Comparative study on the severity of heart failure based on NYHA classification and the levels of NT-proBNP, BNP and NT-proBNP/BNPin pmol/L

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Background

To our knowledge, BNP and NT-proBNP have been already used to evaluate the severity of heart failure (HF), the therapeutic effect and the prognosis. However, there have been few comparative studies between the severity of HF and the levels of BNP, NT-proBNP and the ratio of NT-proBNP/BNP in pmol/L.
Aim

The purpose of this study is to clarify relations between the severity of HF and BNP, NT-proBNP and the ratio of NT-proBNP/BNP in pmol/L in patients with HF.
Subjects and methods

After written informed consents were obtained, 1062 consecutive patients with HF were recruited into this clinical study. An average age was 67.5 years and male/female;685/377. NYHA HF classification and blood sampling for the measurement of BNP and NT-proBNP were performed to clarify relations between the severity of HF and BNP, NT-proBNP and the ratio of NT-proBNP/BNP in pmol/L in the patients with HF. Both BNP and NT-proBNP were measured by immunoluminescence methods. Other medical information was obtained from their medical records whenever necessary. Statistics was performed by JMP9.0. A p-value of < 0.05 was considered statistically significant.
According to NYHA HF classification, 84% was in NYHA I, 13.9% in NYHA II, 2.6% in NYHA III, and 2.2% in NYHA IV. Medians of BNP, NT-proBNP and NT-proBNP/BNP in pmol/L were 68,311pg/ml and 1.67 in NYHA I, 244, 1315pg/ml and 2.29 in NYHA II, 253, 1371pg/ml and 2.43 in NYHA III, 472, 5110pg/ml and 2.35 in NYHA IV, respectively. BNP and NT-proBNP were significantly different in NYHA I vs NYHA II, III, IV, in NYHA II vs IV and not different in NYHA II vs III, NYHA III vs IV by nonparametric ANOVA. The ratio of NT-proBNP/BNP in pmol/L was increasing, corresponding to increasing NT-proBNP and BNP concentration.
Summary Result - 2

NT-proBNP and BNP were divided into 5 quintiles (Q1-5). Median of $\text{pmolRatio}$ in each quintile of NT-proBNP was 0.94(Q1), 1.35(Q2), 1.81(Q3), 2.19(Q4), and 2.58(Q5), respectively. Median of $\text{pmolRatio}$ in that of BNP was also similar. According to NYHA class, BNP and NT-proBNP were divided into 4 groups. Median of $\text{pmolRatio}$ in each NYHA class was 1.62 in NYHA class -I, 2.21 in NYHA class -II, 2.34 in NYHA class -III, 2.26 in NYHA class –IV, respectively.
Summary Result - 3

Using the same model of multivariate linear regression analysis (one dependent variable: BNP or NT-proBNP, 15 independent variables), on BNP, E/e', LVEF, NYHA class, LVMI and cystatin C were significant and on NT-proBNP, cystatin C, LVMI, NYHAc, E/e' and LVEF were significant in order. Influential variables essentially were very similar on both peptides but renal failure only a little more influenced NT-proBNP than BNP.
Age Distribution of the Patients With Heart Failure Based on NYHA HF Classification (N=1059)

- N1 = 862
- N2 = 147
- N3 = 27
- N4 = 23
NYHA HF Classification, and NT-proBNP and BNP Concentration (Median) in the HF Patients (N=1059)

<table>
<thead>
<tr>
<th>NYHA HF Classification</th>
<th>Median NT-proBNP (pg/ml)</th>
<th>Median BNP (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>311</td>
<td>68</td>
</tr>
<tr>
<td>II</td>
<td>1315*</td>
<td>244*</td>
</tr>
<tr>
<td>III</td>
<td>1371*</td>
<td>253*</td>
</tr>
<tr>
<td>IV</td>
<td>5110*,**</td>
<td>1050*,**</td>
</tr>
</tbody>
</table>

*:I vs II,III,IV (statistically significant)  *?:II vs IV (statistically significant?)
NYHA HF Classification, and BNP and NT-proBNP Concentration (Median) in the HF Patients (N=1059)

**Median BNP (pg/ml)**

- Quintile 1: 17.6
- Quintile 2: 42.5
- Quintile 3: 87.9
- Quintile 4: 176
- Quintile 5: 540

**Median NT-proBNP (pg/ml)**

- Quintile 1: 51.9
- Quintile 2: 153.9
- Quintile 3: 402.1
- Quintile 4: 986.6
- Quintile 5: 3031.5
Association Between the Ratio of (NT-proBNP pmol/L / BNP pmol/L) and NYHA HF Classification in the Patients With Heart Failure (N=954)

<table>
<thead>
<tr>
<th>NYHA HF Classification</th>
<th>Ratio (NT-proBNP / BNP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA I</td>
<td>1.61</td>
</tr>
<tr>
<td>NYHA II</td>
<td>2.21*</td>
</tr>
<tr>
<td>NYHA III</td>
<td>2.34*</td>
</tr>
<tr>
<td>NYHA IV</td>
<td>2.26*?</td>
</tr>
</tbody>
</table>

*: I vs II,III (statistically significant)
*? : I vs IV (statistically significant?)
NYHA HF Classification, and LVMI and LVEF in the HF Patients

N=1059

Mean LVMI (g/m²)

Mean LVEF (%)

* I vs II, V (statistically significant)

*? I vs III (statistically significant?)

NYHA HF Classification
The Change of NT-proBNP and BNP Concentration in Natural Log Scale Associated With Increasing of Left Ventricular Mass Index in the Patients With Heart Failure (N=1059)
The Relation of (NT-proBNPpmol/L)/(BNPpmol/L) With eGFR in the Patients with Heart Failure (N=1059)

30(ml/min/1.73m²)
The Change of (NT-proBNPpmol/L)/(BNPpmol/L) With Increasing of LnBNP and LnNT-proBNP Concentration in the Patients with Heart Failure (N=1059)
The Changes of (NT-proBNPpmol/L)/(BNPpmol/L) Associated With Increasing of Cystatin C Concentration and Creatinine in the Patients With Heart Failure (N=1059)
The Changes of \( \ln(\text{NT-proBNP}) \) and \( \ln(\text{BNP}) \) Concentration Associated With Increasing of Cystatin C Concentration in the Patients With Heart Failure (\( N=1059 \))
The Association of BNP and NT-proBNP in Natural Log Scale With Increasing of LVMI
Stepwise multivariate linear regression analysis

**Dependent variables:** natural log NT-proBNP, BNP

**Independent variables:** Age, Gender, BMI, NYHA class, Af, OMI, Hemodialysis, LAD, LVDd, LVDs, LVEF, LVMI, E/e', E/A, DcT
Conclusion

NYHA HF classification may well correspond to the levels of BNP and NT-proBNP in mild to moderate grade but may not well correspond to the levels of BNP and NT–proBNP in moderate to severe grade. With advancing heart failure, however, NT-proBNP/BNP in pmol/L increased proportionally. NT-proBNP/BNP in pmol/L may reflect the severity of HF. Renal failure or impairment affects BNP levels as well as NT-proBNP levels in the patients with HF judging from cystatin C levels. Inconsistency between NYHA HF classification and the ratio of NT-proBNPpmol/L / BNPpmol/L may be attributed to ambiguity inherent in NYHA HF classification, itself.