There was a statistically significant difference when comparing EMP levels fasting, at one hour (p = 0.0002) and three hours (p = 0.0001) after the high fat meal. When low fat meal was given, there was no statistical difference when comparing EMP levels fasting and one hour and three hours after low meal.

**CONCLUSION:** EMP are shed in the circulation and may represent an early marker of endothelial injury. There is a direct correlation between cholesterol and EMP levels in healthy volunteers. A single high fat meal may lead to a detectable elevation of EMP in the circulation even in subjects with normal fasting baseline total cholesterol.

### 1159-192

**The Influence of Simvastatin on the Angiotensin AT1 Receptor Density, Oxidative Stress, and Endothelial Function in Patients With Coronary Disease**

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**Background:** On the base of experimental studies we formulated the hypothesis on the development of the endothelial dysfunction: LDL cholesterol $\rightarrow$ angiotensin AT1 receptors ($A_T R\rightarrow$ oxidative stress $\rightarrow$ endothelial dysfunction. We tested this hypothesis in patients (pts) with stable angina. We tested also whether statins: (i) improves endothelial function by reducing oxidative stress and (ii) that this effect is due to the reduction in angiotensin $A_T R$ density.

**Methods:** Lipid profile, platelet $A_T R$ receptor density, serum F2-isoprostanes (marker of oxidative stress) and nitrate $+$ nitrite concentration, and brachial artery flow mediated dilation (FMD, index of endothelial function) were assessed in 20 pts (LDL cholesterol 75-230 mg%) with proven coronary heart disease, which were not on hypolipemic treatment. These measurements were performed at baseline and after treatment with simvas- tatin 40mg/d for 12 weeks.

**Results:** At baseline there was a significant linear correlation between (i) LDL cholesterol concentration and $A_T R$ density ($r=0.56; p<0.05$) and (ii) $F_2$-isoprostanes and FMD ($r=-0.66; p<0.05$). Simvastatin treatment caused a significant reduction in LDL cholesterol (152±39 vs. 89±27mg/dl; p=0.0001), $A_T R$ density (14.42±5.42 vs. 7.58±6.88 receptors/platelet; p<0.0001), $F_2$-isoprostanes (39.85±14.03 vs. 27.90±10.65pg/ml; p=0.017), a significant improvement in FMD (8.85±4.80% vs. 11.04±3.85%; p<0.001), and significant increase in nitrate $+$ nitrite concentration (17.23±3.03 vs. 20.94±7.93µmol/l; p=0.038). Among these simvastatin-induced effects, only changes in $A_T R$ receptors and $F_2$-isoprostanes concentrations showed strong linear correlation ($r=0.65; p<0.05$).

**Conclusions:** For the first time we have shown in one study that statins causes, in addition to LDL cholesterol reduction and endothelial function improvement, reduction in $A_T R$ density and oxidative stress. Baseline results suggest relationship between LDL cholesterol, $A_T R$ density, oxidative stress and endothelial dysfunction. Our results suggest that simvastatin-induced reduction in oxidative stress is due to reduction in $A_T R$ density.

### 1159-193

**Simvastatin Combined With Ramipril Improved Endothelium-Dependent Vasodilation and Fibrinolysis Potential and Reduced Oxidative Stress and Inflammation Markers in Hypercholesterolemic Patients**

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**Background:** Because the mechanisms of the biological effects of statin and antitensin converting enzyme inhibitor therapies differ, we studied the vascular responses to these therapies in hypercholesterolemic patients.

**Methods:** We administered simvastatin 20 mg and placebo or ramipril 10 mg daily during 2 months with washout 2 months to 50 hypercholesterolemic patients. This study was randomized, double-blind, placebo-controlled, crossover in design. $\ast P<0.05; \ast \ast P<0.01; \ast \ast \ast P<0.001$ vs Baseline. Data= mean±SEM.

**Results:** Simvastatin alone did not reduce blood pressure, however, simvastatin combined with ramipril significantly reduced blood pressure after 2 months administration compared with baseline. Compared with each baseline, simvastatin alone or combined with ramipril significantly changed lipoproteins, and improved the percent flow-mediated dilator response to hyperemia by 30.5% and by 53.6%, respectively (both P<0.001) and reduced plasma levels of malondialdehyde (MDA) levels by 4×7% (P=0.026) and by 25×4% (P=0.001), respectively and MCP-1 levels by 3×3% and by 12×2%, respectively (P=0.049 and P=0.001, respectively), and C-reactive protein levels by 4×14% and by 26×5%, respectively (P=0.036 and P=0.001, respectively), and PAI-1 antigen levels by 7×7% and by 17×5%, respectively (P=0.028 and P=0.001, respectively). However, simvastatin combined with ramipril significantly changed more percent flow-mediated dilator response to hyperemia and plasma levels of MDA, MCP-1, CRP, and PAI-1 antigen than simvastatin alone independent of lowering blood pressure.

**Conclusions:** Compared with simvastatin alone, simvastatin combined with ramipril significantly improved endothelium-dependent vasodilation and fibrinolysis potential and reduced plasma levels of oxidative stress and inflammation markers in hypercholesterolemic patients.

**Baseline1 Statin+Placebo**

- Apo B (mg/dl) 131±4 99±3*** 124±5 92±3***
- FMD (%) 4.8±1.5 8.2±0.29*** 4.96±0.25 6.58±0.25***
- Nitrate (umol): 92±7 83±6 94±7 µmol**

**Baseline2 Statin+Ramilpr**

- Apo B (mg/dl) 131±4 99±3*** 124±5 92±3***
- FMD (%) 4.8±1.5 8.2±0.29*** 4.96±0.25 6.58±0.25***
- Nitrate (umol): 92±7 83±6 94±7 µmol**

**MDA (um) 1.36±0.01 1.17±0.07* 1.45±0.09 1.01±0.07***

**MCP-1 (gg/ml) 194±8 178±5* 202±8 174±6***

**PAI-1 (gg/ml) 64±3 63±4 68±5 53±3***