHD than is apparent by the detection of LVH or overt DD. It should be emphasized that reduced strain and strain rate, which is a sensitive marker for preclinical HHD, are nonspecific and have also been reported in preclinical infiltrative and hypertrophic cardiomyopathy, and are likely to be present in a broad range of other disease states as well. Thus, strain and strain rate data must be put in context of the clinical situation.

2D-speckle imaging

Newer methods, such as 2D-speckle imaging, appear to provide a direct angle- and geometry-independent measure of circumferential strain (ϵ) [67]. A principal advantage of speckle tracking imaging is that it offers measurements of strain that, unlike tissue Doppler, are not dependent on insonation angle. Amundsen *et al.* showed a good correlation between longitudinal 2D strain values and those obtained by CMR tagging [68]. This method permits measurement of the three principal systolic strains: circumferential, longitudinal and radial. Narayanan *et al.* noted that HHD with normal ejection fraction is associated with reduced myocardial velocities and reduced regional function but normal global systolic strain (ϵ) [69]. Velocity abnormalities occur early in hypertension and may be an appropriate target for preventive strategies because they occur before abnormalities in global ϵ [69]. These data suggest that velocity abnormalities occur relatively early in hypertensive subjects, are associated with (or even responsible for) diastolic filling abnormalities, and thus may be a target for preventive strategies [70].

CMR for diastolic dysfunction

There is homology between CMR and transthoracic echo-cardiography for the assessment of diastolic inflow, with excellent agreement of quantitative velocity measurements [71]. Diastolic blood flow assessment by CMR can be performed in a single scan, either in a single breath-hold or averaged over approximately 3 min. This can be part of a routine CMR examinations, either as an adjunctive test when evaluating systolic function or even as a primary test when echocardiographic data cannot be obtained. Thus, CMR has a demonstrated potential to define diastolic function and quantify its properties in terms of active and passive stages, and its relaxation and compliance characteristics. CMR is also useful for assessing inflow and myocardial velocities, and revealing properties of the chamber and myocardium [72], thus providing insights not fully available with other invasive and noninvasive strategies.

Myocardial fibrosis

A common end point of many cellular and noncellular pathologic processes in HHD is myocardial fibrosis. Fibrosis quantification in endomyocardial samples obtained via transjugular biopsy showed a significantly greater collagen volume fraction in patients with hyper-tension than in normotensive controls [73]. Myocardial fibrosis in animals is associated with worsening ventricular systolic function, abnormal cardiac remodeling and increased ventricular stiffness [74]. The link between collagen turnover and myocardial fibrosis is not fully understood, but it is thought to play an important role in the development of diastolic dysfunction [75,76].

Imaging myocardial fibrosis

Various imaging techniques have emerged to quantify myocardial fibrosis noninvasively. Echocardiography with integrated backscatter show good correlation with collagen volume fraction, recognizing that slightly less than half of patients may have suitable backscatter signal for analysis [77]. A more robust approach for visualization of myocardial fibrosis is late gadolinium enhancement (LGE)-CMR (**Figure 6**) [78].

This technique shows enhancement in regions of fibrosis with appropriate T1-weighted techniques 10–15 min after intravenous administration of gadolinium-based contrast because of:

- Expanded extravascular volume in fibrotic myocardium that is occupied by this extracellular contrast agent;
- Impaired efflux of gadolinium-based contrast due to vascular changes in fibrotic myocardium.

A recent study showed that approximately half of patients with LV hypertrophy due to arterial hypertension manifested patchy enhancement on LGE imaging [79]; this pattern is clearly distinguishable from the subendocardial enhancement of infarcted myocardium. Raman *et al.* have shown that severity of diastolic dysfunction increases with extent of fibrosis by LGE [80].

Visibly enhanced myocardial regions by LGE-CMR may be absent in HHD even in the presence of diffuse interstitial fibrosis. A critical drawback to the technique of LGE-CMR in the detection of more diffuse myocardial fibrosis is that it is qualitative, not quantitative, and it relies on the difference in signal intensity between scarred and normal adjacent myocardium to generate image contrast. Because collagen deposition in LVH is commonly diffuse, the technique of delayed contrast enhancement often shows no regional scarring.

This has prompted the development of the technique of T1 mapping by which quantification of global T1 time can help to quantify diffuse myocardial fibrosis. These studies are in the early phases of technique development and application. T1 mapping may be applied to the entire myocardium allowing quantification of differences in T1 relaxation, an intrinsic property of spins or protons in fibrotic versus normal myocardium. These differences are further exaggerated after gadolinium administration, which showed good correlation with collagen volume fraction in a small study of post-orthotopic heart transplant patients by Iles

et al. [81]. Their data demonstrated profound differences in myocardial contrast accumulation between normal and heart failure subjects utilizing post-contrast T1 mapping, with histologic data supporting their assertion that these changes reflect diffuse fibrosis. The differences also correlated with echocardiographic measurements of diastolic function, indicating shortening of T1 time may reflect altered diastolic function as a functional consequence of myocardial fibrosis. T1 mapping has the potential to be an end point in future therapeutic trials targeting fibrosis in HHD, eliminating the need for serial invasive endomyocardial biopsies [82].

Ischemia in HHD

In hypertensive patients, coronary arterial insufficiency may occur as a consequence of increased coronary arterial resistance, including diminished coronary flow and flow reserve, and altered blood rheology. These changes in the coronary circulation are independent of occlusive atherosclerotic epicardial arterial disease. Diminished coronary flow and flow reserve, increased coronary vascular resistance and blood viscosity in hypertension, and the increased myocardial oxygen demand engendered by the elevated arterial pressure and increased cardiac mass all play a major part in the high prevalence of sudden death and silent ischemia associated with hypertension. Abnormalities in the coronary micro circulation that accompany cardiac hypertrophy play a significant role in the pathogenesis of the complications associated with LVH [83].

Imaging for ischemia in HHD

Myocardial perfusion scintigraphy may be valuable and could have a potential role in the detection of diminished coronary flow and flow reserve in HHD. However, there are issues with the technique in this patient population. Since myocardial thallium uptake is dependent on regional $\text{Na}^+ - \text{K}^+$ pump function, and technetium uptake is dependent on myocardial blood flow, any myocardial pathology may produce an abnormal image. It may thus be postulated that hypertensive patients, especially those with LVH, may have perfusion abnormalities unrelated to epicardial coronary artery disease that serve to alter the kinetics of radio-isotope tracer agent and result in abnormal images interpreted as representing ischemia or infarction [84]. In HHD, Picano *et al.* have shown that ST segment depression and/or myocardial perfusion abnormalities are frequently found with angiographically normal coronary arteries associated with LVH and/or microvascular disease [85]. Although stress echocardiography tends to have a higher specificity in HHD for angiographically proven epicardial CAD [85], the sensitivity of wall motion abnormalities for detection of ischemia is markedly reduced in the presence of LVH.

Microvascular disease as a cause of endothelial dysfunction has been proposed as one of the etiologies of chest pain and myocardial ischemia in patients with hypertension and/or diabetes and normal coronary arteries on angiography [86]. Patients with positive stress testing for coronary ischemia and exclusion of significant coronary stenosis invasively were found to have subendocardial perfusion deficits on stress perfusion CMR [87]. Stress perfusion CMR allows noninvasive differentiation between patients with significant stenosis and patients with micro vascular disease caused by hypertension and/or diabetes based on the temporal and spatial extent of perfusion deficits. Patients with microvascular disease

more often have diffuse perfusion deficits with shorter persistence than patients with significant epicardial coronary artery disease [88].

Clinical applications of imaging HHD

In clinical practice the ECG is usually the first test performed to assess for the presence of LVH. Although LVH on ECG has the potential to identify the subgroup of patients with the highest LVM and the highest risk [89,90], false positives are very common in the young and in patients of African-American origin. In addition, a normal ECG does not exclude the presence of LVH [91], and these patients should be evaluated further with imaging.

Echocardiography is the preferred initial imaging strategy since it can confirm the presence of LVH as well as provide additional information such as LV systolic/diastolic function and the presence or absence of other potential causes of LVH. CMR can provide useful information in patients with suboptimal echo windows. It must be noted that at the present time, there is limited data available on CMR techniques such as T1 mapping and LGE in hypertensive LVH. The relative expense of CMR precludes its routine use in patients with hypertensive LVH, but for clinical trials of LVH and LV mass reduction with antihypertensive therapy, CMR or 3D echocardiography should be the imaging modality of choice.

Expert commentary

In spite of advances in therapies, the hypertensive patient's risk of heart failure has changed little since its recognition by large population-based studies over the past decades. Hypertensive LVH is an established predictor of cardiovascular events in hypertension. Since a normal ECG does not exclude the presence of LVH, imaging is important for diagnosis and prognostication in HHD. 2D echocardiography still remains the imaging technique of choice for the initial assessment of HHD. However, advanced echocardiographic tools (including 3D echocardiography) and CMR techniques offer a more comprehensive assessment of HHD, although they are limited by inadequate acoustic windows in a third of patients and cost, respectively. The newer real-time 3D echocardiographic technology now offers second-generation matrix array probes, solving the acquisition difficulties, while advances in computer technology and analysis software have shortened the duration of postprocessing. CMR is a reliable means of evaluating cardiac morphology, and therefore well suited for identifying and characterizing hypertensive patients with LVH and accurately measuring LV mass. Such precise measurements of LV mass using CMR or 3D echocardiography allows a smaller sample size to detect changes in clinical trials of LVH regression on hypertensive therapy.

Five-year view

Advances in imaging have provided tools for comprehensive noninvasive imaging of LVH, diastolic dysfunction, myocardial fibrosis and ischemia observed in HHD. The currently available echocardiographic techniques such as TDI, strain, strain rate and speckled tracking will continue to evolve and become more routine and user friendly in the years ahead. 2D-speckle imaging appears to provide a direct angle- and geometry-independent measure of

circumferential strain. Advances in understanding myocardial mechanics in hypertension, coupled with targeted therapies, suggest that routine clinical application of these advanced echocardiographic methods could benefit patients in the detection of subclinical disease, quantification of myocardial tissue dynamics, and tracking changes in disease progression or in response to hypertensive therapies. Since diastolic dysfunction often precedes the development of LVH, these techniques will help early detection of diastolic dysfunction in the absence of LVH.

Cardiac magnetic resonance has demonstrated great potential to define diastolic function in terms of active and passive stages, and its relaxation and compliance characteristics. In the future, CMR is likely to be utilized more often in HHD to assess inflow and myocardial velocities, and revealing properties of the LV, thus providing insights not fully available via other invasive and noninvasive strategies. Imaging fibrosis may improve the understanding of the pathophysiology of HHD. Novel CMR methods, such as T1 mapping, could become established as a tool for non invasive quantification of diffuse myocardial fibrosis in LVH, which could be used to evaluate newer therapies aimed at reducing myocardial fibrosis.

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• of interest

•• of considerable interest

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Key issues

- Hypertensive left ventricular hypertrophy (LVH) represents a powerful predictor for cardiovascular morbidity and mortality, independent of other cardiovascular risk factors, even blood pressure itself.
- A normal ECG does not exclude the presence of LVH, and therefore patients should be evaluated further with imaging.
- Echocardiography is clinically useful in the detection of LVH and the assessment of diastolic function.
- Cardiac magnetic resonance (CMR) has been demonstrated to be more accurate and reproducible for the estimation of left ventricular (LV) mass.
- Precise measurement of LV mass using CMR or 3D echocardiography allows a smaller sample size to detect changes in clinical trials.
- Myocardial fibrosis, a common end point in hypertensive heart disease (HHD), has been linked to the development of LVH and diastolic dysfunction.
- Recent developments in CMR techniques, such as T1 mapping, can help us quantify diffuse fibrosis that occurs in HHD.
- Noninvasive quantification of diffuse myocardial fibrosis in LVH is highly desirable in evaluating newer therapies aimed at reducing myocardial fibrosis.

Figure 1. Classification of left ventricular geometry on the basis of left ventricular mass and relative wall thickness

LVH: Left ventricular hypertrophy.

Adapted with permission from [18].

Figure 2.
Marked left ventricular hypertrophy noted on 2D-guided M-mode echo.

Figure 3. Left ventricular hypertrophy on 2D echo
(A) Parasternal long-axis view. (B) Parasternal short-axis view.

Figure 4.
Four-chamber long-axis view on an end-diastolic frame from a steady-state free precession cine image set demonstrating left ventricular hypertrophy by cardiac magnetic resonance.

Figure 5. Tissue Doppler imaging in a patient with hypertension demonstrating reduced early diastolic mitral annular velocity (Ea), suggestive of diastolic dysfunction.

Figure 6.
Late gadolinium enhancement–cardiac magnetic resonance in a patient with hypertensive left ventricular hypertrophy demonstrating a mid-wall region of late gadolinium enhancement in the inferoseptum.

Table 1

Accepted criteria and cut-off values for left ventricular hypertrophy and left ventricular mass by currently available imaging techniques.

Imaging technique	Male g/m ²	Female g/m ²
<i>Echocardiography</i>		
M-mode LVM indexed BSA	>125	>110
2D echo LVM indexed BSA	>102	>88
<i>Cardiac magnetic resonance</i>		
TGE LVM indexed BSA	>96	>77
SSFP indexed BSA	>83	>67

BSA: Body surface area; LVH: Left ventricular hypertrophy; LVM: Left ventricular mass; SSFP: Steady-state free precession; TGE: Turbo gradient echo.

Modified from [25].

Table 2

Advantages and disadvantages of the various methods currently available to assess left ventricular hypertrophy.

Measure	ECG	M-Mode	2D echo	3D echo	CMR
Cost	+	++	++	++	+++
Sensitivity	+	++	++	+++	+++
Specificity	+++	+++	+++	+++	+++
Availability	+++	+++	+++	+	+
Complexity	+	+	++	++	++

+: Low; ++: Moderate; +++: High; CMR: Cardiac magnetic resonance.

Modified from [25].