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Review

Endothelial dysfunction in heart failure

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Abstract:
Endothelial dysfunction crucially contributes to the development of impaired coronary and systemic perfusion as well as reduced exercise capacity in patients with congestive heart failure, with fundamental impact on morbidity and mortality. Reduced bioavailability of nitric oxide (NO) and abundant formation of reactive oxygen species (ROS) within the vascular wall are the key determinants in endothelial dysfunction. The disbalance between NO and ROS mainly results from neurohumoral activation associated with heart failure. As endothelial derived NO is a major endogenous modulator of platelet function, reduced intravascular bioactivity of NO contributes to platelet activation, adhesion and thromboembolic events in heart failure. Treatment with angiotensin converting enzyme (ACE) inhibitors, angiotensin and aldosterone antagonists, and statins beneficially modulates endothelial dysfunction in heart failure. All these therapies increase NO bioactivity by either modulation of ROS generation, thereby preventing the interaction of superoxide anions with NO, and/or increasing endothelial NO synthase (eNOS) expression/activity. AVE9488, a novel eNOS transcription enhancer, attenuates cardiac remodeling and endothelial dysfunction in rats after large myocardial infarction. Endothelial progenitor cell (EPC) levels and their mobilization are regulated by eNOS. After myocardial infarction in rats, EPC levels and formation of endothelial colony forming units are markedly reduced. AVE 9488, ACE or HMG-CoA reductase inhibition result in significant increases in EPC levels, and beneficial effects on bone marrow molecular alterations after myocardial infarction.

Key words:
endothelial dysfunction, congestive heart failure, nitric oxide, reactive oxygen species