Introduction

Cardiomyopathies are heart muscle diseases originated from a series of aggressions, such as genetic defects, cardiac myocyte injury or infiltration of myocardial tissue. Dilated cardiomyopathy (DCM) is characterized by an impairment of the left ventricular or biventricular contraction, caused by familial, genetic, viral, autoimmune, alcoholic, toxic, or of unknown cause. It is also associated with other recognized cardiovascular diseases, being considered a major cause of heart failure (HF) and the main indication for heart transplantation, which, on average, appears in the fourth decade of life [4,5]. Subsequent studies in experimental models have shown that the disease caused by troponin T changes results in calcium desensitization of the ATPase of the actomyosin, which in turn reduces the rate of contraction of the sarcomere and consequently its contractile force. Not always changes in the mutations in the cardiac troponin genes are pathogenic, and to become so, it require genetic or environmental changes. Presenilin is an essential protein to γ-secretase, the enzyme responsible for the proteolytic processing of multiple proteins associated with the cell membrane. It is widely expressed in the brain, where it is responsible for the regulation of intracellular calcium currents and is implicated in the pathophysiology of Alzheimer’s disease, but also expressed in the heart, where it is essential to cardiac morphogenesis. Mutations in PSEN1 and PSEN2 genes were proposed as possible causes of DCM. Thus, alterations of PSEN1 and PSEN2 genes are potential candidates for disease, as they increase intracellular protein aggregates, which in turn alter calcium homeostasis and provoke cytotoxicity [6,7]. Its’ appearance in younger subjects suggests an early senility of the cardiac apparatus. Recently, studies have identified a polymorphism of the HSPB7 gene as being associated with increased susceptibility to DCM. HSPB7 is a gene encoding a small heat shock protein, cvHsp (also known as HspB7), usually activated when the cell is under stress, whether by elevated temperature, hypoxia or ischemia. Although the pathophysiological mechanism of this polymorphism is not well defined, its prevalence in patients included in the studies was 49% of cases of DCM [8].

Another important discussion is the discovery of three troponin subunits that cause the disease, namely TNNC1 (troponin C), TNNT2 (troponin T) and TNNI3 (troponin I) genes. These changes in the troponin complex are present in about 6% of DCM cases, and the clinical manifestations of these mutations are generally severe, causing sudden cardiac death and need for heart transplantation, which, on average, appears in the fourth decade of life [4,5]. Subsequent studies in experimental models have shown that the disease caused by troponin T changes results in calcium desensitization of the ATPase of the actomyosin, which in turn reduces the rate of contraction of the sarcomere and consequently its contractile force. Not always changes in the mutations in the cardiac troponin genes are pathogenic, and to become so, it require genetic or environmental changes. Presenilin is an essential protein to γ-secretase, the enzyme responsible for the proteolytic processing of multiple proteins associated with the cell membrane. It is widely expressed in the brain, where it is responsible for the regulation of intracellular calcium currents and is implicated in the pathophysiology of Alzheimer’s disease, but also expressed in the heart, where it is essential to cardiac morphogenesis. Mutations in PSEN1 and PSEN2 genes were proposed as possible causes of DCM. Thus, alterations of PSEN1 and PSEN2 genes are potential candidates for disease, as they increase intracellular protein aggregates, which in turn alter calcium homeostasis and provoke cytotoxicity [6,7]. Its’ appearance in younger subjects suggests an early senility of the cardiac apparatus. Recently, studies have identified a polymorphism of the HSPB7 gene as being associated with increased susceptibility to DCM. HSPB7 is a gene encoding a small heat shock protein, cvHsp (also known as HspB7), usually activated when the cell is under stress, whether by elevated temperature, hypoxia or ischemia. Although the pathophysiological mechanism of this polymorphism is not well defined, its prevalence in patients included in the studies was 49% of cases of DCM [8].

The adequate investigation and the progression of the pathophysiological knowledge of DCM advances every year with new genetic discoveries. It’s better understanding is very important for the introduce of appropriate treatment. Even though, nowadays in many centers, genetic research in these patients is still not a reality.
References