Insulin resistance is associated with increased large artery stiffness in normotensive healthy adults

Ochoa JE¹, Balparda JK², García E², Correa M², Valencia AM², Alvarez M², Gallo J², McEwen J³, Bilo G⁴, Salvi P⁴, Aristizabal D², Parati G¹⁴

1. Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Milan, Italy.
2. Clinical and Research Center, SICOR, Medellín, Colombia.
3. Corporación para Investigaciones Biologicas, Medellín, Colombia.
4. Department of Cardiology, S. Luca Hospital, Istituto Auxologico Italiano, Milan, Italy.
Authors declare no conflicts of interest for this work.
Aim

1. Relationship between IR and measures of large artery stiffness and wave reflections in normotensive healthy adults.

2. Relationship between IR and cardiac BRS
Methods: subjects

- Population study
- Medellín, Colombia
- Prevalence of CV risk factors in (n=800).
- Subjects with DBP \( \leq 30^{\circ} \) percentile of DBP distribution curve
Methods: Subjects

Further inclusion criteria

- **Normotensive** 24h mean SBP/DBP 107/69 mmHg
- **No history of HT or taking antihypertensive treatment**
- **Normoglicemic** mean fasting glucose 76.1± 10.0 mg/dL
- **Non-obese** mean BMI 25.40 ± 3.66 Kg/m²
- **Healthy adults** mean age 48±10 yrs, no previous history of CVD.

A total of 90 subjects were included
**Methods: BP measurement**

- 24h ABPM was performed
- HR, SBP and DBP levels were averaged over the 24-h, day- and night-time.

**Mobil-O-Graph NG, IEM, Stolberg, Germany.**
Methods: Pulse wave analysis

- Recordings of pulse waveform
- In-built transfer-function like method (ARCSolver algorithm).

Mobil-O-Graph NG, IEM, Stolberg, Germany.
Methods: Hemodynamic parameters derived from PWA

- Central SBP (mmHg)
- Central DBP (mmHg)
- Central PP (mmHg)
- Aortic PWV (m/s)
- Augmentation index at 75 bpm (%)

Methods: assessment of cardiac BRS

- Computer analysis of 10 min beat-to-beat BP and RRI recordings in supine position (Task Force Monitor®, Graz, Austria)
Methods: assessment of cardiac BRS

Sequence method, Parati et al. 1988
Methods: Statistical analysis

- Subjects were classified into HOMA tertiles
- ANOVA to test differences in clinical, autonomic and hemodynamic parameters among tertiles of HOMA-Index.
- ANCOVA Adjusting for age, sex, smoking, and BMI
Results: Clinical characteristics by tertiles of HOMA-Index

<table>
<thead>
<tr>
<th>Variable</th>
<th>All</th>
<th>T1 (&lt;0.94) (n=32)</th>
<th>T2 (0.94-1.90) (n=28)</th>
<th>T3 (&gt;1.90) (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.27 ± 10.5</td>
<td>48.3 ± 9.6</td>
<td>46.8 ± 8.1</td>
<td>46.9 ± 11.1</td>
<td>0.833</td>
</tr>
<tr>
<td>BMI</td>
<td>25.40 ± 3.66</td>
<td>22.7 ± 2.9</td>
<td>25.8 ± 2.9</td>
<td>27.2 ± 3.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Sex (Male, %)</td>
<td>50</td>
<td>50.1</td>
<td>41.9</td>
<td>58.0</td>
<td>0.452</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>16.4</td>
<td>17.0</td>
<td>29.1</td>
<td>7.7</td>
<td>0.072</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>76.17± 10.0</td>
<td>70.4 ± 7.5</td>
<td>75.5 ± 7.3</td>
<td>82.4 ± 8.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Insulin (mU/mL)</td>
<td>8.7 ± 5.8</td>
<td>3.6 ± 1.0</td>
<td>7.3 ± 1.5</td>
<td>15.1 ± 5.5</td>
<td>0.001</td>
</tr>
<tr>
<td>HOMA-Index</td>
<td>1.69 ± 1.26</td>
<td>0.62 ± 0.2</td>
<td>1.35 ± 0.3</td>
<td>3.07 ± 1.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>201.9± 37.1</td>
<td>203 ± 41</td>
<td>205 ± 38</td>
<td>200 ± 33</td>
<td>0.879</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>45.3 ± 12.24</td>
<td>51.8 ± 11</td>
<td>43.9 ± 11</td>
<td>39.5 ± 10</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>129.2± 34</td>
<td>131 ± 37</td>
<td>136 ± 35</td>
<td>125 ± 29</td>
<td>0.462</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>153.6± 79</td>
<td>119 ± 55</td>
<td>142 ± 71</td>
<td>201 ± 89</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Results: 24h HR and BP levels by tertiles of HOMA-Index

<table>
<thead>
<tr>
<th>Variable*</th>
<th>T1 (&lt;0.94) (n=32)</th>
<th>T2 (0.94-1.90) (n=28)</th>
<th>T3 (&gt;1.90) (n=30)</th>
<th>adjusted p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>24h HR (bpm)</td>
<td>68.3 ± 1.4</td>
<td>71.5 ± 1.3</td>
<td>73.0 ± 1.3</td>
<td>0.04</td>
</tr>
<tr>
<td>24h SBP (mmHg)</td>
<td>103.7 ± 1.7</td>
<td>106.7 ± 1.5</td>
<td>111.3 ± 1.6</td>
<td>0.008</td>
</tr>
<tr>
<td>24h DBP (mmHg)</td>
<td>70.2 ± 1.1</td>
<td>71.7 ± 0.8</td>
<td>73.1 ± 0.9</td>
<td>0.091</td>
</tr>
<tr>
<td>24h PP (mmHg)</td>
<td>33.5 ± 1.0</td>
<td>35.0 ± 0.9</td>
<td>38.4 ± 1.0</td>
<td>0.004</td>
</tr>
</tbody>
</table>
Results: Central and peripheral BP levels by tertiles of HOMA-IR

- **Central SBP (mmHg):**
  - T1: 103.7, T2: 106.7, T3: 115.3
  - p = 0.001

- **Central DBP (mmHg):**
  - T1: 77.8, T2: 81.1, T3: 86.1
  - p = 0.001

- **Central PP (mmHg):**
  - T1: 25.5, T2: 25.1, T3: 29.2
  - p = 0.06

- **Peripheral SBP (mmHg):**
  - T1: 111.7, T2: 114.3, T3: 123.2
  - p < 0.001

- **Peripheral DBP (mmHg):**
  - T1: 76.8, T2: 79.8, T3: 84.7
  - p = 0.001

- **Peripheral PP (mmHg):**
  - T1: 33.5, T2: 35, T3: 38.4
  - p = 0.004
Results: PWV and AIx by tertiles of HOMA-IR

Aortic PWV (m/s) *

Augmentation index (%) At 75 bpm

*Corrected by MAP, HR, sex, age and BMI
Results: BRS by tertiles of HOMA-IR

- BRS up-slope (ms/mmHg): T1, T2, T3
  - p = 0.045

- BRS down-slope (ms/mmHg): T1, T2, T3
  - p = 0.042

- BRS total slope (ms/mmHg): T1, T2, T3
  - p = 0.045
Insulin resistance was associated with:

- ↑ Ambulatory HR and SBP (during day, night and 24h)
- ↑ Central and peripheral SBP and DBP levels
- ↑ arterial stiffness
- ↓ Cardiac BRS
Conclusion

Insulin Resistance

↓ Arterial compliance

↓ BRS

↑ Central Sympathetic drive

↑ Central BP

↑ peripheral BP

↑ CV outcomes and mortality

↑ CV outcomes and mortality
Thanks for your attention.