

## Editorial

# Dynamic Evaluation of Exercise Limitation and Functional Class in Patients With Hypertrophic Cardiomyopathy

## Evaluación dinámica de la capacidad funcional y la limitación con el esfuerzo de los pacientes con miocardiopatía hipertrófica

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*Article history:*

Available online 26 November 2012

Hypertrophic cardiomyopathy (HCM)<sup>1,2</sup> is a myocardial disease characterized by left ventricular hypertrophy which is not attributable to valvular disease or hypertension. In most cases the underlying cause is genetic and is inherited as an autosomal dominant trait with variable penetrance. HCM has been attributed to mutations in genes encoding sarcomere proteins. Ten such genes are known and very many mutations that cause HCM have been identified. In recent decades, advances in genetics have led to increased knowledge and identified many gaps in our understanding of the results obtained using the most recent generation of genetic sequencing technologies. Recently, data processing using computerized algorithms has opened up many fascinating issues, and the added complexity involved in interpreting the results obtained means that patients will benefit from consultations with specialists in cardiogenetics for improved care and genetic counseling.

One of the characteristics of HCM is that the age at which the patients present the disease can markedly differ; in fact, it may occur at any age, and the degree of hypertrophy or ventricular thickness can be mild, moderate, or severe. The location of ventricular hypertrophy also varies considerably: it may be predominantly apical or distal, may have an eccentric or more often an asymmetric pattern, and principally affects the basal septum. The ventricular cavity is generally smaller, although in cases of very localized hypertrophy it can be close to normal. In addition to hypertrophy, there may be mitral valve abnormalities, whether intrinsic—affecting the length of the leaflets (often redundant) or the subvalvular apparatus—or functional, due to insertion of the papillary muscles.

The symptoms and prognosis of HCM also differ to great extent; decreased functional capacity with exercise limitation is one of the most common symptoms of HCM due to dyspnea, chest pain, or both.

Echocardiographic assessment can help classify patients with HCM into those with left ventricular obstruction or not and aid in the development of a treatment plan.

The assessment of patients with cardiomyopathy at rest is of limited use in understanding the origin of symptoms, most of which are associated with stress. It is normal practice to perform gradient provocation maneuvers, such as the Valsalva maneuver, during echocardiography. The problem with provocative maneuvers is their degree of reproducibility. Echocardiographic study should be as complete as possible; together with morphologic echocardiographic values and valvular velocities it is also important to make a detailed analysis of diastolic tissue and tissue Doppler velocities.

Electrocardiographic study at rest does not always identify the functional limitations of some patients who may be initially classified as having obstruction. An ECG stress test is of great use in the identification of this group of patients; according to some authors, up to 70% of patients with HCM and symptoms under stress conditions have obstruction.<sup>3,4</sup>

The best protocol to identify patients with obstruction maximizes provocation factors such as stress and orthostasis; the patient is assessed while standing or using a cycle ergometer or treadmill.<sup>5</sup>

The factors that hypothetically limit exercise capacity in patients with HCM depend on ventricular systolic and diastolic filling characteristics, peripheral pressor response, and an appropriate response of the heart rate to adrenergic stimulation with exercise.<sup>6</sup>

Although it is theoretically easy to list the possible causes of functional limitations in these patients, there is great variation in baseline findings and the theoretical prediction of functional limitations. The reserve capacity and the minute volume increase through increased relaxation are characteristics that vary dynamically. At the molecular level, although the degree of ventricular hypertrophy is genetically determined during the patient's life, an active process of remodeling and adaptation develops in parallel to the aging process, with decreased relaxation and diastolic failure. The histological finding of fibrosis is characteristic of disease progression and therefore of cardiac aging, with progressive diastolic and systolic heart failure.<sup>7</sup>

Patients with obstructive disease benefit from therapeutic strategies that reduce the left ventricular outflow tract gradient. The severity of symptoms is not directly related to the maximum ventricular thickness or the maximum gradient in the left ventricular outflow tract, but indicates functional

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<http://dx.doi.org/10.1016/j.rec.2012.06.011>, Rev Esp Cardiol. 2013;66:98–103.

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reserve capacity, the ability to instantly adjust to the demands of exercise, and the hemodynamic consequences of dynamic obstruction of the left ventricular outflow tract.

One study<sup>8</sup> assessed the use of stress Doppler echocardiography in 87 HCM patients; a large percentage of these patients had obstruction, which is one of the determining factors. They had a greater degree of greater left atrial dilatation and mitral valve regurgitation. The diastolic function and age indexes were also independent factors in the patients with obstruction. In the remaining patients, limited functional capacity was associated with left chamber volumes.

The data presented partly explain the functional limitation under conditions of stress; the adjusted *R* (0.49) is low, but is still better than the adjusted *R* at rest.

Patients with hereditary cardiovascular disease would benefit from follow-up in units with experts who would participate in assessment and specific treatments. The dynamic assessment of patients with HCM aids in understanding the symptoms of these patients, improving treatment plans, and assessing risk assessment.

A deep assessment of the phenotype and better characterization of patients will help to choose the best treatment at the right time, since the slow, progressive process of aging in HCM subtly affects the parameters under conditions of stress, but only affects the parameters under resting conditions in the terminal phase.<sup>9,10</sup>

#### CONFLICTS OF INTEREST

None declared.

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