114. GENETICS IN HEART FAILURE

Author: Abiah Maria Joseph

Scientific adviser: Snejana Vetrilă, MD, PhD in Medical Sciences, Associate Professor, Discipline of Cardiology, Department of Internal Medicine, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

Introduction. One of the causes of heart failure is dilated cardiomyopathy (DCM) and a major proportion of DCM cases are of genetic mutation and most common is TTN gene which encodes for titin and causes cardiac dysfunction.

Aim of study. To analyse literature data about TTN mutation and severity of dilated cardiomyopathy and its genetic correlation.

Methods and materials. A literature review of a number of two articles in PubMed publications, including studies conducted to evaluate the type of mutation, genetic inheritance, and their effect on cardiac structure and function.

Results. The most common cause of dilated cardiomyopathy is structural mutation of titin, a giant gene encoded by TTN, which maintains structural integrity and acts as a molecular spring in the cardiomyocyte. TTN mutations have an autosomal dominant inheritance pattern. The TTN gene not only maintains the structure of the sarcomere but also multiple signalling pathways in cardiomyocytes, which are striated, involuntary, and branched muscle cells. When there is a genetic mutation in TTN, it leads to the formation of irregular trabeculae in the cardiomyocyte and causes left ventricular non-compaction (LVN), which is a type of dilated cardiomyopathy. Congestive heart failure caused by familial dilated cardiomyopathy occurs in approximately 20 to 30% of cases, due to mutations in cytoskeletal proteins, contractile proteins, and inner nuclear membrane proteins. The inheritance pattern of the TTN mutation is autosomal dominant with dilated cardiomyopathy, linked to chromosome 2q31 and known as CMD1G and MIM 604145. If we consider a large family of TTN mutations, there is a 2-base pair insertion mutation in exon 326 of TTN, which causes a frameshift mutation and leads to the truncation of a region of the titin loop. The truncation of titin leads to the formation of a premature stop codon that is incorporated into the sarcomere and acts as a poisonous peptide, ultimately destroying contractile function. If we consider another family of familial dilated cardiomyopathy with CMDIG that has a missense mutation, instead of tryptophan there is an arginine substitution Try930Arg, which leads to destabilization of the protein structure, may weaken the structural integrity of titin and disconnect the Z disc from the M line.

Conclusions. Genetics play a crucial role in the development of DCM, and the identification of the TTN gene sheds light on the genetic mechanism. This contributes to early diagnosis, thus ensuring early management, prevention and optimal treatment of heart failure.

Keywords. TTN mutation, Dilated cardiomyopathy, Autosomal dominant.

https://doi.org/10.66603/medespera2026.645