HIV is an Independent Predictor of Aortic Pulse Wave Velocity

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Key Findings
- Pulse wave velocity (a measure of aortic stiffness; PWV) was 16% higher in patients with HIV and in those with metabolic syndrome (MS) compared to those without.
- Patients with HIV and MS had a 19% higher PWV than those with HIV but without MS.
- The ST2 level of those with MS was 26% higher than those without MS.

Background
- People with HIV have an increased risk of cardiac disease including MI [1], preclinical atherosclerosis [2] and sudden cardiac death [3].
- Potential causes include dyslipidemia [4], chronic inflammation [5], HAART toxicity [6], endothelial dysfunction [7] and traditional cardiovascular risk factors [8].
- Aortic pulse wave velocity (PWV) is a clinical measure of arterial stiffness.
- PWV predicts cardiovascular events and mortality [9, 10] and is a surrogate marker of atherosclerosis [11].
- Soluble ST2 levels have been associated with cardiovascular mortality [12], prognosis after myocardial infarction [13], heart failure [14, 15], right ventricular function [16] and atherosclerosis [17]. One small study showed high levels of sST2 with HIV [18].

Aims
To examine the relationship between HIV, metabolic syndrome (MS) and PWV and to assess the ST2 level of those with HIV and those with MS.

Methods
90 patients with documented HIV infection (13 naive to anti-retroviral therapy) and 119 subjects with no history of HIV infection were recruited.

Anthropometric data were collected, a fasting blood sample was taken and HIV details were extracted from the patient records. A subset of blood samples were tested for ST2 using the Human ST2/IL-1 R4 Immunoassay (R&D Systems Europe, Abingdon, UK).

Aortic PWV was assessed using vascular MRI (1.5-Tesla, Avanto, Siemens Medical Solutions, Erlangen, Germany). Image analysis was performed using Siemens analytical software (Argus ©, Siemens Medical Solutions, Erlangen, Germany).

Results

Table 1: HIV Specific Data for the HIV+ve/MS+ve and HIV+ve/MS+ve groups

<table>
<thead>
<tr>
<th>Group</th>
<th>HIV+ve/MS+ve (n=73)</th>
<th>HIV+ve/MS+ve (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of HIV infection (years)</td>
<td>6 ± 5</td>
<td>7 ± 5</td>
</tr>
<tr>
<td>On HAART (%)</td>
<td>84 ± 37</td>
<td>94 ± 24</td>
</tr>
<tr>
<td>Time on HAART (years)</td>
<td>4 ± 4</td>
<td>6 ± 5</td>
</tr>
<tr>
<td>Nadir CD4 cell count (10^6/l)</td>
<td>257 ± 186</td>
<td>179 ± 125</td>
</tr>
<tr>
<td>Current CD4 cell count (10^6/l)</td>
<td>354 ± 186</td>
<td>559 ± 201</td>
</tr>
<tr>
<td>HIV viral load (copies/ml)</td>
<td>2097 ± 9317</td>
<td>3263 ± 13557</td>
</tr>
</tbody>
</table>

The Effect of HIV on PWV
PWV was 16% higher in the HIV+ve/MS+ve (n = 73) group compared to the HIV+ve/MS+ve group (n = 77) (6.2 ± 1.9 vs 5.4 ± 1.0 m/s, p = 0.008).

Figure 1: Pulse Wave Velocity

Comparing the Effects of HIV and the Metabolic Syndrome
The HIV+ve/MS+ve and the HIV+ve/MS+ve groups had similar PWV (6.3 ± 1.7 vs 6.2 ± 1.9 m/s), both of which were 16% higher than the HIV+ve/MS+ve group (p<0.05 for both).

Table 2: ST2 Level

<table>
<thead>
<tr>
<th>Number</th>
<th>Mean ST2 level (pg/ml)</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+ve+MS+ve</td>
<td>17</td>
<td>13330.81</td>
</tr>
<tr>
<td>HIV+ve+MS-ve</td>
<td>85</td>
<td>11382.49</td>
</tr>
<tr>
<td>HIV-ve+MS+ve</td>
<td>8</td>
<td>18708.13</td>
</tr>
<tr>
<td>HIV-ve+MS-ve</td>
<td>30</td>
<td>12822.53</td>
</tr>
</tbody>
</table>

Multivariable Regression
Age (b=0.07, p<0.001), SBP (b=0.02, p=0.02) and HIV infection (b=0.62, p=0.01) were all independent predictors of aortic PWV.

ST2 and Metabolic Syndrome and HIV
The mean ST2 for participants with MS (14812.79 pg/ml) was significantly higher than the mean ST2 for those without MS (11862.12 pg/ml; p value 0.038).

Conclusion
- HIV infection is associated with higher PWV.
- The effect size of HIV alone is the same as the effect size of MS alone.
- HIV and MS have an additive effect: having HIV and MS leads to a higher PWV than either condition alone.
- ST2 level is highest in those with MS and without HIV and lowest in those with HIV and without MS.