Clinical Phenotype and Outcome of Hypertrophic Cardiomyopathy Associated With Thin-Filament Gene Mutations

Definitions:

**Hypertrophy** – The thickening of an organ or tissue  
**Arrhythmic** - Without rhythm or regularity  
**Phenotype** – the appearance of a genetic disease; in the case of HCM, the complex abnormalities picked up by cardiologists using a variety of tests  
**Filament** – A slender threadlike fiber  
**LV Outflow Tract** – Portion of the left ventricle of the heart through which blood passes in order to enter the arteries  
**Systolic Dysfunction** – A decrease in the hearts ability to contract and push the blood into the circulatory system.  
**Restrictive LV Filling** – Limited filling of the blood from the atria to the left ventricle  
**Triphasic LV Filling** – Filling of the left ventricle in three stages as opposed to the normal 2 stage pattern  
**Malignant Ventricular Arrhythmia** – An especially severe and dangerous arrhythmia usually requiring defibrillation to be stopped  
**Diastolic Dysfunction** – A decrease in the hearts ability to push the blood from the atria into the ventricle.

Objectives This study aimed to assess clinical features and outcomes in a large cohort of patients with HCM associated with thin-filament mutations compared with thick-filament HCM.

Methods: Adult HCM patients (age >18 years), 80 with thin-filament and 150 with thick-filament mutations, were followed for an average of 4.5 years.

Results: Compared with thick-filament HCM, patients with thin-filament mutations showed: 1) milder and atypically distributed left ventricular (LV) hypertrophy and less prevalent outflow tract obstruction 2) higher rate of progression to class III or IV of the New York Heart Association heart failure classification 3) higher prevalence of systolic dysfunction or restrictive LV filling at last evaluation 4) 2.4-fold increase in prevalence of triphasic LV filling pattern and 5) similar rates of malignant ventricular arrhythmias and sudden cardiac death.

Conclusion: In adult HCM patients, thin-filament mutations are associated with increased likelihood of advanced LV dysfunction and heart failure compared with thick-filament disease, whereas arrhythmic risk in both subsets is comparable.
Triphasic LV filling is particularly common in thin-filament HCM, reflecting profound diastolic dysfunction.

The importance of this study lies in the possibility of further understanding genotype-phenotype correlation in HCM. This is of relevance in the perspective of designing and testing personalized therapies for HCM.