DIVERSE MECHANISMS OF HEART FAILURE DUE TO MYOCARDIAL INFARCTION

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It is now well known that heart failure due to myocardial infarction is associated with elevated levels of several vasoactive hormones such as catecholamines angiotensins, endothelins and serotonin. These hormones not only induce cardiac hypertrophy but also produce functional hypoxia, metabolic derangements, oxidative stress, inflammation, subcellular defects for Ca^{2+}-handling abnormalities and arrhythmias in the failing heart. Particularly, prolonged exposure of the hypertrophied heart promotes the oxidation of catecholamines and serotonin by monoamine oxidase as well as activation of NADPH oxidase by angiotensin II and endothelin for the generation of oxyradicals and oxidants which result in oxidative stress. These pathophysiological events affect different signal transduction pathways and play a critical role in the development of apoptosis, necrosis and fibrosis as well as activation of different proteases and dramatic alterations in the extracellular matrix for the occurrence of adverse cardiac remodeling and cardiac dysfunction. There also occurs a loss of adrenergic support for maintaining cardiac function in the failing heart. Thus, heart failure due to myocardial infarction is not only a consequence of the loss of myocardium but also involves a set of complex mechanisms in both viable cardiomyocytes and extracellular matrix. It is suggested that multi-target therapy should be developed for delaying the progression of heart failure.

Keywords: vasoactive hormones, metabolic defects, Ca^{2+}-handling abnormalities, oxidative stress, extracellular matrix.