Hypercholesterolemia exacerbates transplant arteriosclerosis via increased neointimal smooth muscle cell accumulation: studies in apolipoprotein E knockout mice.

李文森

Shi C;Lee WS;Russell ME;Zhang D;Fletcher DL;Jr.;John B. Newell and Haber E

Abstract

Hypercholesterolemia is thought to be a significant risk factor for coronary vasculopathy in cardiac transplant recipients. Methods and Results We examined the development of arteriosclerosis in mouse carotid artery loops allografted from B.10A(2R) (H-2h2) donors to normocholesterolemic C57BL/6J (H-2b) recipients and hypercholesterolemic C57BL/6J recipients in which the apolipoprotein (apo) E gene had been knocked out. Luminal occlusion and cross-sectional neointimal area were greater in arteries allografted into hypercholesterolemic recipients at 15 and 30 days after transplantation. We also measured cellular and extracellular matrix components of the neointima by computerized planimetry of the fractional areas subtended by smooth muscle cells (anti–-actin stain), collagen (Masson's trichrome), lipid (oil red O), and leukocytes (anti-CD45). The neointimal area stained for smooth muscle cells was significantly greater in hypercholesterolemic recipients than in normocholesterolemic recipients at 15 and 30 days after allografting. Lipid contributed to neointimal area to a lesser degree, and there was no significant increase in the contribution of collagen or leukocytes. Conclusions Smooth muscle cell accumulation appears to be the principal contributor to the increase in neointimal area observed in arteries allografted into hypercholesterolemic mice.