Public Abstract
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Title:RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS BLOCKADE IMPROVES ENDOTHELIAL DEPENDENT VASCULAR FUNCTION IN ATHEROSCLEROTIC MICE

Atherosclerosis is a progressive inflammatory disease that is predominantly present in large vessels in the body. Among other effects, a noted impairment of endothelial-mediated vasodilation is especially prominent. We hypothesized that either adiponectin treatment or soluble Receptor for Advanced Glycation Products (sRAGE) treatment would rescue the decreased endothelial function of aortae in apolipoprotein-E knockout (ApoE-/-) mice, a murine model of atherosclerosis. Both adiponectin and sRAGE are hypothesized to mediate signaling pathways that counteract and promote inflammation, respectively. We examined endothelial-dependent vasorelaxation to acetylcholine (ACh) in aortae removed from atherosclerotic ApoE-/- and control wild (WT) mice. Relaxation to ACh was blunted in ApoE-/- compared with WT controls while endothelial-independent vasorelaxation to sodium nitroprusside (SNP) was comparable. Soluble receptor of advanced glycation end products/receptor (sRAGE) improved ACh-induced vasorelaxation in ApoE-/- mice without affecting dilator response to SNP.
However, adiponectin treatment did not show significant improvement of endothelial function in aortae of ApoE-/- mice. Dilation to ACh was significantly attenuated after administration of nitric oxide (NO) synthase inhibitor NG-monomethyl L-arginine in WT mice, which indicates that vasodilation to ACh was NO mediated while L-NMMA did not further inhibit endothelial-dependent vasodilation in ApoE-/- mice. Immunostaining showed RAGE to co-localized with the endothelium in murine aortae. These results suggest that AGE/RAGE signaling may play a pivotal role in processes that lead to endothelial dysfunction in atherosclerosis.