Plasma NT-proBNP mirrors the deleterious cardiovascular and renal continuum in hypertension

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Disclosure Statement of Financial Interest

I currently have, or have had over the last two years, an affiliation or financial interests or interests of any order with a company or I receive compensation or fees or research grants with a commercial company: NONE
Background

- NT-proBNP predicts mortality and cardiovascular events in hypertensive patients
- Integrative aspects of NT-proBNP plasma concentration in cardiovascular assessment

Paget V, Hypertension 2011
Welsh P, Hypertension 2014
Bricca G, Archives Cardiovasc Dis 2011
**Objectives**

- **Primary objective**: to test the ability of NT-proBNP to detect in hypertensive patients without heart failure the following target organ damages:
  - LVH,
  - aortic stiffness
  - renal dysfunction (eGFR, microalbuminuria)

- **Secondary objective**: in an ancillary study to test NT-proBNP day-night variability for a routine clinical practice
Methods

• **Target organ damages**
  • **Left ventricular hypertrophy:**
    • ECG: Sokolow index >3.5 mV, RaVL >1.0 mV, Cornell Voltage >2.8 mV (+0.8 mV for women), Cornell Product >2440 mm.ms
    • Transthoracic echocardiography: Left ventricular mass index >115 g/m2 in men and >95 g/m2 in women or >51g/m2.7 for both gender
  • **Pulse wave velocity** (Complior, real travel distance) : >10 m/s
  • **Renal dysfunction:**
    • eGFR (MDRD) <60 mL/min/1.73m2
    • Microalbuminuria >30mg/day
Methods

• **Heart Failure definition**
  - Previous hospitalization for acute heart failure
  - Transthoracic echocardiography criteria:
    - LVEF <50%
    - E/e’ ratio >13

• **NT-proBNP assessments**
  - Elisa kit (Roche Diagnostics, Meylan, France)
  - At the end of the nighttime period for all patients
  - During the daytime period for a subset of patients (N=325)
913 patients with a complete work-up of hypertension

76 patients with missing data

837 patients had a complete TOD assessment: ECG, TTE, PWV, eGFR, microalbuminuria and NT-proBNP

72 patients had a history of heart failure

765 patients without history of heart failure and 1 NT-proBNP assessment

325 patients without history of heart failure and 2 NT-proBNP assessments
## Results: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All (N=837)</th>
<th>Men (N=426)</th>
<th>Women (N=411)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>50.3 ± 23.8</td>
<td>50.6 ± 23.3</td>
<td>50.0 ± 24.3</td>
<td>0.715</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 [23.2-29.7]</td>
<td>26.8 [24.3-29.7]</td>
<td>25.3 [21.8-30.0]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24-hour ambulatory SBP (mm Hg)</td>
<td>148 [136-163]</td>
<td>150 [139-164]</td>
<td>145 [133-161]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24-hour ambulatory DBP (mm Hg)</td>
<td>90 [81-98]</td>
<td>91 [82-99]</td>
<td>89 [80-97]</td>
<td>0.043</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>10.5</td>
<td>10.3</td>
<td>10.7</td>
<td>0.859</td>
</tr>
<tr>
<td>Heart Failure (%)</td>
<td>8.6</td>
<td>8.1</td>
<td>9.1</td>
<td>0.652</td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>4.7</td>
<td>6.8</td>
<td>2.4</td>
<td>0.003</td>
</tr>
<tr>
<td>NT-proBNP (pg/mL)</td>
<td>82 [40-179]</td>
<td>71 [30-166]</td>
<td>96 [49-192]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Microalbuminuria &gt;30 mg/24h</td>
<td>26.6</td>
<td>29.8</td>
<td>23.4</td>
<td>0.025</td>
</tr>
<tr>
<td>eGFR &lt;60 mL/min (%)</td>
<td>10.2</td>
<td>8.2</td>
<td>12.2</td>
<td>0.060</td>
</tr>
<tr>
<td>TTE or ECG LVH (%)</td>
<td>68.9</td>
<td>71.6</td>
<td>66.2</td>
<td>0.088</td>
</tr>
<tr>
<td>PWV &gt;10 m/s (%)</td>
<td>21.7</td>
<td>23.7</td>
<td>19.7</td>
<td>0.156</td>
</tr>
<tr>
<td>Anti-hypertensive treatment (N)</td>
<td>1.4 ± 1.1</td>
<td>1.5 ± 1.1</td>
<td>1.4 ± 1.2</td>
<td>0.304</td>
</tr>
</tbody>
</table>
Results: Association between target organ damages

- Aortic Stiffness (N=167)
- MDRD<60mL/min or microalbuminuria >30mg/day (N=247)
- ECG or TTE LVH (N=524)

Intersection:
- 15
- 12
- 74

Overall:
- 259
- 121
- 70
- 40

No TOD: 174
1 TOD: 314
2 TOD: 203
3 TOD: 74
Results: NT-proBNP values according to TOD

Whole Cohort

Gender

Aetiologies

TOD: Target Organ Damage
HF: Heart Failure
## Results: Univariate and Multivariate Regression

<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (+1 year)</td>
<td>Coefficient</td>
<td>P values</td>
</tr>
<tr>
<td></td>
<td>0.237</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (Female vs. Male)</td>
<td>0.183</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (+1 kg/m2)</td>
<td>-0.032</td>
<td>0.376</td>
</tr>
<tr>
<td>Coronary artery disease (Yes)</td>
<td>0.138</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type 2 Diabetes (Yes)</td>
<td>0.127</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary hypertension (Yes)</td>
<td>-0.101</td>
<td>0.004</td>
</tr>
<tr>
<td>SBP on 24 hours ABPM (+1 mmHg)</td>
<td>0.386</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP on 24 hours ABPM (+1 mmHg)</td>
<td>0.182</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PWV &gt;10 m/s (Yes)</td>
<td>0.299</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ECG or TTE LVH (Yes)</td>
<td>0.238</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR &lt;60 mL/min (Yes)</td>
<td>0.326</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Microalbuminuria &gt;30 mg/24h (Yes)</td>
<td>0.147</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of anti-HT treatment (+1)</td>
<td>0.256</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Results: ROC Curves to detect at least 1 TOD

TOD defined as:
- TTE or ECG LVH
- PWV >10m/s
- eGFR <60mL or microalbuminuria >30mg/day

AUC=0.796
Sp 95%
Se 36%
90 pg/mL

AUC=0.706
Sp 94%
Se 37%
144 pg/mL

AUC=0.740
Sp 94%
Se 36%
120 pg/mL

AUC=0.718
Sp 96%
Se 41%
148 pg/mL
Results: NT-proBNP day-night variability

Daytime 70 (34-165) pg/mL / Nighttime 60 (30-165) pg/mL p=0.002

N=325

94.8%

R=0.952
P<0.001
Discussion

• NT-proBNP is influenced in a dose-dependent manner by the presence of TODs
• Good specificity but low sensitivity: cost-effectiveness to detect high-risk patients
• Independent association with LVH, eGFR and PWV but not with microalbuminuria
• Coupling with MR-proANP to detect microvascular damages? (Stehouwer CD, Kidney Int 2004; Schnabel RB, Hypertension 2012)
• Good day-night reproducibility for clinical routine use
• Limits: patients with heart failure
Conclusion

• NT-proBNP mirrors the silent heart, vascular and renal damages induced by hypertension

• Fair reproducibility for measuring it in ambulatory conditions

• Correlation between NT-proBNP and target organ damages changes?

• Specific threshold may be defined to tailor treatment strategy in hypertension?