Aortic Valve Calcification and C-Reactive Protein

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Background: Recent studies suggest that inflammation and aortic valve calcium (AVC) play a role in the pathogenesis of subsequent cardiovascular events. We sought to determine whether C-reactive protein (CRP) and AVC are associated with events.

Methods: 856 non-diabetic participants in the South Bay Heart Watch cohort without underlying coronary heart disease underwent baseline risk factor screening (including CRP measurement). Total CRP was defined as > 75th percentile of the non-zero values (>140 score units) and was present in 41 participants (4.8%). Mean follow-up was 7.0 +/- 0.5 years. AVC was measured using the method of the MESA study. Abnormal CRP was defined as > 75th percentile (>3.97 mg/L). Outcomes of non-fatal myocardial infarction, coronary death, coronary revascularization, or stroke were considered. Cox regression analysis was performed to determine the effect of AVC and CRP on clinical outcomes.

Results: As shown in the table, participants with both elevated AVC and CRP were more likely to suffer subsequent events than participants with only one of these findings (p=0.0004).

A high AVC score in combination with elevated CRP in an asymptomatic person portends a higher risk for future cardiovascular events than either high AVC or CRP alone.

<table>
<thead>
<tr>
<th>CRP, AVC</th>
<th>CRP, AVC+</th>
<th>CRP+, AVC</th>
<th>CRP+, AVC+</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR</td>
<td>1.0</td>
<td>1.63</td>
<td>1.32</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.70-3.79</td>
<td>0.86-2.02</td>
<td>1.92-9.57</td>
</tr>
<tr>
<td>P</td>
<td>0.26</td>
<td>0.21</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

Conclusion: Maternal undernutrition and early postnatal diet affect vascular parameters in offspring. This activation is partially abolished by atorvastatin, supporting anti-inflammatory effects of statins.

POSTER SESSION

1159 Vascular Function and Structure: Translational Research

Tuesday, March 09, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1159-183 Circulating T Cell Perturbation and Macrophage Activation in Stable Coronary Artery Disease Patients: Effect of Atorvastatin Therapy

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Background: Coronary artery disease (CAD) is characterized by both T lymphocyte and macrophage activation. Statins have anti-inflammatory effects beyond lipid lowering. Whether these also affect the global immune system is unclear. The aim of this study was to investigate the influence of atorvastatin (atorv) on circulating inflammatory T helper lymphocytes (TH1), on their circulating activation marker soluble CD40 ligand (sCD40L) on the soluble intercellular adhesion molecule-1 (sICAM-1), involved in lymphocyte recruitment and on neopterin, a macrophage activation marker.

Methods: 30 hypercholesterolemic patients with angiographically documented stable CAD were randomized in a double-blind study to placebo or atorv (20mg/d) for 3 months. Eight healthy volunteers served as controls. sCD40L, sICAM-1, neopterin and C-reactive protein (CRP) levels were measured with ELISA. TH1 and anti-inflammatory T helper (TH2) lymphocytes were determined by FACS analysis.

Results: TH1 cells (47.9±10.8 vs. 31.5±9.5%; p<0.002), neopterin (7.0±2.5 vs. 4.5±1.3nmol/L; p<0.002), sCD40L (10.4±4.5 vs 6.6±1.6ng/mL; p<0.001), sICAM-1 (251.8±83.6 vs 127.9±44.8ng/mL; p<0.01) and CRP levels (0.47±0.40 vs 0.07±0.05mg/dL; p<0.001) were decreased in the atorv group, but remained similar in the placebo group. By contrast, neopterin (p<0.02), sCD40L (10.4±4.5 vs. 6.6±1.6ng/mL; p<0.01), sICAM-1 (p=0.01) and CRP (p=0.01) were decreased in the atorv group, but remained similar in the placebo group.

Conclusion: A high AVC score in combination with elevated CRP in an asymptomatic person portends a higher risk for future cardiovascular events than either high AVC or CRP alone.