

Arginine and Endothelial and Vascular Health

Heather L. Gornik and Mark A. Creager

Vascular Medicine Section, Cardiovascular Division, Brigham and Women's Hospital, Boston, MA 02115

ABSTRACT The vascular endothelium is a crucial regulator of vascular function and homeostasis. Nitric oxide (NO) is an important paracrine substance released by the endothelium to regulate vasomotor tone. Risk factors for atherosclerosis, as well as atherosclerosis per se, are associated with endothelial dysfunction and decreased bioavailability of NO. Indeed, endothelial dysfunction is integral to the pathogenesis of atherosclerosis and other cardiovascular diseases. Moreover, endothelial dysfunction relates to an increased risk of adverse cardiovascular outcomes. L-Arginine is an essential amino acid required by the constitutive enzyme, endothelial NO oxide synthase (eNOS), to produce NO. Administration of L-arginine improves endothelial function in animal models and in humans with hypercholesterolemia and with atherosclerosis. Clinical trials to date support potential clinical applications of L-arginine in the treatment of coronary artery disease and peripheral arterial disease, as well as in the prevention of in-stent restenosis. The mechanism of benefit of L-arginine on endothelial function is unclear, because intracellular concentrations of L-arginine far exceed that required by eNOS. One potential explanation of this "arginine paradox" is that L-arginine restores endothelial function in atherosclerotic patients, in whom there are elevated levels of asymmetric dimethylarginine, an endogenous inhibitor of eNOS. Given the promising findings of early studies of L-arginine as a potential therapy for cardiovascular disorders, large-scale clinical trials are warranted.
