Association of plasma B-type natriuretic peptide concentration with myocardial infarct size in patients with acute myocardial infarction

J.M. Niu¹, Z.L. Ma², C. Xie¹ and Z.Q. Zhang¹

¹Department of Cardiology, Laiwu People's Hospital, Laiwu, Shandong, China
²Special Need Sickroom, Laiwu People's Hospital, Laiwu, Shandong, China

Corresponding author: Z.Q. Zhang
E-mail: zhiqiangzhangcn@163.com

Received May 17, 2013
Accepted October 1, 2013
Published February 21, 2014
DOI http://dx.doi.org/10.4238/2014.February.21.6

ABSTRACT. B-type natriuretic peptide (BNP) is widely used in the treatment of early-stage heart failure and coronary heart disease. In this study, the association of plasma BNP concentration with myocardial infarct (MI) size in patients with acute myocardial infarction (AMI) was investigated. Eighty patients with AMI were enrolled in the MI group and 30 healthy volunteers were selected as the control group. Magnetic resonance imaging of the heart and plasma BNP concentration detection were carried out, and then the relationship between plasma BNP concentration and MI size was analyzed in the two groups. Results showed that the plasma BNP concentration was positively related to MI size (r = 0.645, P < 0.0005), whereas it was negatively correlated to the left ventriculus ejection fraction (r = 0.297, P = 0.047). Multiple regression analysis showed that MI size was the only parameter that was independently associated with BNP (r² = 0.32, F = 7.712, P = 0.007). Moreover, when the BNP level reached 150 pg/mL, it had 85.1% sensitivity and 70.4% specificity of determining MI sizes exceeding 10%. The plasma concentration of BNP is highly related to MI size in patients with AMI, and can be clinically used to evaluate MI size.

Key words: Myocardial infarction; B-type natriuretic peptide; Myocardial infarct size; Magnetic resonance perfusion imaging
INTRODUCTION

B-type natriuretic peptide (BNP) is secreted by ventricles through the bioactivities of natriuresis, diuresis, anti-aldosterone, vasodilation, blood pressure lowering, myocardial fibrosis inhibition, and vascular smooth muscle hyperplasia, etc. (Schirger et al., 2000). Recently, BNP has been widely used for the treatment, danger delamination, and prognosis evaluation of early-stage heart failure and coronary heart disease (Clerico, et al., 1999; McCullough and Sandberg, 2003; Omland, et al., 2007). Some researchers have reported a correlation between the plasma concentration of BNP and myocardial infarct (MI) size in patients with acute myocardial infarction (AMI). Mayr et al. (2011) and Mistry et al. (2011) evaluated the correlation between BNP and MI size after 66 ± 8 h, 3 months, and 3 days from AMI occurrence, respectively. However, the stage at which BNP in AMI can best reflect the MI size is still under investigation. No correlation study has yet addressed the relationship between BNP and MI size 1 month after AMI occurrence. In this study, the BNP content of 80 AMI patients was evaluated after 28-30 days of AMI occurrence, and magnetic resonance perfusion imaging (MRPI) was used to determine MI size for investigating the correlation between BNP and MI size. By investigating the correlation 1 month after AMI, these results contribute to the ongoing discussion related to the optimal time stage of correlating BNP with MI size. The objective of this study was to provide basic evidence for further research on the correlation between BNP and MI.

MATERIAL AND METHODS

Subjects

Eighty patients with AMI were enrolled in this study. All patients met the standards of AMI diagnosis (Anderson et al., 2007; Antman, et al., 2008) and were treated with percutaneous coronary intervention (PCI) combined with coronary artery stent implantation. The blood flow reached TIMI Level 3. The exclusion criteria were as follows: ischemic stethalgia occurred after PCI, past medical history, electrocardiogram, and color Doppler ultrasound revealed obsolete MI, previous percutaneous coronary bypass grafting or PCI, heart failure, valvular heart disease, atrial fibrillation, pacemaker installation, kidney insufficiency, taking digitalis, left ventricular hypertrophy, and severe lung diseases. Of the 80 patients, 51 cases were males and 29 cases were females, with an average age of 58.5 ± 9.8 years. Among them, 22, 20, and 24 cases had hypertension, diabetes, and a history of smoking, respectively. The average body mass index (BMI) was 27 ± 2 kg/m². Thirty healthy volunteers without severe disease histories were selected as controls. Electrocardiograms, color Doppler ultrasounds, and other normal health examinations all showed normal results. The control group comprised 18 males and 12 females with an average age of 25.1 ± 1.2 years. Fifteen cases had a history of smoking, with one case of hypertension or diabetes. The average BMI of the control group was 25 ± 3 kg/m².

Determination of BNP concentration

After 28-30 days of PCI, 2 mL venous blood was collected at resting state before MRPI and was injected into an EDTA tube. Then, 250-μL venous blood was injected into the Triage checking board, followed by determination of BNP using the Triage BNP diagnosis instrument (Biosite, USA).
MRPI

A Philips Intera 1.5 T Master superconduction short magnetic resonance instrument was used in the experiment. Subjects were intravenously injected with 0.1 mmol/kg gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) at a 2-5 mL/s injection speed. Double-echo steady-state scanning was conducted 2, 5, 10, and 15 min after contrast media injection. The graphical analysis was carried out according to the 17-segment model of the American Heart Association/American College of Cardiology (AHA/ACC). MI size was calculated in the following manner (de Roos et al., 1990). First, every layer’s MI area was calculated from the apex cordis to the cardiac base, and then all areas were summed. Second, the sum of every layer’s cardiac muscle capacity was calculated from the apex cordis to the cardiac base. Third, the ratio of the two sums was obtained, which represented the MI content proportion. The room wall shapes of ventriculus sinister diastasis and end-systolies were drawn manually for the left ventriculus ejection fraction (LVEF) with a computer. In the AMI group, the cut-off point was set every other 0.5 ng/L BNP, and the receiver operating characteristic (ROC) curve was drawn accordingly. The area under the curve (AUC) was determined using the non-parametric method.

Statistical analysis

The SPSS13.0 statistical software was used for the statistical analysis. The normally distributed measurement data are reported as means ± SD, and were analyzed using the Student t-test. The chi-squared test was used for analyses of enumeration data. BNP, a numerical value, showed a significantly skewed distribution and is reported as median (interquartile interval). The Wilcoxon rank test was used for comparisons between 2 separate samples. The factors affecting the difference in BNP concentration were analyzed with Spearman interclass correlation analysis, and the sensitivity and specificity were calculated with the ROC curve.

RESULTS

BNP and MRPI results in the two groups

The BNP concentrations in the AMI group and in the control group were 190.3 ng/L (range: 80.4-325.8 ng/L) and 8.1 ng/L (range: 6.7-12.5 ng/L), respectively, which showed a significant difference (P < 0.01). MRPI showed that the MI size of the AMI group was 16.58 ± 9.73% and the LVEF was 45 ± 8%, whereas in the control group they were 0 and 59 ± 8%, respectively, and the difference between the two groups was significant (P < 0.01).

Correlation of BNP and MI size

BNP showed a positive correlation with MI size in the AMI group (r = 0. 645, P < 0.01) and a negative correlation with LVEF (r = 0. 297, P < 0.05), which showed a stronger correlation with MI size. There was no correlation of BNP with age, gender, diabetes, hypertension, smoking, or BMI (Table 1).
Multiple regression analysis

BNP was set as the dependent variable, and age, gender, MI size, LVEF, hypertension, diabetes, smoking, and BMI were set as the independent variables. Multiple regression analysis showed that MI size was the only independent correlation factor for BNP ($r^2 = 0.297$, $F = 7.69$, $P < 0.01$).

ROC curve in the AMI group

The ROC curve in the AMI group is shown in Figure 1. When the BNP level was set to 150 ng/L, the sensitivity for judging MI size >10% was 85.1%, and the specificity was 70.4%. The positive prediction value was 80.5% and the negative prediction value was 89.9%. The AUC was 0.835%, and the 95% confidence interval ranged from 0.768 to 0.906 (Figure 1).

---

**Table 1. Correlation factors affecting ΔBNP (B-type natriuretic peptide).**

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>Gender</th>
<th>MI size</th>
<th>LVEF</th>
<th>Age</th>
<th>Gender</th>
<th>MI size</th>
<th>LVEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI</td>
<td>0.099</td>
<td>0.514</td>
<td>0.159</td>
<td>0.295</td>
<td>0.645</td>
<td>&lt;0.0005</td>
<td>0.297</td>
<td>0.047</td>
</tr>
<tr>
<td>Control</td>
<td>0.056</td>
<td>0.702</td>
<td>0.145</td>
<td>0.307</td>
<td>-</td>
<td>-</td>
<td>-0.136</td>
<td>0.221</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Diabetics</th>
<th>Smoking</th>
<th>BMI</th>
<th>Hypertension</th>
<th>Diabetics</th>
<th>Smoking</th>
<th>BMI</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI</td>
<td>0.102</td>
<td>0.146</td>
<td>0.062</td>
<td>-0.082</td>
<td>0.603</td>
<td>0.102</td>
<td>0.146</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>-</td>
<td>-</td>
<td>0.057</td>
<td>-0.075</td>
<td>0.681</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

$r =$ Sperman’s rank correlation coefficient. MI = myocardial infarct; LVEF = left ventricular ejection fraction; AMI = acute myocardial infarction; BMI = body mass index.
DISCUSSION

In recent years, research about the application of BNP in the diagnosis of stable coronary heart disease (SCHD) has increased. Sahinarslan et al. (2005) reviewed data of approximately 62 SCHD patients and found that the BNP plasma concentration increased in SCHD patients with normal left heart function, and that the degree of increase was correlated with the degree of pathological changes of the coronary artery disease and the anterior descending branch. Schnabel et al. (2006) detected the BNP plasma concentration in SCHD patients who had cardiovascular issues for 2.5 years, and showed that BNP was an independent factor of other known danger factors of heart function, and was the important dependent predicting factor for the long-term prognosis of SCHD patients. Omland et al. (2007) investigated the BNP and N-terminal prohormone-BNP (NT-proBNP) plasma concentrations in 3761 low-danger SCHD (with normal heart function) patients. Results showed that BNP levels were closely correlated with cardiac death, congestive heart failure, MI, and apoplexia. This indicated that BNP levels could predict congestive heart failure and that NT-proBNP levels could predict cardiac death.

Many researchers have tested the BNP concentration before and after exercise for analyses of SCHD. Sabatine et al. (2004) conducted exercise tests in 112 patients, and evaluated heart muscle perfusion nuclide imaging and BNP at the baseline level, after 4 h of exercise, and immediately following the end of exercise. The results showed that transient myocardial ischemia induced plasma BNP levels to rise with a positive curve relationship. Foote et al. (2004) carried out the same tests in 74 SCHD patients, and detected BNP and NT-proBNP levels before and after exercise. The changes in BNP and NT-proBNP levels were almost twice as high in myocardial ischemia sensitivity induced by exercise compared to the pure exercise test. Zaid et al. (2007) found that the ΔBNP of 203 targets could be used to improve the sensitivity of exercise tests, specificity the negative prediction value and accuracy of prediction.

Recent studies have indicated that BNP would significantly increase in accurate coronary syndrome (ACS), and was closely related with prognosis. Through analyzing the BNP plasma level in 1676 unstable angina pectoris (UAP)/non-ST elevation myocardial infarction (NSTEMI) patients, the TACTICS-TIMI 18 study (Morrow, et al., 2003) found that the BNP plasma levels were higher than 80 pg/mL in 25.2% NSTEMI and 15.6% UAP patients. Furthermore, the BNP plasma level was higher than 80 pg/mL in 13.6% of UAP cases without a history of symptoms of heart failure. Bassan et al. (2005) tested the BNP level in patients with 3-6 h stethalgia without ST stage increase, and found that the median BNP levels were 204 pg/mL for MI, 78 pg/mL for UAP, and 28 pg/mL for non-ACS cases. They set the BNP threshold value at 100 pg/mL, which could diagnose AMI with 70.8% sensitivity and 68.9% specificity. The determination of BNPs could help the early diagnosis of ACS and provide important information for ACS Danger Classification (Mueller, et al., 2004). In 2007, the Guide of UAP and NSTEMI of the ACC/AHA added BNP as a biomarker for the first time, suggesting it be used to evaluate the complete heart risk of ACS (Anderson, et al., 2007).

Animal models and clinical studies have already demonstrated that delayed-enhancement MRI has the advantage of high resolution and could be used to identify the MI of the endocardium and to distinguish the degree of wall penetration; therefore, it is the best method to quantitatively evaluate MI (Bondarenko, et al., 2005; Hsu, et al., 2006). In this study, 80 AMI patients were evaluated with PCI revascularization, and the blood flow reached TIMI Level 3. MRPI was used for the detection of MI size after 28-30 days, and BNP was detected before the MRPI. The results showed that BNP was positively correlated with MI size (r =
0.645, \( P < 0.01 \), and was negatively correlated with LVEF \( (r = 0.297, P < 0.05) \). Multiple regression analysis revealed that MI size was the dependent related factor of the BNP level; when the threshold value of BNP was set to 150 ng/L, the sensitivity of MI size >10% was 85.1% and the specificity was 70.4%. Cochet et al. (2004) detected the MI size with MRPI and NT-proBNP plasma levels in 84 AMI patients, and found that the NT-proBNP plasma concentration was correlated with MI size \((P < 0.01)\) and LVEF \((P < 0.01)\). Steen et al. (2007) found that NT-proBNP and troponin had important value in the evaluation of LVEF and MI size. Bruder et al. (2010) reported that in 41 accurate ST stage increase patients, NT-proBNP was correlated with MI size \((r = 0.74, P < 0.01)\), which was stronger than its relationship with LVEF \((r = -0.47, P = 0.01)\). Furthermore, their multiple regression analysis revealed that BNP was the only dependent factor that was correlated with MI size, which was also confirmed in the present study. Nijveldt et al. (2008) reported that BNP was more strongly correlated with necrotic cardiac muscles than with ischemic cardiac muscles, and Grabowski et al. (2007) reported that BNP was more informative than other clinical indexes, such as the Killip grade, TIMI risk points, etc. Mayr et al. (2011) found that the NT-proBNP concentration was closely correlated with heart function and could accurately predict chronic MI size after 3 days of MI, and that the heart function of the patients could not recover if the NT-proBNP level was >1115 pg/mL. Mistry et al. (2011) reported that the NT-proBNP plasma concentration showed a stronger correlation when AMI occurred within 3 months compared to only 3 days.

In conclusion, the BNP plasma level has high sensitivity and specificity for judging MI size, and can help in classifications of the AMI risk degree, prognosis evaluation, and further directions for treatment.

REFERENCES


Foote RS, Pearlman JD, Siegel AH and Yeo KT (2004). Detection of exercise-induced ischemia by changes in B-type...
Association of BNP with MI size in AMI patients


