A statement of the conclusions reached: Higher serum IL-15 levels were found in patients with severe organ damages, especially cardiovascular diseases such as CAD or PAD. These data suggested systemic inflammatory response including IL-15 might be involved in occurrence of cardiovascular diseases in patients with essential hypertension.

Key Words: IL-15, Essential Hypertension, Cardiovascular Complications

P-579
NONDIPPING STATUS AND HIGH PULSE PRESSURE: RELATIONSHIP TO ENDOTHELIAL DAMAGE/DYSFUNCTION

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On 24 hour ambulatory blood pressure monitoring (ABPM), patients with nondipping pattern of BP (a circadian nocturnal fall in systolic BP of <10%) have a greater risk of target organ damage than do patients with a dipping pattern. Pulse pressure (PP) has been shown to be independently associated with the presence of coronary artery disease (CAD) and as an independent predictor of cardiovascular risk. We hypothesized that there is a greater degree of impaired endothelial function in patients with CAD who have higher 24-hr mean PP and/or nondipping pattern of circadian BP.

We studied 72 patients (58 male, 59±11 yrs) with stable CAD and preserved left ventricular function (ejection fraction 61±10%). All completed a 24-hr ABPM. Patients were divided into groups according to high (≥median, 51 mmHg) or low (< median) values of 24-hr mean PP, and dippers or nondippers according to their circadian nocturnal fall in systolic BP. Flow-mediated dilation (FMD, an index of endothelium-dependent vasodilation) and nitroglycerine-mediated dilation (NMD) of the brachial artery assessed by high-resolution ultrasound and plasma von Willebrand factor (vWF, an index of endothelial damage/dysfunction, ELISA) were measured in all patients blinded from the ABPM results. Baseline FMD and vWF values were compared with 35 matched healthy controls (23 male, 57±6 yrs). Patients with CAD had significantly ab-

<table>
<thead>
<tr>
<th>Dippers (n = 27)</th>
<th>Nondippers (n = 39)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>57 ± 11</td>
<td>60 ± 11</td>
</tr>
<tr>
<td>24-hr PP (mmHg)</td>
<td>47 ± 11</td>
<td>55 ± 14</td>
</tr>
<tr>
<td>vWF (μg/dl)</td>
<td>163 ± 44</td>
<td>216 ± 54</td>
</tr>
<tr>
<td>FMD (%)</td>
<td>0.64 (±1.1–2.5)</td>
<td>0.96 (±0.9–4.6)</td>
</tr>
</tbody>
</table>

(normal vWF levels and FMD but not NMD compared to controls (p<0.001). In the overall group, vWF levels were correlated with FMD (r=0.48), age (r=0.35) and 24-hr PP (r=0.37)(all p<0.001). Patients with high 24-hr PP had significantly elevated vWF levels (212±58 vs 172±49 μg/dl, p=0.004) but not FMD (0.54[1.1–2.9] vs 1.2[0.2–3.8]%), p=0.21) compared to patients with low 24-hr PP. Nondippers with high 24-hr PP had the highest vWF levels (225±55 vs 150±34 μg/dl, p<0.001), but not FMD (0.5[1.1–3.6] vs 0.8[1.1–3.9]%, p=0.58), when compared to dippers with low 24-hr PP.

Patients with CAD who were nondippers and with higher ambulatory PP had the highest vWF levels, whereas dippers with lower ambulatory PP had the lowest levels. vWF levels were closely associated with FMD, whilst ambulatory PP and circadian BP patterns had no relationship with FMD.

Key Words: Endothelial Damage/Dysfunction, Pulse Pressure, Nondipping

P-580
ANGIOTENSIN II RECEPTOR BLOCKADE REDUCED INTERLEUKIN-6 LEVEL IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Angiotensin II promotes superoxide anion generation, endothelial dysfunction, and inflammation. Interleukin-6 (IL-6), which is produced by vascular endothelial cells, smooth muscle cells, and leukocytes, is a pleiotropic cytokine and a central mediator of acute-phase response, with a broad range of effects on the diverse immune cells. IL-6 is also expressed human atherosclerotic lesions and associated with atherosclerotic cardiovascular disease.

We evaluated the relationship between serum IL-6 and carotid atherosclerosis in patients with essential hypertension and further estimated the effects of angiotensin II receptor blockade (ARB) on IL-6 level. In study 1, we examined 41 patients with essential hypertension (20 men, 21 women; mean age, 62±12 years). These patients were evaluated blood pressure, serum creatinine, urine albumin to creatinine ratio, serum IL-6, serum high sensitivity C-reactive protein (hsCRP), and performed Doppler carotid ultrasound in the common carotid artery. We measured the peak systolic and peak diastolic flow and the mean flow rate, and used these data to calculate the pulsatility index (PI) and the resistive index (RI).

hsCRP was significantly correlated with PI and RI (r=0.367, p<0.018 and r=0.376, p<0.015). IL-6 also significantly correlated with PI and RI (r=0.316, p<0.044 and r=0.317, p<0.044). In study 2, we examined 39 patients of these patients (20 men, 19 women; mean age, 61±13 years) to measure these data after 3 months of the treatment with ARB. Blood pressure was significantly reduced (161±18/91±13 mmHg vs. 143±16/85±12 mmHg, p<0.0001). There was no significant difference in serum creatinine levels between before and after ARB treatment. Serum IL-6 was significantly reduced after 3 months of ARB therapy (9.26±1.52 vs. 8.91±1.23 pg/ml, p<0.0001). There was no significant difference in serum hsCRP between before and after ARB treatment.

In patients with essential hypertension, serum IL-6 level was a marker of atherosclerosis in the carotid artery and ARB may inhibit development of atherosclerosis by lowering serum IL-6.

Key Words: Interleukin-6, Hypertension, Angiotensin II Receptor Blockade

P-581
ESTROGENIC VASOPROTECTION IS LOST IN AGED RATS

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Background: 17β-estradiol (E2) negatively modulates the neointimal response to vascular injury in young (10 wk old) ovariectomized (OVX) rats, at least in part, by limiting inflammation early in the injury response. Trials in elderly women treated with hormone therapy after many hormone-free years have not confirmed a vasoprotective effect.

Hypothesis: The beneficial effects of E2 on the vascular injury response are blunted in aged (10-14 mo old) rats.

Methods: In morphometric studies, young and aged OVX rats were treated with vehicle (V) or E2, sacrificed 2 wks after balloon injury of the right common carotid artery, and cross-sectional neointimal areas and intima-to-media ratios were determined. In studies of early vascular inflammation, 24 hrs post-injury, rats were euthanized and carotid arteries (injured and control) were analyzed for inflammatory cells by flow cytometry.

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