

EDITORIAL

Echocardiographic profiles in hypertrophic cardiomyopathy: imaging beyond the septum and systolic anterior motion

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Introduction

Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease with enormous diversity in phenotype expression (1). The classic description of HCM is that of hypertrophy of the basal anterior septum, systolic anterior motion (SAM) of the mitral valve (MV) resulting in dynamic left ventricular outflow tract (LVOT) obstruction at rest or with provocation in the majority of patients (Fig. 1). Since the first noninvasive description of the entity was made using M-mode echocardiography, advances in cardiac imaging in recent years have brought to light that the structural and functional abnormalities in HCM are indeed a large and heterogeneous spectrum beyond just septal hypertrophy, including the MV and subvalvular apparatus (2, 3, 4, 5, 6, 7, 8). A variety of genetic mutations are responsible for the diverse phenotypical expression and clinical course. Recognition of such morphological and functional manifestations has diagnostic, prognostic and therapeutic implications and will be reviewed here (9, 10, 11, 12, 13).

Left ventricular hypertrophy

The most common region for increased left ventricular (LV) wall thickness is the basal anterior septum in continuity with the anterolateral wall, although hypertrophy can involve any region of the myocardium including increased wall thickness confined to the apex (Fig. 2). While the anterior portion of the septum is more commonly involved in HCM, hypertrophy limited to the posterior septum can be observed in some patients. Regions of LV hypertrophy that may be encountered

other than the septum in HCM include anterior free wall, lateral wall and rarely posterior wall. Although the majority of HCM patients have increased wall thickness involving more than half of the LV wall, a subgroup of patients have much more limited hypertrophy, with increased wall thickness confined to only one or two LV segments. It is imperative to determine the maximal LV wall thickness anywhere in the LV wall, because extreme hypertrophy, LV wall thickness of ≥ 30 mm, is a risk factor for sudden cardiac death and may lead to recommendation of primary prevention with intracardiac defibrillator therapy (14). In patients in whom accurate delineation of the LV borders cannot be reliably determined, the administration of trans-pulmonary ultrasound contrast is useful. Alternatively, cardiovascular magnetic resonance imaging provides very accurate definition of the myocardial walls, making wall thickness measurements reliable and accurate.

In patients who are considered for surgical myectomy or catheter-based alcohol septal ablation (ASA), it is particularly important to delineate the location and the extent of hypertrophy and the relationship between areas of hypertrophy and MV contact (9, 15). Extended myectomy beyond the basal septum may be required in some patients who have to reliably eliminate outflow obstruction and improve symptoms (16). Transesophageal echocardiography performed intra-operatively helps the surgeon to determine the length and extent of myectomy trough to adequately relieve obstruction. In these patients, ASA is unlikely to be effective in abolishing the gradient. In selected patients undergoing ASA, contrast-enhanced

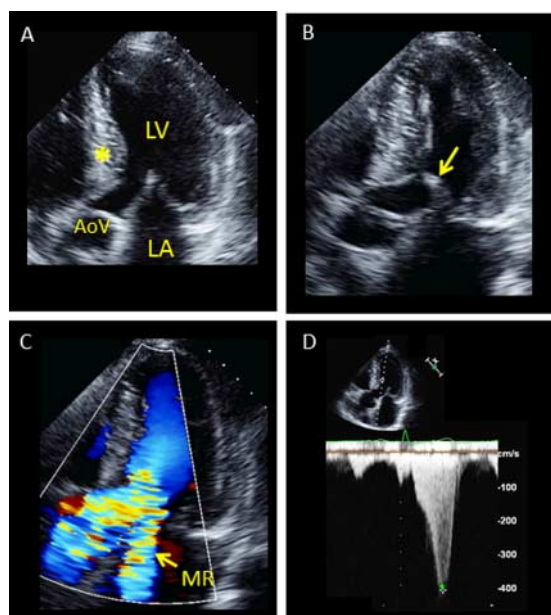


Figure 1

Images from a patient with HCM. (A) Asymmetrical septal hypertrophy (*). (B) Systolic anterior motion of the mitral valve (arrow). (C) Turbulence in the left ventricular outflow tract and mitral regurgitation jet. (D) Increased flow velocity secondary to LV outflow tract obstruction. Abbreviations as in text.

echocardiography helps to guide ASA as the intracoronary injection of contrast agent into a candidate septal perforator artery will help to determine the perfusion supplied to ensure that the appropriate site of perfusion, to area of hypertrophy, is chosen to best relieve obstruction and help to avoid complications.

A subset of patients has hypertrophy limited to the apex, referred to as apical HCM, with a localized intracavitary pressure gradient (Fig. 3). Some of these patients (about 2%) develop a thin-walled LV apical aneurysm associated with regional apical scarring (17). These patients are at high risk of developing adverse clinical events during follow-up, including progressive heart failure (HF), sudden death, and thrombo-embolic events presumably due to clot formation within the aneurysm. The identification of this anomaly alters treatment strategy, with consideration for primary prevention with an intracardiac defibrillator and anti-coagulation for stroke prophylaxis. Therefore, consideration of apical LV aneurysms is important in patients with mid-ventricular or apical hypertrophy. Echocardiography with contrast imaging or cardiac magnetic resonance imaging will help to identify or delineate the

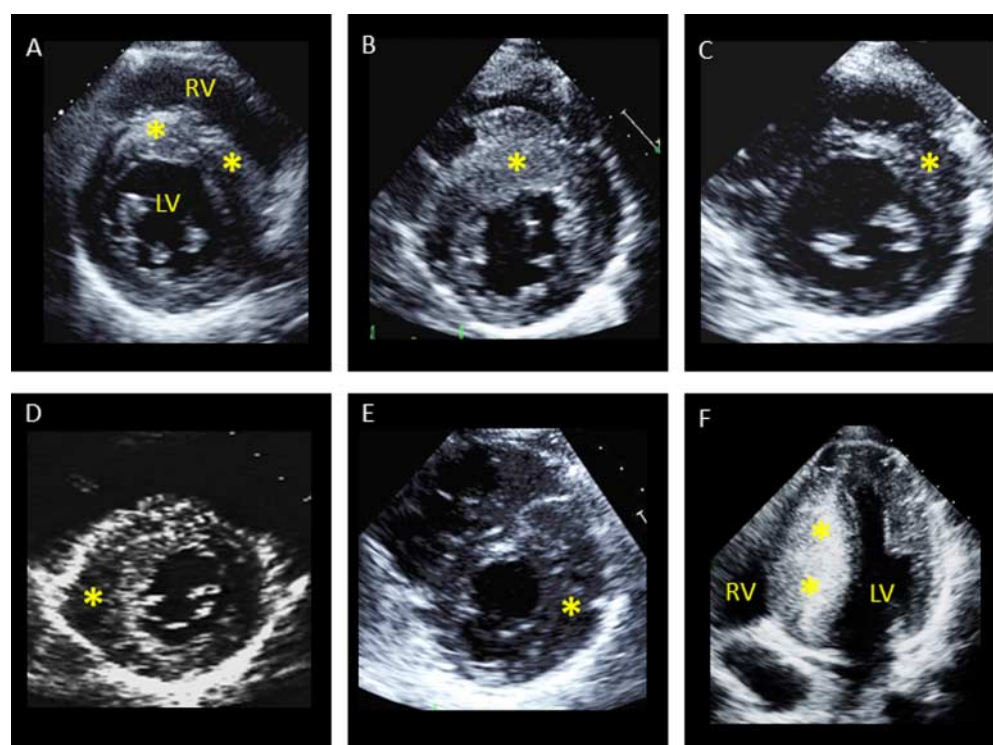


Figure 2

Patterns of LV hypertrophy (*). (A) Hypertrophy involving the whole basal septum. (B) Marked hypertrophy of the anterior septum. (C) Hypertrophy of the septal-anterior wall junction. (D) Hypertrophy

limited to septal-posterior wall junction. (E) Anterior free wall thickening. (F) Massive hypertrophy of the whole septum from base to apex.

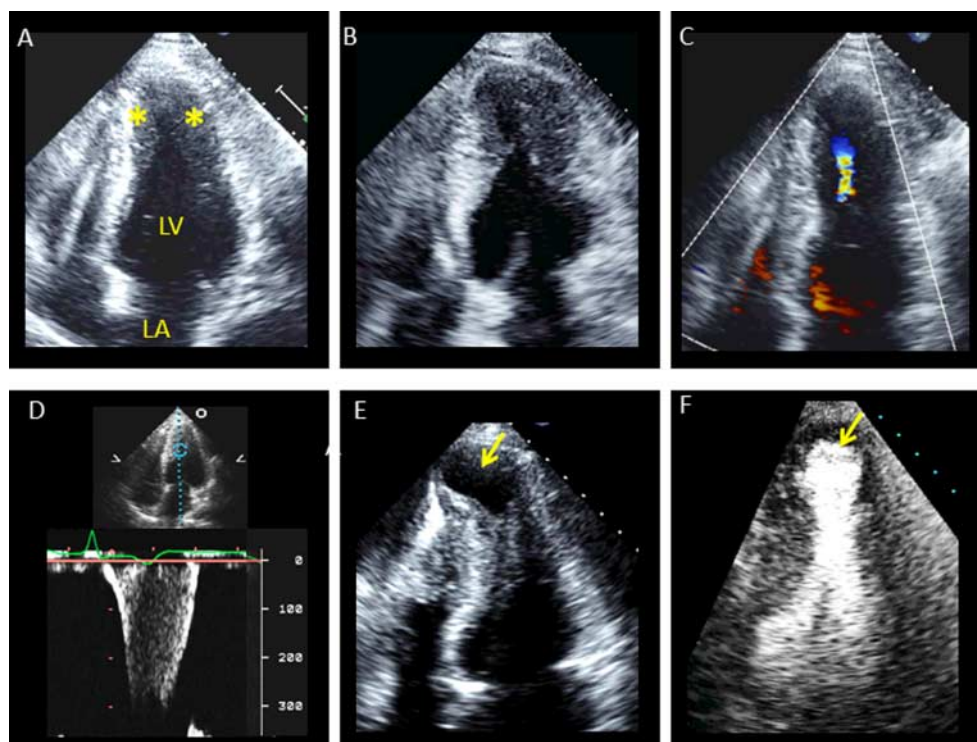


Figure 3

Apical hypertrophic cardiomyopathy. (A and B) Images depicting apical hypertrophy in two patients. * represents hypertrophied myocardium. (C and D) Color-Doppler and spectral Doppler images demonstrating intraventricular gradient. (E and F) Apical aneurysm from two patients with apical HCM (Arrow).

aneurysm in such patients, and in those with technically suboptimal echocardiographic results.

MV and subvalvular abnormalities

A number of morphological abnormalities involving the MV and subvalvular apparatus are part of the phenotypic expression of HCM (18). A vast majority of patients with HCM have substantially elongated mitral leaflets, most commonly involving the anterior leaflet but the posterior or both leaflets can also be involved (Fig. 4). Elongated MV leaflets contribute to LVOT obstruction by making more distal contact with the septum than usually seen. This is clinically relevant in patients undergoing myectomy, because during surgery the anterior mitral leaflet will need to be shortened (i.e. plication) in addition to myectomy to ensure complete relief of obstruction. Mitral regurgitation is a common accompaniment of LVOT obstruction in patients with HCM, resulting from the dynamic, systolic deformation of MV closure. The mitral regurgitation jet is often posteriorly directed in HCM due to inadequate coaptation of the posterior leaflet due to SAM. The degree of mitral regurgitation usually resolves or becomes mild

following surgical relief of obstruction. Some rare patients, however, may have marked intrinsic or degenerative abnormalities of the MV that would require extensive repair or replacement.

Many patients with HCM may have varied abnormalities of the papillary muscles (19) (Fig. 5). HCM patients often have an increased number of papillary muscles (three or four) and these accessory muscles are often hypertrophied and apically displaced toward the ventricular septum. For this reason, these abnormally displaced papillary muscles often contribute to outflow obstruction by pulling the plane of the MV toward the septum. For patients undergoing surgical myectomy, these accessory and apically displaced papillary muscles are often revised or resected in order to facilitate adequate elimination of the gradient. Anomalous insertion of the anterolateral papillary muscle directly into the anterior leaflet of the MV is another morphologic abnormality of the subvalvular apparatus. The anomalous insertion of the papillary muscles is a cause of mid-ventricular obstruction and therefore its identification is important for helping presurgical planning, as a very distal resection with revision of the papillary muscles is necessary in these

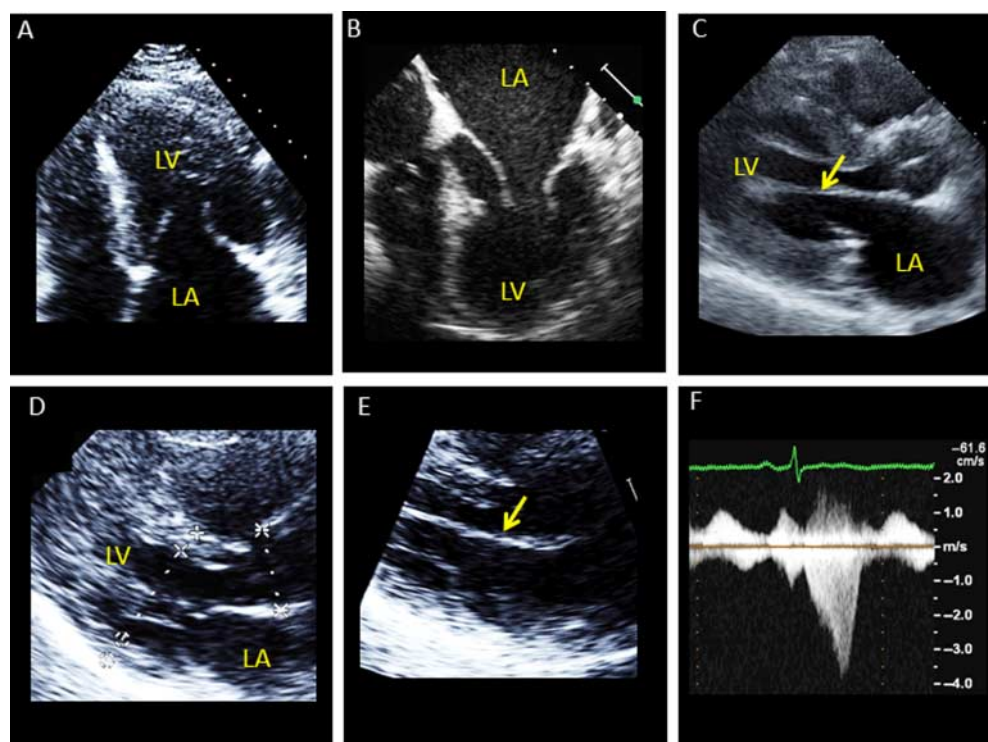


Figure 4

Abnormalities of mitral valve apparatus in HCM patients. (A, B and C) Elongated mitral leaflets (arrows) from three different patients. (D, E and F) Long MV leaflets contributing to obstruction despite minimal septal hypertrophy.

cases to reliably eliminate the outflow obstruction. Finally, LV apical–basal muscle bands have also been described in HCM and often have abnormal chordal connections to the MV, which again contribute to the mechanism of obstruction. These muscle bands are often removed during surgical myectomy for adequate relief of obstruction.

LV outflow obstruction

LV outflow obstruction is an independent predictor of prognosis in HCM patients. It is also a major contributor to symptoms such as dyspnea, syncope, and chest pain (1, 13, 20). It is critical therefore to identify or unmask LVOT gradient in these patients. One-third of patients with HCM exhibit gradients ≥ 30 mmHg at rest. Provocations such as Valsalva manoeuvre, amyl nitrite inhalation, premature ventricular contraction, infusion of dobutamine or isoproterenol, and exercise can provoke latent obstruction in another one-third of patients (Fig. 6). Thus, the majority of HCM patients exhibit impedance to LV outflow either at rest or with provocation. Among the provocative manoeuvres, Valsalva is the simplest to do at bedside or during echocardiographic examination. However exercise is the preferable method because it is

the closest to representing the conditions of real life that result in symptom production in patients during daily activities. This approach also alerts the physician and patient to the effort tolerance of the individual (21). An LVOT gradient of ≥ 50 mmHg at rest or with provocation is the cut-off necessary for recommending invasive septal reduction therapy. Almost all patients with HCM and hyperdynamic ventricle will have some degree of intracavitary gradient; some however may have significant mid-cavitary obstruction, and high intracavitary gradients that can contribute to symptoms. Multiple sites of obstruction may be observed in some individuals and may require attention in those who are undergoing surgery.

The left ventricle

The LV cavity is generally normal or small in size with a hyperdynamic ventricle and a high ejection fraction. Many patients may live without symptoms for many decades. Others may develop HF over time, often due to diastolic dysfunction; this could proceed to systolic dysfunction and advanced HF, ‘burnt-out HCM’ that may eventually require heart transplantation (22). While the diagnosis of HF is based on clinical symptoms, careful

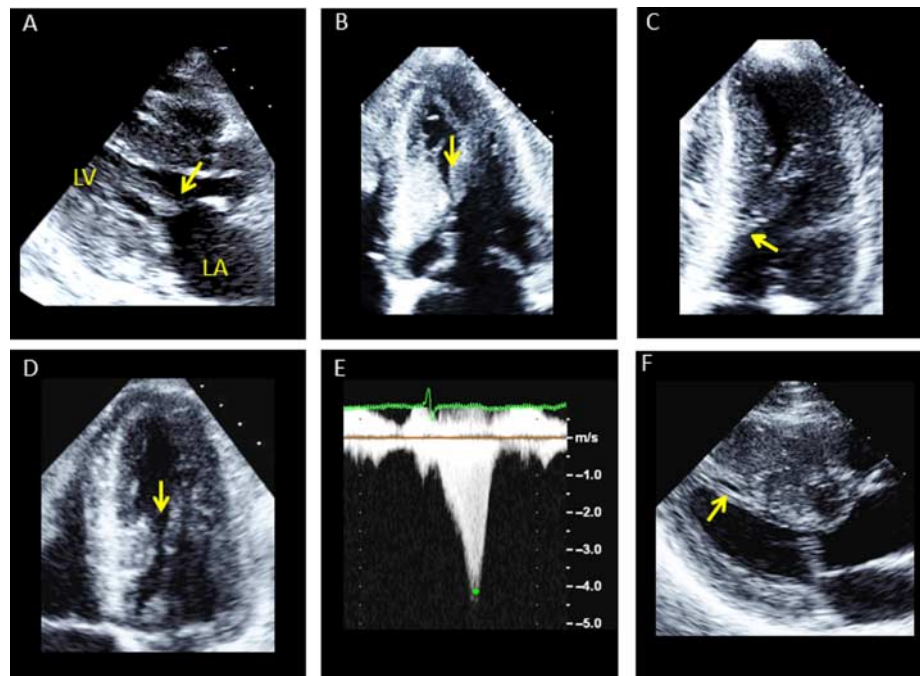


Figure 5

Spectrum of subvalvular abnormalities in HCM. (A) Direct attachment of anterior papillary muscle to anterior MV leaflet (yellow arrow). (B) Hypertrophied papillary muscle narrowing the LVOT. (C, D and E)

Anteriorly oriented papillary muscle encroaching on the LVOT (arrows) and contributing to outflow gradient. (F) Abnormal muscle band with attachment to the septum (arrow).

assessment of LV ejection fraction is important because of management implications. While most patients will have some degree of diastolic dysfunction, Doppler indices of diastolic function do not correlate well to invasive measures of LV filling pressure in individual patients, and for this reason these are not been routinely used in clinical management (23). Recent experience with speckle tracking echocardiography has indicated that reduction in certain strain parameters may be used to identify changes in myocardial function and the likelihood of serious arrhythmias. However, it is too early to derive a certain speckle parameter for use in risk stratification or management decisions (24, 25). Identification of apical LV aneurysms is important in patients with mid-ventricular or apical hypertrophy. Contrast imaging would help to delineate the aneurysm in patients with technically difficult windows.

Right ventricular pathology and other coexistent disorders

The right ventricular (RV) wall thickness and mass are increased in one-third of HCM patients, predominantly as a diffuse process involving the entire or a significant

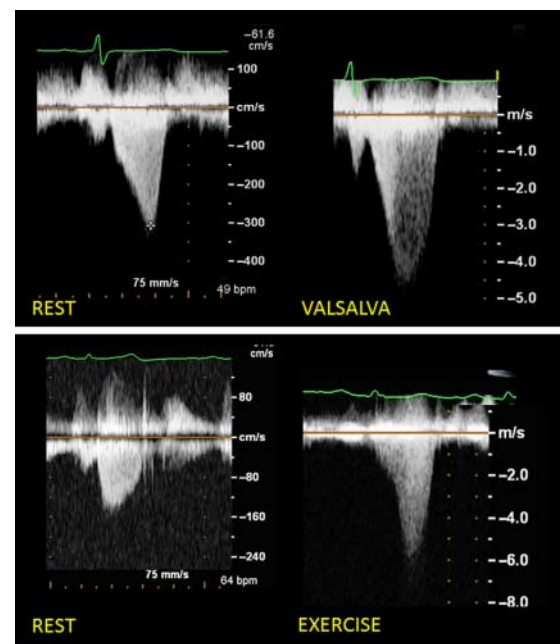


Figure 6

Doppler recordings of LVOT gradients from two patients with HCM. Top panel shows only a mild gradient at rest in a HCM patient, increasing significantly with Valsalva maneuver; bottom panel depicts LVOT velocity in a patient, which increases markedly with exercise.

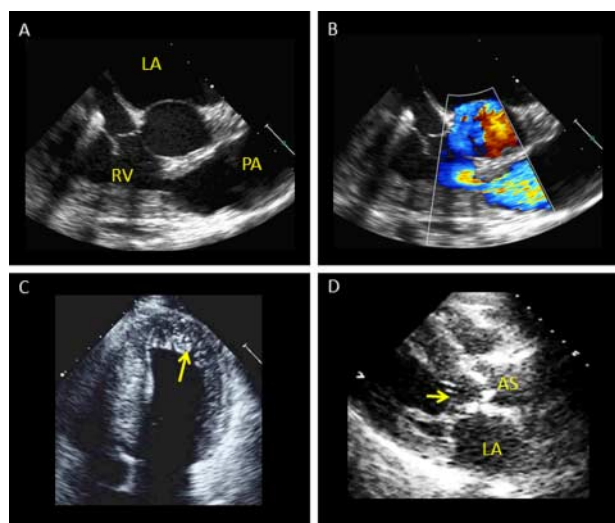


Figure 7

Hypertrophic cardiomyopathy with unusual features. (A and B) Narrowing of right ventricular outflow and turbulent flow in a symptomatic patient who had been operated for LVOT obstruction years earlier. (C) Image showing findings of both HCM and noncompaction (arrow). (D) A patient with HCM and aortic valvular stenosis (arrow).

proportion of the RV wall (26, 27). Rarely, patients may develop RV outflow obstruction secondary to marked hypertrophy of the crista supraventricularis, moderator band, or trabeculae, causing significant obstruction at RV outflow or mid-ventricular regions (Fig. 7). Careful imaging of the RV is thus important in patients with HCM, as this finding may contribute to symptoms, with the potential need to correct at the time of LV myectomy.

Echocardiographic evaluation aids in the identification of any coexistent, obstructive pathology such as aortic valve stenosis and subaortic membrane (28), or any other genetic disorder such as ventricular noncompaction. Failure to recognize dynamic subvalvular obstruction related to HCM in patients with aortic valve stenosis could prove to be disastrous if only the aortic valve is replaced in such patients. Likewise resection of a subvalvular membrane would be required in symptomatic patients with such a combined abnormality.

Conclusion

HCM was initially felt to be a disease characterized by hypertrophy of the basal anterior septum and LV outflow obstruction. However, advances in our understanding of this disease have led us to identify heterogeneous phenotypes within HCM, ranging from minimal to massive hypertrophy in any location of the LV,

subvalvular derangements, presence or absence of outflow obstruction, and a range of LV function from hyperdynamic to end-stage. Advances in noninvasive imaging have allowed for the identification and understanding of these morphological and functional manifestations, leading to alterations in management strategies.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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