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Review

Molecular determinants of heart failure with normal left ventricular ejection fraction

Attila Borbély[1,2], Zoltán Papp[1], István Édes[1], Walter J. Paulus[2]

[1]Division of Clinical Physiology, Institute of Cardiology, University of Debrecen, Medical and Health Science Center, Móricz Zsigmond 22, H-4032 Debrecen, Hungary

[2]Department of Physiology, Institute for Cardiovascular Research, VU University Medical Center, Van der Boechorststraat 7, 1081BT Amsterdam, The Netherlands

Correspondence: Attila Borbély, e-mail: borbelya@dote.hu

Abstract:
In population-based studies, heart failure with normal left ventricular (LV) ejection fraction (HFNEF) is now increasingly recognized and referred to as diastolic heart failure. However, the pathogenic mechanisms underlying HFNEF are incompletely understood, mainly because of limited availability of human myocardial biopsy material. Nevertheless, recent studies have examined *in vivo* hemodynamics, *in vitro* cardiomyocyte function, myofilamentary protein composition, collagen content and deposition of advanced glycation end products from LV endomyocardial biopsies. These measures were compared between HFNEF patients, subjects without symptoms of heart failure (controls), patients with heart failure and reduced ejection function (HFREF), and patients with HFNEF and HFREF with diabetes mellitus. This article summarizes the various findings of these studies and focuses on the possible correlations among altered LV myocardial structure, cardiomyocyte function, myofilamentary proteins, and extracellular matrices. These findings revealed novel mechanisms responsible for diastolic LV dysfunction, and they have important therapeutic implications, particularly HFNEF, for which a specific heart failure treatment strategy is largely lacking.

Key words: heart failure, diastolic function, cardiomyocytes, myofilamentary proteins, fibrosis, diabetes mellitus