46. MOLECULAR REMODELING IN HUMAN HEART FAILURE

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Introduction: Heart failure is a disease in which there is a mismatch between blood supply and demand of the organs, in which case the heart undergoes molecular changes, also known as cardiac remodeling.

Cardiac remodeling is the restructuring and reshaping of the heart that underlies heart failure progression.

The traditional concepts of cellular remodeling in the failing heart are characteristic alterations in cell size, shape, and the ability to perform contractile work.

Aim: Studying the immediate and long-term manifestations of the cardiac remodeling aspects in the body.

Materials and methods : A wide variety of experiments, researches and hours were put into understanding chronic heart failure and its molecular changes, which we were supported by, as well as the facts provided by a couple of cardiologists we seeked.

Discussions and results: Heart failure is a disease in which there is a mismatch between blood supply and demand of the organs, in which case the heart undergoes molecular changes. In the United States, it is estimated that heart failure develops in 465,000 people each year. Heart failure occurs in both men and women and is associated with a high morbidity and mortality rate in both sexes and in all races. The traditional concepts of cellular remodeling in the failing heart are characteristic alterations in cell size, shape, and the ability to perform contractile work. Cellular changes in heart failure include myocyte hypertrophy, abnormalities in calcium homeostasis, excitation-contraction coupling, cross-bridge cycling, and changes in the cytoskeletal architecture.

Myocardial remodeling denotes acquired pathological states of the heart resulting in rearrangement of normally existing structures and generally concerns the two components of the cardiovascular system, the myocardium and the vessels, the structure of both can be altered by unfavorable conditions caused by several noxious stimuli that impose increased biomechanical stress to the cardiomyocytes. In response to an increased workload, individual cardiomyocytes react by adaptive hypertrophic growth, they increase in cell size, volume and mass, or undergo apoptosis, respectively. As a result, there is organ enlargement, cardiac dilation and increased sphericity. Although salutary at the beginning by reducing wall tension, hypertrophy eventually becomes a maladaptive process, leading to chronic heart failure and cardiac mortality. Dilation is followed by increased ventricular wall stress resulting in decreased coronary blood flow, impaired pump function and diminished cardiac output. Moreover, interstitial fibrosis is observed, further hindering systolic and diastolic cardiac function.

Conclusions:

1.Heart failure is compensated through pathogenetic mechanisms, which maintain cardiac performance.

2. Compensatory mechanisms cause molecular remodeling, that compromise systolic and diastolic cardiac function.

3. Finally, the logistical challenges of studying human cardiac gene expression emphasize the need for newer noninvasive approaches to study molecular aspects of cardiac remodeling in human subjects. Many strategies are evolving to do this, including novel circulating biomarkers, studies of inherited gene variation in hypertrophic signaling pathways, and molecular imaging. These techniques will undoubtedly help us test the clinical relevance of mechanisms of cardiac remodeling discovered in animal models and thereby identify novel therapeutic targets for human heart failure.