Format: Abstract


Genetic Risk of Arrhythmic Phenotypes in Patients With Dilated Cardiomyopathy.


Abstract

BACKGROUND: Genotype-phenotype correlations in dilated cardiomyopathy (DCM) and, in particular, the effects of gene variants on clinical outcomes remain poorly understood.

OBJECTIVES: The purpose of this study was to investigate the prognostic role of genetic variant carrier status in a large cohort of DCM patients.

METHODS: A total of 487 DCM patients were analyzed by next-generation sequencing and categorized the disease genes into functional gene groups. The following composite outcome measures were assessed: 1) all-cause mortality; 2) heart failure-related death, heart transplantation, or destination left ventricular assist device implantation (DHF/HTx/VAD); and 3) sudden cardiac death/sustained ventricular tachycardia/ventricular fibrillation (SCD/VT/VF).

RESULTS: A total of 183 pathogenic/likely pathogenic variants were found in 178 patients (37%): 54 (11%) Titin; 19 (4%) Lamin A/C (LMNA); 24 (5%) structural cytoskeleton-Z disk genes; 16 (3.5%) desmosomal genes; 46 (9.5%) sarcomeric genes; 8 (1.6%) ion channel genes; and 11 (2.5%) other genes. All-cause mortality was no different between variant carriers and noncarriers (p = 0.99). A trend toward worse SCD/VT/VF (p = 0.062) and DHF/HTx/VAD (p = 0.061) was found in carriers. Carriers of desmosomal and LMNA variants experienced the highest rate of SCD/VT/VF, which was independent of the left ventricular ejection fraction.

CONCLUSIONS: Desmosomal and LMNA gene variants identify the subset of DCM patients who are at greatest risk for SCD and life-threatening ventricular arrhythmias, regardless of the left ventricular ejection fraction.
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**KEYWORDS**: desmosomal mutations; dilated cardiomyopathy; genotype-phenotype correlation; prognosis

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