Assessment of correlation between Brain Natriuretic Protein test and early prognosis in Acute Coronary Syndrome

Ashkan Tabibzadeh [1], Gholamreza Hemassi [2], Hamidreza Mahboobi [3,4], Reza Yazdani [1], Oveis Salehi [1], Mehrdad Jalalian [5]

[1.] Trauma and Medical Emergencies Research Center, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandarabbas, Iran
[2.] Department of Emergency Medicine, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[3.] Research Center for Behavoural and Neurosciences, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandarabbas, Iran
[4.] Payame Noor University, Tehran, Iran
[5.] M.D., Editor In-Chief, Electronic Physician Journal, Mashhad, Iran
hamidrezamahboobi@yahoo.com

Abstract: The aim of this study was to determine; the relationship between Brain Natriuretic Protein (BNP) and early prognosis in Acute Coronary Syndrome (ACS). In this analytical study, 158 patients with ACS admitting to Emergency Department of Rasul Akram hospital in Tehran entered in study. For each patient, information include of demographic, past medical history, drug therapy, presenting symptoms and signs, results of serum chemistry test, radiographic studies, electrocardiography and NT-proBNT test that measured using immunoassay were collected. Totally 158 patients with mean age of 59.7 ± 0.95 that 86(54.4%) of them were male included in study. The ROC curve showed that BNP more than 612 (pg/ml) had sensitivity and specificity of 98% in predicting the outcome (discharged vs. CCU admission) which had a Positive predictive value (PPV) of 99% and Negative predictive value (NPV) of 96%, while in another ROC curve analysis BNP greater than 3200(pg/ml) had a sensitivity of 81% ,specificity of 92% in predicting heart failure, fatal arrhythmia or death as an outcome with a PPV of 37.5% and NPV of 98.5%. Results demonstrate NT-proBNP for strongly predicted short-term outcomes in subjects with chest pain, with 1.2 increases in risk for death by 7 days among those with marked elevation in NT-proBNP concentration. Other studies have found similar results.

Keywords: Acute Coronary Syndrome; Brain Natriuretic Protein (BNP); Prognosis

1. Introduction

The significance of contribution of Laboratory Medicine to clinical cardiology has grown in importance over the years (1, 2). Until 20 years ago, the clinical laboratory only placed at cardiologist's diaposal a few assays for the retrospective detection of cardiac tissue necrosis, such as enzymatic methods for creatin Kinase (CK) and lactate dehydrogenase catalytic activities (3). However, in the latter part of 20th century, highly sensitive and specific assays for detection of myocardial damage, such as cardiac troponins, as well as assays for reliable markers of myocardial function, such as cardiac natriuretic peptides, have become available, assigning to laboratory a pivotal role in the diagnosis and follow up of patients with cardiac disease. This is witnessed by the incorporation of these markers into international guidelines and the redefinition of myocardial infarction. BNP is a 32 amino acide polypeptide initially found in brain but later found abundant in cardiac ventricle tissue. Baseline NT-BNP measurements, regardless of sample timing (on presentation; early 12-24 hours and sub-acute > 3days), during the index clinical presentation, have consistently been shown to be of utility as a predictive for short and long term mortality in patients with acute heart failure (4), but the importance of this marker as an independent predictor of ACS in debate.

The aim of this study was to determine the relationship between Brain Natriuretic Protein (BNP) and early prognosis in Acute Coronary Syndrome (ACS).

2. Material and Methods

This analytical study was done on patients admitting to Emergency Department of Rasul Akram hospital in Tehran. Totally 158 patients with ACS entered in our study. All four component data sets had comparable information available, including standard demographics, past medical history and drug therapy, presenting symptoms and signs of Physical examination, results of serum chemistry tests,

radiographic studies, (typically plain chest radiographs), electrocardiography results and finally, the results of NT-proBNP testing. Glomerular Filtration Rate (GFR) was estimated using modified diet in renal disease (MDRD) equation. For each trial, blood was collected into EDTA tubes and NT-proBNP was measured using validated, commercially available immunoassay (Elecsys® ProBNP, Roche Diagnostics, Indiapolis), using established methodology. This assay has been reported to have < 0.001% cross-reactivity with bioactive BNP, and had inter-run coefficients of variation ranging from 0.9 to 5.5%. NT-proBNP levels were expressed in pg/ml.

In the next few days, the outcome of patients in 7 days after admission surveyed. Outcome of patients was: Discharge, CCU admission, fatal arrhythmia, Heart failure, expired.

Exclusion criteria were: signs and symptoms of heart failure, and inability to provide informed consent, chronic renal failure. We obtained written informed consent from all study participants.

Mean and standard deviation was used for description of the data. X2 analysis, with appropriate correction, was used to compare the categorical variables. Standard parametric tests were used for continues variables (T test, ANOVA) and spearman correlation was done as a non parametric test. Logistic regression analysis was used for performing multivariate analysis for prediction of related variables with categorized outcome. (End outcome, discharge)

BNP values followed log normal distributions, so correlation and regression analysis were done using natural log transformed BNP.
ROC curve used to find cutoff point and the sensitivity and specificity and predictive values to predict the short term outcome. The analysis was done by SPSS 15 software. A p value of < 0.05 was considered statistically significant.

3. Results

Totally 158 patients included in this study with mean age of 59.7 ± 0.95 that 86(54.4%) of them were male. Normal ECG finding found in 55(34.8%) of patients at presentation. The mean and median of BNP were respectively 1607 ± 154 and 1100. There was no significant difference of BNP between males versus females (1753 ± 218 versus 1433 ± 215) (P > 0.05).

Table 1. Comparing the factors at the presentation of patients with chest pain in two categorized outcome (Discharged group versus End group)

Variables		Discharged group	End group outcome	P value
Age		59.96 ± 1.420	61.5 ± 1.253	N.S
Sex	Male	23(44.2%)	63(59.4%)	N.S
	Female	29(55.8%)	43(40.6%)	
Quality of pain	Pressure	36(69.2%)	84(59.4%)	N.S
Pain duration	>20 min	36(69.2%)	84(79.2%)	N.S
Pain referring	Yes	39(75%)	82(78.1%)	N.S
Exertional pain	Yes	21(40.4%)	60(56.6%)	0.01
Associated symptoms	Yes	51(98.1%)	103(98.1%)	N.S
PMH	Positive	40(67%)	90(85%)	N.S
DH	Positive	36(69%)	92(87%)	0.01

NS: Not significant

The outcome of patients in next 7 days was as below: 52(32.9%) discharged, 95(60.1%) CCU admission, 3(1.9%) heart failure, 4(2.5%) fatal arrhythmia and 4 (2.5%) expired. The comparing variables into two categorized outcome has been shown in Table 1 and 2. The mean of BNP is significantly more in End group than discharge group outcome (2327 ± 194 versus 138 ± 25) (P = 0.001) (Table 2).

The mean of BNP according to the ECG finding is as below: Normal ECG findings (526.93 ± 105.89), ST elevation (2472.50 ± 311.56), ST Depression (2040.30 ± 424.97), T inversion (1861.59 ± 377.64). There was significant difference of mean among four ECG groups. (ANOVA P = 0.001). This difference was not significant between ST depression, T inversion (Post Hoc P > 0.05), but all of them had significant difference with normal ECG findings. (Post Hoc P = 0.001). There was a negative correlation between BNP and Ejection fraction of left ventricle. (Spearman correlation P = 0.001, r = -0.499).

The multivariate analysis showed that BNP was the independent predictive value for 7 days categorical outcome in patients admitting with chest pain. (Logestic regression P = 0.001, R Square =

0.741, Exp (B) = 1.8) and also in another multivariate analysis, predicted the outcome of heart failure, fatal arrhythmia and mortality in next 7 days more strongly than other variables in the model. (P = 0.001, R square = 0.721, Exp (B) = 1.2). The ROC curve showed that BNP, greater than 612 pg/ml had sensitivity and specificity of 98% in predicting of End group outcome and the predictive values were:

PPV = 99% and NPV = 96%. Also in another ROC curve analysis BNP, greater than 3200 pg/ml had sensitivity and specificity of 81% and 92% respectively in predicting of outcome which the heart failure, fatal arrhythmia and death included and the predictive values were: PPV = 37.5% and NPV = 98.5%.

Table 2. Comparing the tests done at the presentation of the patients with chest pain in two categorized outcome (Discharged group versus Ed group)

Variables		Discharged group outcome	End group outcome	P value
BNP		138.35±25.698	2327.46±194.566	0.001
Troponin I	Positive	2(3.8%)	52(49.1%)	0.001
CPK		116.80±27.902	271.96±88.510	N.S
CPK MB		24.22±2.146	156.74±79.104	N.S
Ejection fraction		76.90±1.140	55.63±1.251	0.001
ECG findings	Normal	38(73.1%)	17(16%)	0.001
	ST elevation	0(0%)	47(44.3%)	
	ST Depression	5(9.6%)	20(18.9%)	
	T inversion	9(17.3%)	22(20.8%)	

NS: Not significant

4. Discussions

A reliable biomarker or group of biomarkers that would provide incremental data to predict risk for cardiovascular morbidity and death would certainly enhance clinical care in the outpatient setting. An enhanced appreciation of risk may lead to adequate up-titration of medical therapy and improve patient compliance in high risk subsets. The biomarkers would be most useful if it further guided targeted treatment strategies that would in turn optimize patient outcome. Our results demonstrate NT-proBNP for strongly predicted likhood for short-term outcome in subjects with chest pain, with 1.2 increases in risk for death by 7 days among those with marked elevation in NT-proBNP concentration. Other studies have found similar results as well (5-10). NT-BNP has been shown to be an independent predictor of mortality in these studies. However, a significant proportion of predictive ability of increasing levels of NT-BNP in acute setting due to its association with other well established clinical risk factors: Age, Female gender, diabetes mellitus, hypertension, previous MI, heart failure, resting heart rate, and ST-Segment depression, renal dysfunction and inflammatory markers like CRP (5, 6). We solved this problem by including almost all of these variables in the model as covariates to find the predictive potential of NT-BNP. The admission NT-BNP concentration was so strongly predictive of short-term outcome among our patients with chest pain that its presence in multi-variable models

overwhelmed the prognostic impact of other traditional risk factors. NT-BNP measurement, have also been correlated with myocardium at risk, infarct size, and extent and complexity of coronary artery disease (11-14). It is well known that among healthy subjects, NT-proBNP levels are higher in older female when compared with age-matched malesubjects, possibly due to a higher prevalence of diastolic abnormalities or more significant age-related reductions in GFR in women. No significant gender-related difference in mean of NT-proBNP and BNP appear to deliver important diagnostic and prognostic information in a wide variety of patient types; the choice of which marker to use should be based on difference in analytical performance, the individual clinician comfort with the results from the assays (16). In summary, the findings in this study and the results of other clearly indicate the remarkable ability of NT-BNP to predict short term outcome. It appears to be effective in patients with an ACS. Its value appears to be incremental to that obtained from standard clinical variables. In addition, it seems to integrate risk from an array of clinical variables that may be relatively easy to comprehend.

Corresponding Author:
Dr. Hamidreza Mahboobi,
Research Center for Behavioral and Neurosciences,
Faculty of Medicine,
Hormozgan University of Medical Sciences,
Bandarabbas, Iran
Tel: +98.9172121995
Fax: +98.7643273311
E-mail: hamidrezamahboobi@yahoo.com

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