Hypertrophic Cardiomyopathy: Morphological Differential Diagnosis

Poster No.: C-2230
Congress: ECR 2013
Type: Educational Exhibit
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Keywords: Education and training, Education, MR, Cardiac
DOI: 10.1594/ecr2013/C-2230

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Learning objectives

We aim to provide an overview of Hypertrophic Cardiomyopathy (HCM), presenting the main MRI features and considering the role of imaging in the differential diagnosis.
Background

Hypertrophic cardiomyopathy (HCM) is a genetic disease of the cardiac sarcomere characterized by a diffuse or segmental left ventricular (LV) hypertrophy with a nondilated and hyperdynamic chamber, in the absence of any identifiable cause such as hypertension or valvular disease. It is the most common monogenic disease of the cardiovascular trait, with autosomal dominant inheritance predominates, affecting 1:500 (0.2%) individuals in the general population.

Most cases of HCM are phenotypically expressed in adolescence or early adulthood. Thus, early detection is important because it is the most common cause of sudden cardiac death among young people (from arrhythmias).

Because the clinical manifestations and electrocardiographic findings are nonspecific and diverse, noninvasive imaging modalities, such as cardiac MR, play a important role in detection and assessment of the morphologic, functional, and myocardial contrast-enhancement characteristics of nonischemic cardiomyopathy and is highly recommended as a powerful imaging modality for differentiating HCM from other cardiomyopathies.
Imaging findings OR Procedure details

Cardiac MR imaging can allow excellent characterization of the pattern and distribution of LV hypertrophy in HCM; Furthermore, delayed gadolinium enhancement (LGE) MR imaging techniques can provide unique information for tissue characterization, specifically for the identification of myocardial fibrosis or scarring. The pattern of fibrosis may be useful in the differential diagnosis.

There is a broad range of phenotypic expressions (Fig. 1 on page 9), with asymmetric involvement of the interventricular septum being the most common pattern (60-70% of the cases), followed by symmetric or concentric form of HCM (up to 40%). Other variants include apical, and masslike LVH.

**Asymmetric** (septal) HCM is diagnosed when the septal thickness is greater than or equal to 15 mm or when the ratio of the septal thickness to the thickness of the inferior wall of the left ventricle is greater than 1.5 at the midventricular level.

This phenotype is typically most evident in the anteroseptal myocardium and can be associated with systolic anterior motion (SAM) of the anterior mitral leaflet which can increase left ventricle outflow tract (LVOT) obstruction and decreased coronary and systemic outflow. Mitral regurgitation and left auricle dilation are some other secondary signs.

It is clinically important to distinguish between the obstructive and nonobstructive forms of HCM.

**Symmetric** HCM, is characterized by concentric LV hypertrophy with a small cavity dimension and no evidence of a secondary cause.

1. IMAGING FINDINGS

1.1 - General Features

**Best diagnostic clue:**

- Hallmark is myocardial hypertrophy which cannot be explained by another disease (i.e., hypertension, aortic stenosis).
- Most common diagnostic criterion of HCM is that the maximal LV wall thickness is greater than or equal to 15 mm in the end-diastolic phase (Fig. 2 on page 9) (13-14 mm is considered borderline, particularly so if there is a family history of HCM).
Location:

Degree and distribution of LV hypertrophy in HCM is variable.

- Most common location is basal septum hypertrophy with or without obstruction.
- Asymmetric septal hypertrophy is defined by a ratio of the wall thickness of the septum to a non-hypertrophied segment > 1.3.
- Rare cases exist of concentric hypertrophy, mid-cavity hypertrophy, and apical hypertrophy.

Morphology:

- Nondilated and hyperdynamic LV.

1.2 - MR Findings

- Delayed myocardial enhancement with gadolinium usually representing areas of increased fibrosis (seen in as many as 80% of patients with HCM).
  - Delayed enhancement has been shown to be more common at junction of the RV wall and septum (Fig. 3 on page 10).
  - Delayed enhancement can be diffuse or focal and involve any portion of LV wall (Fig. 4 on page 11).
  - Volume of delayed hyperenhancement on MR correlates with risk for sudden cardiac death.
    - LV outflow tract (LVOT) obstruction with abnormal flow dynamics in some cases (Fig. 5 on page 12, Fig. 6 on page 13).
    - Mitral valve regurgitation and systolic anterior motion (SAM) of the mitral valve leaflet (Fig. 7 on page 14).

2. DIFFERENTIAL DIAGNOSIS

Although sarcomeric HCM accounts for the majority of unexplained left ventricular hypertrophy seen in adults, a number of other non-sarcomeric diseases can produce increased wall thickness of the myocardium as part of their phenotypic expression.

HCM, predominantly the symmetrical type, should be differentiated from other causes of symmetric increased thickness of the LV wall, including amyloidosis, athlete’s heart,
Fabry disease, and the secondary adaptive pattern of LV hypertrophy that is due to hypertension or aortic stenosis, because the treatment strategies are different.

2.1 - Cardiac Amyloidosis

Amyloidosis is a systemic process, thus involvement of all four chambers is common.

Ventricular myocardial thickening affects the right and left ventricles, and a useful distinguishing feature from HCM is that it generally results in a diffuse and symmetric rather than a focal pattern of hypertrophy.

Morphologic changes of a thickened nodular right atrial free wall and interatrial septum are helpful in distinguishing cardiac amyloid from HCM. An increase in the thickness of the interatrial septum and right atrial free wall by more than 6 mm has been shown to be a specific finding for cardiac amyloidosis (Fig. 8 on page 15).

Tickenining of the right ventricular wall is less helpful in the differentiation between amyloidosis and HCM, but the distribution of hypertrophy can be a clue. In HCM right ventricular involvement is typically asymmetric with thickening more commonly identified apically. In cases of amyloid, the right ventricular involvement is more commonly symmetric.

Through the use of DE MR imaging, a distinct pattern of late enhancement, which was distributed over the entire subendocardial circumference, has been shown to have high specificity and sensitivity for cardiac amyloidosis (Fig. 9 on page 16).

2.2 - Hypertensive Heart Disease

Exposure to long-standing systemic hypertension will result in nearly identical wall thickening in the septum and LV lateral wall (ie., concentric or symetric hypertrophy) (Fig. 10 on page 17). In addition, hypertensive cardiomyopathy is very rarely associated with resting LV outflow tract obstruction due to typical systolic anterior motion (SAM) with septal contact. Likewise, LV wall thickening in HCM is almost always asymmetric with resting outflow obstruction present in over one-third of patients.

Hypertensive heart disease is a diagnosis of exclusion, and when the distinction between these two disease entities still remains otherwise ambiguous in an individual patient, detection of HCM in family members who were previously undiagnosed or identification of a sarcomere mutation with genetic testing would provide additional evidence strongly favoring a clinical diagnosis of HCM.

2.3- Valvular disease (Aortic Stenosis) and Aortic Coarctation
Thickening, fusion and/or calcification of the aortic valve apparatus lead to extremely elevated peak systolic pressure gradient.

Aortic stenosis is readily evaluated on cardiovascular MR (Fig. 11 on page 18) and other findings include systolic flow void (jet) on cine exam arises at valve level (not LVOT) and extends into proximal aorta and secondary left ventricular hypertrophy in severe aortic stenosis.

Coarctation of the aorta (Fig. 12 on page 19) refers to a narrowing of the aortic lumen with obstruction to blood flow. MR may reveal bicuspid aortic valve or ascending aortic aneurysm and can estimate of flow velocities and gradient.

Both, severe aortic stenosis and aortic coarctation, leads to concentric left ventricular hypertrophy.

2.4- Athlete's Heart

Although sudden cardiac death is rare among the athletic population (estimated to be less than 1:200,000), it is nonetheless a devastating occurrence. HCM is known to be the most common cause of sudden death in young athletes, usually male.

Morphologic adaptations of an athlete's heart may mimic cardiovascular diseases such as HCM (Fig. 13 on page 20).

Approximately 2% of highly trained male athletes will have mild symmetric increase in wall thickness (usually < 16 mm), increased left ventricular volumes, and increased left ventricular mass, but no evidence of diastolic dysfunction.

The diastolic wall thickness (DWT) divided by the left ventricular end-diastolic volume (LVEDV) ratio (DWT/LVEDV) was identified by Petersen et al. as the best parameter to differentiate an athlete's heart from all other pathologic causes of hypertrophy. A cutoff for the DWT/LVEDV ratio of less than 0.15 mm/m²/mL gave a sensitivity of 80% and a specificity of 99%.

Patients in whom wall thickness regresses greater than 2 mm after a period of deconditioning supports a diagnosis of athlete’s heart, while hypertrophy that remains unchanged suggests HCM.

At present, it does not appear that competitive athletes demonstrate areas of delayed enhancement and therefore the presence of LGE may also provide additional information to confirm diagnosis of HCM. However, it should be noted that the absence of myocardial delayed enhancement does not exclude the diagnosis of HCM.

2.5 - LV non-compaction
Non-compaction of the left ventricle, also known as spongiform cardiomyopathy, is an arrest of myocardial compaction during embryogenesis, leading to hypertrophic ventricular trabeculations and deep inter-ventricular recesses.

Predominantly involves mid to apical aspect of left ventricle.

The best diagnostic clue is a ratio of non compacted telediastolic myocardium to compacted telediastolic myocardium of more than 2,3:1 (Fig. 14 on page 21).

Subendocardial perfusion defects on contrast-enhanced MR can be seen and LGE MR may demonstrate hyperenhancement corresponding to myocardial fibrosis.

2.6 - Fabry's disease

Fabry disease is an X-linked lysosomal storage disease that is caused by deficient activity of lysosomal enzyme α-galactosidase A (α-Gal A), leading to accumulation of glycosphingolipid in multiple organs, including the heart.

Although cardiac manifestations can occur early in life, they are generally not detected until the third or fourth decade but remain a major cause of death in patients with Fabry’s.

Fabry’s disease leads to increased, usually concentric, left ventricular wall thickening. However, asymmetric septal thickening mimicking HCM can occur.

Delayed gadolinium-enhanced occur in up to 50% of patients with Fabry's disease. Enhancement was typically mid wall and occurred in the basal inferolateral segment (Fig. 15 on page 22).

Distinction between Fabry's disease and HCM is important because enzyme replacement or enhancement therapy for patients with Fabry’s disease is now available.
Fig. 1: Cardiac MR end-diastolic images demonstrating diverse patterns of LVH in HCM. (A) involving ventricular septum, but sparing the LV free wall; (B) hypertrophy of the basal anterior free wall and contiguous septum, representing the most common area of LV wall thickening in HCM; (C) massive septal hypertrophy (wall thickness > 30 mm); (D) localized hypertrophy to LV apex; (E) mass-like HCM with obstruction of LVOT; (F) symmetric CHM.

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Fig. 2: Asymmetric (septal) HCM in a 43-year-old women with familial disease. Left ventricular wall thickness should be calculated during end-diastole, preferably in the short axis for assessment of the mid to basal thirds of the left ventricular myocardium. Care should be taken to exclude free muscle bundles when measuring wall thickness.

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Fig. 3: Typical delayed enhancement within the anterior and posterior right ventricular insertion points (arrows) on the short-axis oblique delayed enhancement image, representing fiber disarray instead of fibrosis replacement.

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Fig. 4: Delayed enhancement involving the LV. Enhancement is patchy and involves areas of grossly thickened myocardium.

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**Fig. 5:** Three chambers cine view in a patient with asymmetric HCM and obstruction of LVOT.

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Fig. 6: Two chambers short axis cine view in a patient with asymmetric HCM and obstruction of LVOT.

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Fig. 7: Three chambers cine view in a female patient with asymmetric septal hypertrophic cardiomyopathy (HCM) and systolic anterior motion (SAM) of the mitral valve.

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Fig. 8: T2 FS axial image of 48 year-old man with cardiac amyloidosis shows diffuse thickening of myocardium and atrial enlargement with marked atrial septal thickening (15mm). Note also pericardial effusion.

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**Fig. 9:** 60-year-old men with cardiac amyloid. A-D, Inversion recovery delayed gadolinium enhanced images (A and B) and steady-state free precession images (C and D) in the axial and short-axis oblique projections show extensive mid wall enhancement and symmetric thickening of the left ventricle that are typical of amyloid. Mild right ventricular wall thickening is also present. Although subendocardial extension of delayed enhancement is common in cardiac amyloid, large areas of mid wall enhancement, such as in this patient, are also commonly found.

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**Fig. 10:** Adenosine-stress perfusion, short axis cine view. Stress-induced show typical subendocardial hypoperfusion in a patient with left ventricular hypertrophy due to hypertension. Weren’t evident areas of delayed enhancement.

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Fig. 11: Three-chambers cine view. LVH due to aortic stenosis. Note systolic flow void (jet) at valve level (not LVOT) and extends into proximal aorta.

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Fig. 12: LV concentric hypertrophy secondary to aortic coartaction. Multiplanar reformatation (A) show interruption of aortic arch; long (B) and short (C) axis late gadolium stduys show mild and diffuse areas of late enhancement.

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**Fig. 13:** 32-year-old male athlete with athlete's heart. Steady-state free precession images show maximal left ventricular wall thickness was measured as 16 mm. Note biventricular dilatation. Diastolic wall thickness (DWT) and left ventricular end-diastolic volume (LVEDV) ratio (DWT/LVEDV) of 0.13 falls below the cutoff of 0.15. This quantitative evaluation makes diagnosis of athlete’s heart more likely than other pathologic causes of thickened left ventricles.

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Fig. 14: 27-year-old man with noncompaction of LV. Four-chamber (A) and short-axis oblique (B) projection images allows differentiation of compacted and noncompacted layers of the myocardium. Trabeculae within the right ventricle as seen as well. Ratio of non compacted telediastolic myocardium to compacted telediastolic myocardium was calculated in 3.

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Fig. 15: Cardiac involvement in Fabry’s disease. Delayed inversion recovery gadolinium-enhanced images show symmetric left and right ventricular hypertrophy with mid wall delayed enhancement of the basal inferolateral wall.

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Conclusion

Cardiac MR imaging is known to play an important role in the diagnosis of HCM and can help to differentiating other causes of myocardial hypertrophy from HCM because of the unique ability of LGE MR imaging in order to characterize different enhancement patterns in diseased myocardium (Fig. 16 on page 25).

It is important for the radiologist to be familiarized with the imaging features of HCM to improve the accuracy of diagnosis.
**Images for this section:**

<table>
<thead>
<tr>
<th>Phenocopy</th>
<th>Pattern of LGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCM</td>
<td>Hyperenhancement in up to 80% of patients; Highly variable, in pattern and extent; may be absent. TYPICALLY IN RV INSERTION POINTS</td>
</tr>
<tr>
<td>Amyloid</td>
<td>GLOBAL, SUBENDOCARDIAL the most common pattern; difficult to image; dark blood pool</td>
</tr>
<tr>
<td>Fabry’s</td>
<td>INFEROLATERAL in early disease progressing to extensive LGE</td>
</tr>
<tr>
<td>HT</td>
<td>NONE, unless associated with other conditions (i.e. coronary disease)</td>
</tr>
<tr>
<td>Athlete’s heart</td>
<td>NONE</td>
</tr>
</tbody>
</table>

**Fig. 16:** keypoints in pattern of late gadolinium enheacement in different phenocopies of CHM.

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References


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