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-f**ilament** mutations compared with thick-**filamen**t HCM.

Methods: Adult HCM patients (age >18 years), 80 with thin-**filamen**t 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-f**ilamen**t 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.