Abstract

Heart failure (HF) is a common endpoint for many forms of cardiovascular disease and a significant cause of morbidity and mortality. The development of end-stage HF often involves an initial insult to the myocardium that reduces cardiac output and leads to a compensatory increase in sympathetic nervous system activity. Acutely, the sympathetic hyperactivity through the activation of beta-adrenergic receptors increases heart rate and cardiac contractility, which compensate for decreased cardiac output. However, chronic exposure of the heart to elevated levels of catecholamines released from sympathetic nerve terminals and the adrenal gland may lead to further pathologic changes in the heart, resulting in continued elevation of sympathetic tone and a progressive deterioration in cardiac function. On a molecular level, altered beta-adrenergic receptor signaling plays a pivotal role in the genesis and progression of HF. beta-adrenergic receptor number and function are decreased, and downstream mechanisms are altered. In this review we will present an overview of the normal beta-adrenergic receptor pathway in the heart and the consequences of sustained adrenergic activation in HF. The myopathic potential of individual components of the adrenergic signaling will be discussed through the results of research performed in genetic modified animals. Finally, we will discuss the potential clinical impact of beta-adrenergic receptor gene polymorphisms for better understanding the progression of HF.

Keywords

heart failure, sympathetic nervous system, adrenergic receptors.