Epidemiology and Clinical Aspects of Genetic Cardiomyopathies

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KEYWORDS

• Hypertrophic cardiomyopathy • Nonischemic dilated cardiomyopathy
• Arrhythmogenic right ventricular cardiomyopathy • Restrictive cardiomyopathy • Clinical registry

KEY POINTS

- Cardiomyopathies are an increasingly recognized cause of heart failure and sudden death, particularly in young patients.
- Since their original description, major advances were achieved in the phenotype knowledge, natural history, and nosography of cardiomyopathies leading to different classification systems.
- Deeper knowledge of the natural history of the disease and its phases (preclinical, overt disease, and end-stage disease) is needed.
- Large-scale clinical registries provide the opportunity to bridge knowledge gaps and improve risk prediction and management of patients with cardiomyopathies.

INTRODUCTION

Cardiomyopathies (CMPs) are myocardial disorders in which the heart muscle is structurally and functionally abnormal in the absence of abnormal conditions that can explain the observed myocardial abnormality.[1] Although considered rare diseases, the estimated combined prevalence of all CMPs is at least 3%.[2] Furthermore, their recognition is increasing because of advances in imaging techniques[3] and greater awareness in both the lay and medical communities. CMPs are typified by clinical and genetic heterogeneity and are associated with significant morbidity and mortality.[4] In this article, the authors summarize the classification, epidemiology, and phenotypic spectrum of genetic CMPs. (**Tables 1** and **2**)

CLASSIFICATION OF CARDIOMYOPATHIES

In 1957, Brigden[5] first used the term *cardiomyopathies* to describe a group of uncommon myocardial diseases not related to coronary artery diseases. Later in the 1960s, Goodwin and colleagues[6] defined CMPs as "*myocardial diseases of unknown cause*"[6] and identified 3 different entities, namely, dilated CMP (DCM), hypertrophic CMP (HCM), and restrictive CMP (RCM).

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Table 1
Classification systems for cardiomyopathies

Author/Year	CMP Definition	Classification
Goodwing/1972	Myocardial diseases of unknown cause	Hypertrophic CMP Dilated CMP Restrictive CMP
WHO/ISFC/1995	Diseases of the myocardium associated with cardiac dysfunction	Hypertrophic CMP Dilated CMP Restrictive CMP Arrhythmogenic right ventricular CMP Unclassified CMP • Fibroelastosis • Noncompacted myocardium Specific CMPs • Ischemic CMP • Valvular CMP • Hypertensive CMP • Inflammatory CMP • Metabolic CMP • Associated to general system diseases (eg, sarcoidosis) • Associated to muscular dystrophies • Associated to neuromuscular diseases • Caused by toxic reaction (eg, alcoholic CMP) • Peripartal CMP
AHA/2006	A heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic	Genetic • Hypertrophic CMP • Arrhythmogenic right ventricular CMP/dysplasia • Left ventricular noncompaction • Channelopathies Mixed • Dilated CMP • Restrictive CMP Acquired • Inflammatory CMP • Takotsubo CMP • Peripartum CMP • Tachycardia-induced CMP
ESC/2008	A myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular disease, and congenital heart disease sufficient to cause the observed myocardial abnormality	Hypertrophic CMP • Familial ◦ Unknown gene ◦ Sarcomeric protein mutation ◦ Glycogen storage diseases ◦ Lysosomal storage disease ◦ Disorder of fatty acid metabolism ◦ Carnitine deficiency ◦ Mitochondrial cytopathies ◦ Noonan syndrome ◦ Leopard syndrome ◦ Friedreich ataxia ◦ Amyloid (mutated TTR) • Nonfamilial ◦ Obesity ◦ Infants of diabetic mothers ◦ Athletic training ◦ Amyloid (AL/prealbumin, wild-type TTR)

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