B-type Natriuretic Peptide in Predicting Short-term Mortality in Patients with Acute Coronary Syndromes: A Preliminary Report

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Abstract: Objective. This study was designed to investigate the usefulness of B-type natriuretic peptide (BNP) in predicting the short-term mortality in patients with acute coronary syndromes (ACS). **Methods.** A total of 106 patients with ACS, whose blood BNP concentration were measured with Triage BNP test, within 1 – 3 days after onset of ischemic symptoms, were divided into two groups: the survival and the non-survival group, according to the results of 4-week follow-up. **Results.** The blood BNP concentration was significantly higher in the non-survival than in the survival ($P<0.0001$) group; univariate analysis showed that BNP ($\geqslant$ 172 ng/L, median) and Killip class (Ⅱ-Ⅳ) were prognostic factors of the short-term cardiac death in patients with ACS ($P<0.0005$ and $P=0.001$); stepwise logistic regression analysis indicated that smoking and BNP ($\geqslant$ 596 ng/L, 75% percentile) were independent predictors of short-term cardiac death in patients with ACS (OR=5.5, $P=0.028$; OR=21.19, $P<0.0005$). **Conclusion.** BNP might predict the 4-week mortality in patients with ACS. [Life Science Journal. 2005;2(1):61 – 64] (ISSN: 1097 – 8135).

Keywords: B-type/brain natriuretic peptide; acute coronary syndrome; prognosis

1 Introduction

Acute coronary syndromes (ACS) encompass a continuum of cardiac ischemic events, ranging from unstable angina pectoris with no biochemical evidence of myocardial necrosis to ST-elevation acute myocardial infarction (AMI)[1]. Acute prediction of the mortality in patients with ACS is critically important to facilitate the application of preventative measures. B-type/brain natriuretic peptide (BNP), which is mainly secreted by ventricular myocytes, is increased in patients with systolic or diastolic heart failure[2,13]. Numerous clinical trials have demonstrated that BNP could be used to diagnose cardiac dysfunction[4,5]. It has also been shown that an increase in BNP values is associated with a higher mortality and morbidity rate in patients with ventricular failure or ACS[6-10]. In this study, we investigated the usefulness of blood BNP in predicting 4-week cardiac death in patients with ACS.

2 Materials and Methods

Patient selection

Patients were included if they presented within 72 hours after onset of ischemic discomfort and met one or more of the following criteria: electrocardiographic changes (ST-segment depression or elevation of at least 0.5 mm, T-wave inversion of at least 3 mm in at least three leads, or left bundle-branch block), elevated levels of cardiac markers, or a history of coronary disease.

One hundred and six patients admitted to the coronary care unit (CCU) at the First Affiliated Hospital of Zhengzhou University, were enrolled in the study between September 2003 and May 2004. Thirty-three patients had ST elevation myocardial infarction (STEMI), 7 had non-ST elevation myocardial infarction (NSTEMI) and 66 had unstable angina pectoris (UAP). Seventy-one patients were male and 35 were female. Mean age was 62 years (37 – 85). They were divided into 2 groups ac-

cording to the 4-week follow-up results: the survival ($n = 93$, 88%) and the non-survival ($n = 13$, 12%).

2.2 Measurement of blood BNP level

A point-of-care test of fluorescence immunoassay for the quantification of BNP was used (Biosite Diagnostics Inc, USA), 2 ml of intravenous blood was collected at the early morning after 1 – 3 day on admission and BNP was determined within 20 min. The range of measurement was 5 – 5000 ng/L.

2.3 Statistical analysis

Data of BNP were presented with categorical variables and with continuous variables. The difference of circulating BNP between the survival and the non-survival were compared by Wilcoxon signed rank test. Categorical variables were compared by χ^2-test. Both univariate and stepwise multivariate Logistic forward regression analysis were used to evaluate the prognostic value of the parameters. The criterion for inclusion in the regression equation was $P<0.05$. The criterion for exclusion from the regression equation was $P>0.1$. A value of $P<0.05$ was considered statistically significant. All data analysis was performed using the Statistical Package for Social Sciences (SPSS 11.0).

3 Results

The mean of BNP for all patients was 511.05 ± 799.57 ng/L (5 – 5000 ng/L), median was 172 ng/L, and quartile range was 37.5 – 596 ng/L. There were 12 patients whosecirculating BNP was above 172 ng/L (median) and 10 patients whose circulating BNP was above 596 ng/L (75 percentile) in the non-suverial ($n = 13$). Patients with circulating BNP above 172 ng/L and those with circulating BNP above 596 ng/L had a mortality of 23.1% (12/52) and 40.0% (10/25) at 4 weeks, respectively. Rank correlation analysis demonstrated that the circulating BNP levels and Killip class were positively correlated with cardiac death ($r = 0.429$, $P<0.0005$; $r = 0.316$, $P = 0.001$).

The circulating BNP level in the non-survival group was significantly higher than the survival group (median 1169 vs 126 ng/L, $U = 148$, $P<0.0001$, Figure 1). Univariate analysis (Table 1) showed that BNP (≥172 ng/L, median) and Killip class (Ⅱ – Ⅳ) were prognostic factors of short-term cardiac death in patients with ACS ($P<0.001$ and $P = 0.001$).

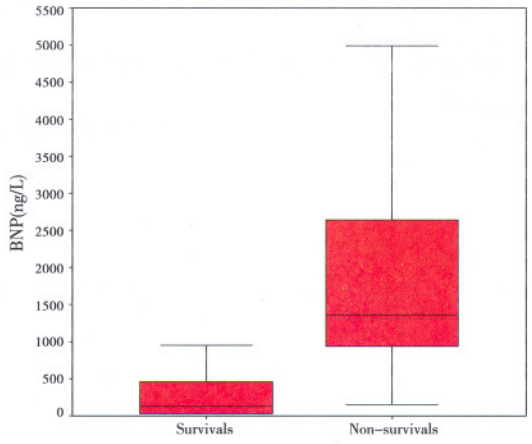

Figure 1. Comparison of circulating B-type natriuretic peptide between the survival and non-survival groups.

Table 1. Comparison between the survival and non-survival groups

Variables	Non-survival group($n = 13$)	Survival group($n = 93$)	P value
Sex(men/women)	9/4	62/31	0.99
Age(<60/≥60)	2/11	33/60	0.26
Smoking	6	19	0.09
Drinking	5	17	0.19
Family history	1	11	0.99
H/O DM	3	12	0.56
H/O Hypertension	7	45	0.71
H/O HF	5	19	0.27
H/O MI	3	13	0.66
Killip class (stage Ⅰ/Ⅱ – Ⅳ)	1/12	52/41	0.001
BNP (<172 ng/L/≥172 ng/L)	1/12	52/41	<0.0005

H/O: history of; DM: diabetes mellitus; HF: heart failure; MI: myocardial infarction.

Stepwise logistic forward regression analysis demonstrated that smoking and circulating BNP (above 596 ng/L, 75 percentile) were independent predictors of cardiac death at 4 weeks (OR = 5.5, 95% confidence interval 1.20 – 25.30, $P = 0.028$; OR = 21.19, 95% confidence interval 4.53 – 99.06, $P<0.0005$); covariates were age, sex, smoking, drinking, history of heart failure, history of myocardial infarction, hypertension, diabetes mellitus, Killip class and circulating BNP (above 596 ng/L). The risk of death in patients with smoking and circulating BNP level above 596 ng/L were 5.5 times and 21 times higher than non-smokers and those with circulating BNP level under 596 ng/L, respectively.

4 Discussions

BNP is a 32-amino-acid polypeptide secreted by the cardiac ventricles in response to increased stretch or wall tension[3,4]. Its diverse actions include natriuresis, vasodilation, inhibition of the rennin-angiotensin-aldosterone system, and inhibition of sympathetic nerve activity[8]. Previous studies have shown that BNP could be used to diagnose and to evaluate the prognosis of congestive heart failure[6]. This study showed that BNP is an independent predictor of short-term prognosis in patients with ACS. The risk of death in patients with circulating BNP level above 596 ng/L was 21 times higher than those with circulating BNP level under 596 ng/L.

A recent study found that the base-line level of BNP was correlated with the risk of death, heart failure, and myocardial infarction 10 months after the ischemic event[7]. In patients with non-ST elevation ACS, the mortality at 7 day and 6 month also increased significantly in patients with BNP above 80 ng/L[8]. Our preliminary study on 4-week mortality yielded similar results, indicating that measuring the circulating BNP levels within 3 days of ischemic event can give clinical physicians critical information in evaluating the severity of the disorder. For patients with very high circulating BNP levels (above 596 ng/L), regardless the severity of ischemic symptoms, physicians should pay great attention to these patients and treat them aggressively, in order to decrease mortality, and improve the short-term prognosis.

It is unclear why BNP is elevated in our patients with ACS who did not have noticeable heart failure. The release of BNP from myocardial cells is provoked by a variety of stimuli, including hyposia, ischemia, increased wall stress, and dilation of ventricles[10]. In rats, rapid induction of ventricular BNP gene expression and BNP production was found in the infarct region and the ischemic periinfarct region. BNP expression was also identified in the nonischemic surrounding myocardium 4 hours after ischemia or infarction[11]. Transient increase in BNP secretion can be found in patients undergoing percutaneous transluminal coronary angioplasty (PTCA)[12]. Above studies indicate that myocardial ischemia can induce synthesis and secretion of BNP, even without myocyte necrosis and overt left ventricular dysfunction.

The pathophysiologic mechanisms and clinical significance that inducing BNP synthesis and secretion by myocardial ischemia are follows[10]. First, elevation of BNP may result from acute ventricular dysfunction caused by myocyte necrosis, and the risk associated with elevated levels could therefore be related to the effect of ventricular impairment on mortality or to a new or progressive heart failure. Second, elevation of BNP levels may result from acute myocardial stretch caused by ischemia without myocyte necrosis, and the risk associated with elevated levels could therefore be related to the extent of ischemia and the consequent risks of future infarction and arrhythmia.

This study also demonstrated that smoking was a significant predictor of cardiac death in patients with ACS. Smoking and hyperlipidemia were the main clinical risk factors for coronary spasm among Chinese[13]. Brummett's study indicated that depressive symptom, smoking, and sedentary behavior were independent predictors of mortality in patients with coronary artery disease[14]. This study accords with above two studies.

The limitations of this study are that the samples were relatively small and the time of follow-up was very short. Larger and double-blinded trials may be required to validate the values of BNP in the risk stratification for patients with ACS.

5 Conclusions

Measuring blood BNP within 1 – 3 days of admission could provide important clinical information for predicting the prognosis of ACS. The risk of death in patients with circulating BNP level above 596 ng/L is 21 times higher than those with circulating BNP level under 596 ng/L. Therefore, aggressive treatment should be applied to patients with very high circulating BNP levels.

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