407-3 Estrogen Augments Incorporation of Bone Marrow-Derived Endothelial Progenitor Cells Into Sites of Myocardial Neovascularization

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Background: We hypothesized that estrogen augments incorporation of bone marrow-derived endothelial progenitor cells (EPCs) into sites of neovascularization after myocardial infarction (MI). Methods and Results: MI was induced by ligation of left coronary artery in 67 ovariectomized FVB mice receiving either 17β-estradiol or placebo. Left ventricular (LV) function within 2 weeks after MI, assessed by echocardiography and catheter-based manometer, was similar between the groups. However, LV systolic and diastolic dimensions and fractional shortening in the estrogen group were preserved 3 and 4 weeks after MI as compared to placebo. LV dP/dt and -dP/dt at 4 weeks after MI in the estrogen group were also higher than placebo. Capillary density 4 weeks after MI was significantly greater in estrogen group (P<0.01). Furthermore, ratio of fibrosis area to LV area in the estrogen group was significantly lower than placebo (P<0.05). In cultured EPC assay, significant increases in circulating EPCs 2 and 3 weeks after MI were observed in the estrogen group as compared to placebo (2 wks, 3 wks: P<0.01). To evaluate the effects of estrogen on BM-derived EPCs at the sites of myocardial neovascularization, we made MI models using 21 ovariectomized FVB mice transplanted with BM from transgenic donors expressing β-galactosidase transcriptionally regulated by endothelial-cell-specific Tie-2 promoter. More X-gal positive cells were observed in viva by MRI as a signal void and post-mortem using confocal fluorescent microscopy. VESF expression in the estrogen group was increased both in the infarcted and non-infarcted areas 1 week after MI, although eNOS expression was similar between the groups. Conclusions: Estrogen attenuates LV remodeling and preserves LV function after MI by augmenting incorporation of SM-derived EPCs into sites of myocardial neovascularization that might partially be mediated by VEGF.

407-4 C-Reactive Protein Directly Attenuates Nitric Oxide Release and Bioactivity

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Background: C-reactive protein (CRP) is an acute-phase protein released in response to bacterial infection or tissue injury. CRP is a positive acute-phase reactant protein and is involved in the pathogenesis of atherosclerosis. CRP has been shown to affect the functional properties of endothelial cells. In the present study, we investigated the effect of CRP on the expression and release of nitric oxide (NO) and cyclic guanosine monophosphate (cGMP) in endothelial cells. Methods: Human umbilical vein endothelial cells (HUVECs) were treated with concentrations of CRP ranging from 0 to 100 µg/mL for 24 hours. The production of NO was measured using the Griess reaction. The effect of CRP on the release of NO was determined using radiolabeled NO (NaNO2) incorporation. Results: CRP significantly reduced the production of NO and cGMP in HUVECs. The inhibitory effect of CRP on NO production was dose-dependent. Conclusion: CRP reduces the release of NO and cGMP in endothelial cells, which may contribute to the pathogenesis of atherosclerosis.

407-5 Circulating and Tissue Angiotensin II Type 1 Receptors From Perioperation Through One-Year of Transplantation: A Potential Molecular Mechanism for Cardiac Allograft Vasculopathy

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The precise molecular mechanism underlying the accelerated progression of cardiac allograft vasculopathy (CAV) after transplantation is not known. Objectives and Methods: We, therefore, attempted to determine whether type 1 angiotensin II (AT1) receptor expression, which was assessed by real-time quantitative RT-PCR using Taqman Man system (Applied Biosystems, CA) during perioperative period through one year after transplantation of CAV manifests the development of CAV. Results: We observed a significant increase in AT1 receptor transcript (AT1R) expression in biopsies of CAV patients compared to those of non-CAV patients. Conclusion: These findings suggest that AT1R expression may play a role in the development of CAV and that inhibition of AT1R may be a potential therapeutic strategy for the prevention and treatment of CAV.