UNFAVOURABLE EFFECTS OF LOW TESTOSTERONE LEVELS ON LEFT VENTRICULAR DIASTOLIC RELAXATION, AORTIC STIFFNESS AND EXERCISE CAPACITY IN MIDDLE-AGED MALES WITH HYPERTENSION

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Objective

* Impaired left ventricular diastolic (LVD) relaxation, reduced exercise capacity and increased aortic stiffness identify hypertensive patients at increased CV risk.
* Low testosterone concentration has been associated with increased risk for CV events, however, the influence of androgen deficiency on LVD function, exercise workload and aortic stiffness in patients with essential hypertension (HTN) is unknown.

Methods

Study population: 82 non diabetic hypertensive men (56±8 y/o, BMI±30kg/m²) and 75 age-matched subjects with normal blood pressure who were referred to the Cardiovascular Diseases and Sexual Health Unit of our Department for evaluation of ED were enrolled (Table). Evaluation of diastolic function: Detailed two-dimensional and Doppler echocardiograms were obtained in all the patients. Transmitral early (E) and late (A) diastolic velocities and deceleration time were recorded in the apical four-chamber view as well. The wall motion velocity pattern was recorded by the pulsed tissue Doppler method, and the peak early diastolic velocity (Em) as well as the peak atrial systolic velocity (Am) were estimated at the lateral border of the mitral annulus in the apical four-chamber view.

Exercise testing: All patients underwent maximal EST under the standard Bruce protocol. All medications were discontinued for at least five half-lives before testing performance. Exercise was terminated because of severe angina, fatigue, dyspnea or severe arrhythmias. In the absence of symptoms, the test was terminated at the occurrence of a 2 mm ST-segment depression or a 1 mm ST-segment elevation, a decrease in systolic blood pressure >10 mmHg or an inability to exercise further because of fatigue.

Measurement of aortic stiffness: Pulse Wave Velocity (PWV) is a well-established index of arterial stiffness. Carotid-femoral pulse wave velocity was calculated from measurements of pulse transit time and the distance traveled between two recording sites, using a validated non-invasive device (Complior®), which allows online pulse wave recording and automatic calculation of pulse wave velocity. Two different pulse waves were obtained simultaneously at two sites (at the base of the neck for the common carotid and over the right femoral artery) with two transducers. The time delay between the two signals (the transit time of the pulse) is determined by the device automatically using appropriate signal processing. The distance was defined as: (distance from the suprasternal notch to femoral artery) - (distance from carotid artery to the suprasternal notch).

Laboratory methods: The serum total testosterone (TT) level was measured by enzyme immunoassay from a blood sample taken between 8 and 11 AM. Hypo6 was defined when TT levels were below 3.4 ng/ml.

Results

- Compared to normotensive subjects, patients with HTN had decreased TT (3.9 vs 4.6 ng/ml) and a higher prevalence of Hypo6 (34 vs 16%), (all P<0.01).
- According to regression analysis, TT was positively associated with METS (b = 0.29, p<0.01) and negatively associated with PWV-f (b = -0.38, p<0.001), independent of age, BP and metabolic profile. Furthermore, TT was positively associated with E/A ratio (b = 0.19, p<0.05) and negatively associated with E/Em ratio (b = -0.26, p<0.01).
- All participants were subdivided according to presence/absence of Hypo6. Patients with both HTN and Hypo6 exhibited lower maximum workload and greater impairment of LVD function and aortic elastic properties compared to all the other groups (Figures 1-3).

Conclusions

- Androgen deficiency confers an incremental unfavourable impact on maximal workload, LV early diastolic relaxation and aortic elastic properties in patients with essential hypertension.
- Our data allow identification of hypertensive patients without overt cardiovascular disease who might warrant more intensive follow-up.

Table. Patient population clinical, EST and Doppler characteristics

<table>
<thead>
<tr>
<th>Control n=75</th>
<th>HTN n=82</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>56±12</td>
<td>56±8</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>28±4</td>
<td>29±4</td>
</tr>
<tr>
<td>Peripheral SP (mmHg)</td>
<td>121±10</td>
<td>143±12</td>
</tr>
<tr>
<td>Peripheral DP (mmHg)</td>
<td>77±9</td>
<td>86±11</td>
</tr>
<tr>
<td>Peripheral PP (mmHg)</td>
<td>44±9</td>
<td>57±12</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>72±13</td>
<td>72±16</td>
</tr>
<tr>
<td>Pulse Wave Velocity (m/s)</td>
<td>7.9±1.0</td>
<td>8.9±1.6</td>
</tr>
</tbody>
</table>

EST and Doppler characteristics

- METS: 11.5±2 vs 9.8±2 <0.01
- Decel. Time: 225±26 vs 231±42 <0.05
- Em/Am: 0.69±0.16 vs 0.87±0.25 <0.01
- E/Em: 6.7±1.8 vs 9.1±2.5 <0.001
- Laboratory tests:
  - Cholesterol (mg/dl): 210±48 vs 208±52 NS
  - Triglycerides (mg/dl): 101 (85-112) vs 116 (82-151) NS
  - HsCRP (mg/l): 1.7±1.2 vs 2.2±1.8 NS
  - Total testosterone (mg/ml): 4.6±1.4 vs 3.9±1.0 <0.01
  - Drug therapy:
    - α-blockers (n, %): - vs 9 (11)
    - ACE inhibitors/ ARBs (n, %): - vs 27 (33)
    - Calcium antagonists (n, %): - vs 22 (27)
    - Diuretics (n, %): - vs 14 (17)

Maximal workload

- Normal BP: 16.0±2.4
- HTN: 13.4±3.1

LVD function

- Normal BP: 14.8±2.0
- HTN: 12.3±3.9

Aortic stiffness

- Normal BP: 10.4±2.5
- HTN: 8.2±3.1

Figure 1
Figure 2
Figure 3