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Echocardiography to Individualize Treatment for Hypertrophic Cardiomyopathy

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Abstract Treatments for hypertrophic cardiomyopathy are largely selected based on patient symptoms and echocardiographic findings. Moreover, all the advanced treatments for heart failure symptoms depend on such imaging for planning and monitoring response to therapy. Risk of sudden death correlates with maximum left ventricular (LV) wall thickness. Massive LV thickening of 30 mm or more is an indication for primary prevention of sudden death with an implanted defibrillator. In this review, we will underscore potential pitfalls in echocardiographic diagnosis. Also we will review, a newly appreciated pathophysiologic mechanism in obstruction dynamic systolic dysfunction due to gradient. (Prog Cardiovasc Dis 2012;54:461-476)

Keywords: Echocardiography; Doppler echocardiography; Hypertrophic cardiomyopathy; Dynamic systolic dysfunction; Left ventricular dysfunction; Heart failure

Hypertrophic cardiomyopathy is marked by extreme anatomical diversity, which figures prominently in the selection of treatment options and prognosis.[1-3] First, echocardiography allows for the determination of the site of the hypertrophy and its magnitude. Hypertrophy of the anterior and posterior septum, and of the anterior wall is the most common variant. Other patients have thickening confined to the apex, termed *apical HCM*. In still others, thickening restricted to the most proximal septum is termed a *discrete subaortic septal bulge*. Finally, some have midventricular hypertrophy, which can progress to the uncommon but important variant of mid–left ventricular (LV) obstruction with an apical akinetic chamber.

The phenotypic expression of HCM may give clues as to whether an abnormal gene will be detected on genotype analysis. Binder and colleagues[4] reported that the pattern of septal hypertrophy to the apex, resulting in a partially crescent-shaped ventricular cavity and reversal of the normal concave curve at the apex, predicts an abnormal genotype—found in 79% of such patients with HCM. In comparison, in patients with a discrete subaortic bulge, only 8% had a positive genotype yield.

The indications and use for resting, transesophageal, and exercise echocardiography are addressed in the current guidelines.[5] In this review, we will highlight abnormalities that direct therapy.

Echocardiography is particularly useful in detecting functional abnormalities that cause symptoms in HCM. Diastolic dysfunction is a hallmark of the disease and may frequently be diagnosed with transthoracic echo.[6] One should always evaluate transmitral flow velocities, pulmonary vein velocities, and tissue Doppler velocities, for an assessment of global and segmental diastolic dysfunction. Often, the thickened septum will have the most marked diastolic abnormalities on tissue Doppler or strain imaging. The systolic abnormalities discussed in the bulk of this review are additive in pathologic effect to impaired relaxation and reduced compliance. Matsubara and colleagues[7] have elegantly shown how systolic load due to dynamic LVOT obstruction can reversibly impair diastolic relaxation. Indeed, at present the only way to

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Abbreviations and Acronyms

CMR = cardiac magnetic resonance

HCM = hypertrophic cardiomyopathy

LVOT = left ventricular outflow tract

SAM = systolic anterior motion

SAS = subaortic stenosis

TEE = transesophageal echocardiography

partially improve LV diastolic dysfunction in HCM is to relieve or abolish LVOT obstruction. Improvement in diastolic function with relief of obstruction has been shown after disopyramide, surgery and ablation.

Approximately two-thirds of patients with HCM have LV outflow tract (LVOT) obstruction either at rest or after physiologic provocation.[3,8-11] Thus, on top of their LV hypertrophy (LVH) and their diastolic dysfunction, such patients have either resting or a provocable LVOT gradient of 30 mm Hg or greater, which contributes to symptoms of exercise intolerance, dyspnea, angina, or syncope. Moreover, resting gradient is associated with decreased survival.[12] Left ventricular outflow tract obstruction is associated with increased systolic LV work, decreased diastolic aortic perfusion pressure, supply-demand ischemia, load-related impairment in diastolic relaxation, and a midsystolic drop in instantaneous LV ejection flow velocities and volumetric flow.[3,13-15]

The most common cause of LVOT obstruction is systolic anterior motion (SAM) of the mitral valve and mitral-septal contact (Figs 1-3). Although LV outflow obstruction at rest occurs in only about a quarter of patients, after provocation with exercise, two-thirds of patients have LVOT obstruction. Shah and colleagues[16] first demonstrated with m-mode that SAM of the mitral valve is the principal cause of LV outflow gradients in HCM. Before this demonstration in 1969, outflow tract gradients detected by catheterization were thought to be due to a muscular sphincter constricting the LVOT. The detection of SAM and mitral-septal contact revolutionized our understanding of this phenomenon. If not for echocardiography, SAM's importance in causing obstruction might not have been ascertained till the advent of cardiac magnetic resonance (CMR) imaging.

The pathophysiology of SAM and mitral-septal contact is now better understood. We find understanding these mechanics to be helpful in devising patient-tailored therapies. All efforts to treat obstruction are based on a correct understanding of its cause, which is an altered internal geometry of the LV, leading to an overlap between the inflow and outflow portions of the LV.[11,17-19] Besides septal hypertrophy, this overlap is caused by anterior displacement of the mitral apparatus (papillary muscles and mitral leaflets),[11] mitral leaflet elongation,[20-22] and mitral slack.[11] Drag, the pushing force of flow, is the dominant hydrodynamic force that causes SAM; flow gets behind the mitral leaflets and sweeps them into the septum[3,11,17,18,23,24] (Figs 2 and 3, left panel). Moreover, there is often a protruding redundant portion of the anterior mitral valve leaflet that extends past the coaptation point.[25] On occasion, it is the posterior leaflet that protrudes past the coaptation point and obstructs.[26] These protruding portions are untethered because there is no LV/left atrium pressure difference to keep them in place.

Systolic anterior motion begins at low velocity and may begin during isovolumetric systole, even before the aortic leaflets open.[11,17] Systolic anterior motion is a flow drag–triggered phenomenon; it has been described as anteriorly directed mitral valve prolapse. The necessary conditions for SAM are: anterior position of the mitral valve in the

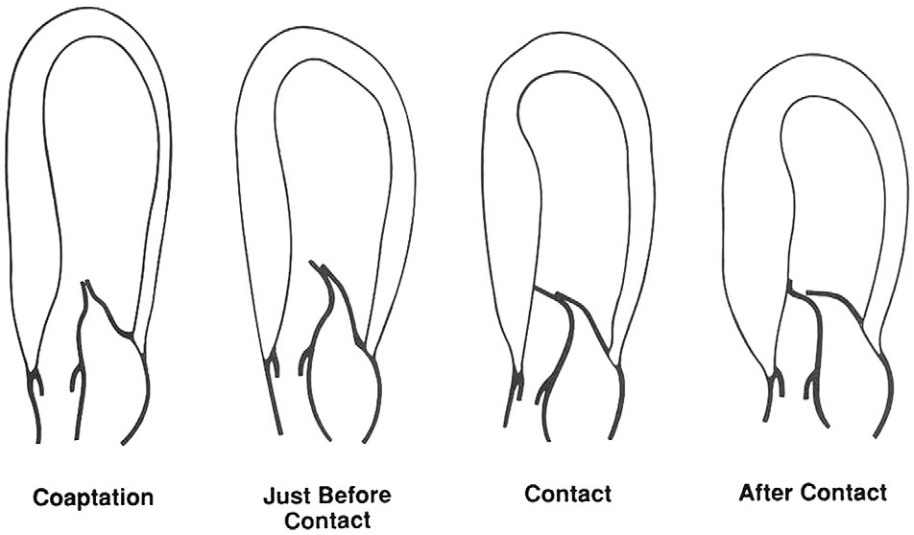

Fig 1. Systolic anterior motion of the mitral valve. Systolic anterior motion of the mitral valve, drawn from an apical 5-chamber view, as it proceeds in early systole. Reproduced with permission from Sherrid et al.[17]