Electrophysiological abnormalities and arrhythmias in alpha MHC mutant familial hypertrophic cardiomyopathy mice

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Abstract

A new mouse cardiac electrophysiology method was used to study mice harboring an alpha-myosin heavy chain Arg403Gln missense mutation (alpha-MHC403/+), which results in histological and hemodynamic abnormalities characteristic of familial hypertrophic cardiomyopathy (FHC) and sudden death of uncertain etiology during exercise. Wild-type animals had completely normal cardiac electrophysiology. In contrast, FHC mice demonstrated (a) electrocardiographic abnormalities including prolonged repolarization intervals and rightward axis; (b) electrophysiological abnormalities including heterogeneous ventricular conduction properties and prolonged sinus node recovery time; and (c) inducible ventricular ectopy. These data identify distinct electrophysiologic abnormalities in FHC mice with a specific alpha-myosin mutation, and also validate a novel method to explore in vivo the relationship between specific genotypes and their electrophysiologic phenotypes.

Version history

Version 1 (February 15, 1997): No description
Hypertrophic cardiomyopathy (HCM) is one of the major cardiac genetic disorders among South Asians, leading to contractile dysfunction, heart failure, and sudden cardiac death. This disease displays autosomal dominant inheritance, and it is associated with a large number of variants in both sarcomeric and non-sarcomeric proteins. The South Asians, a population with large ethnic diversity, potentially carries region-specific polymorphisms. There is high variability in disease penetrance and phenotypic expression of variants associated with HCM. Thus, extensive studies are required to decipher p

Electrophysiological abnormalities and arrhythmias in alpha MHC mutant familial hypertrophic cardiomyopathy mice. C I Berul, M E Christe, M J Aronovitz, C E Seidman, J G Seidman, and M E Mendelsohn. Division of Pediatric Cardiology, Tufts University School of Medicine, Massachusetts 02111, USA. charles.berul@es.nemc.org. Find articles by Berul, C. in: JCI | PubMed | Google Scholar. A new mouse cardiac electrophysiology method was used to study mice harboring an alpha-myosin heavy chain Arg403Gln missense mutation (alpha-MHC403/+), which results in histological and hemodynamic abnormalities characteristic of familial hypertrophic cardiomyopathy (FHC) and sudden death of uncertain etiology during exercise. Sarcomere protein gene mutations cause hypertrophic cardiomyopathy (HCM), a disease with distinctive histopathology and increased susceptibility to cardiac arrhythmias and risk for sudden death. Myocyte disarray (disorganized cell–cell contact) and cardiac fibrosis, the prototypic but protean features of HCM histopathology, are presumed triggers for ventricular arrhythmias that precipitate sudden death events. To assess relationships between arrhythmias and HCM pathology without confounding human variables, such as genetic heterogeneity of disease-causing mutations, background genotypes, and I