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A Study of N-terminal pro-Brain Natriuretic Peptide as a Predictor of Adverse Outcome of STEMI

MOHAMMAD ZAKIR HOSSAIN[1], MD ABU SIDDIQUE[1], TANJIMA PARVEEN[1], MANZOOR MAHMOOD[1], KHANDAKER AISHA SIDDIKA[1], SOHEL MAHMUD[1], DMMF OSMANY[1], NASIMUL BARI[2]

[1]Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, [2]Kustia Sadar Hospital, Kustia

Address of Correspondence: Mohammad Zakir Hossain, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, E-mail: dr_zakirmmc@yahoo.com

Abstract:

Background: Mortality risk is quite variable among fibrinolytic treated ST elevation myocardial infarction patients. Careful and early risk evaluation of each patient is therefore important. Until now, the most evaluated biomarker has been troponin I on admission, which gives strong prognostic information. NT pro BNP has shown reasonable promise in predicting the adverse outcome of STEMI. This research will provide the information regarding its efficacy as a predictor of adverse outcome following STEMI. Objective: To assess the prognostic value of N-terminal pro-brain natriuretic peptide in fibrinolytic treated ST elevation myocardial infarction (STEMI) patients. Method: This short term prospective study was done in Cardiology dept. of BSMMU. We valuated 115 patients of STEMI admitted within 12 hours and receiving thrombolytic therapy. Venous blood sample was collected for NT pro BNP before starting fibrinolytic therapy. Additional clinical data was recorded including detailed complications of STEMI. Results: Out of 115 patients of STEMI 32.2% patient had adverse outcome among them 9.6% patients died, heart failure 13.0%, cardiogenic shock 7.8%, VT & VF 5.2%, acute MR 2.6%, VSR 0.9%, CHB 2.6% and 67.8% patient had no adverse outcome. According to association between hospital outcomes with N-terminal pro BNP level, it was observed that the mean N-terminal pro BNP level was higher in adverse outcome group. Based on the receiver-operator characteristic (ROC) curves N-Terminal Pro BNP level gave a cut off value ≥480.0 pg/ml, with 88.5% sensitivity and 100.0% specificity for prediction of complications and similarly N-terminal pro BNP level gave a cut off value ≥725.5 pg/ml, with 72.7% sensitivity and 93.3% specificity for prediction of mortality. Conclusion: N-Terminal Pro BNP level was highly sensitive and very much effective in the evaluation of adverse outcome of fibrinolytic treated ST elevation myocardial infarction (STEMI).

Key words: STEMI, NT- pro BNP.

Introduction:

Coronary artery disease (CAD) is predicted to be the most common cause of death and disability globally by 2020.[1] Acute myocardial infarction patients increasing in our country and remain a leading cause of morbidity and mortality. Careful and early risk evaluation of each patient is therefore important. Until now, the most evaluated biomarker has been troponin I on admission, which gives strong prognostic information. NT-pro BNP levels rise soon after the onset of symptoms in patients with ACS and this may help to risk stratify patients early in the course of the disease.[2]

NT pro BNP has shown reasonable promise in predicting the adverse outcome of STEMI. This research will provide the information regarding its efficacy as a predictor of adverse outcome following STEMI. The results if satisfactory may be adopted as practice guideline and regular investigation marker for early risk stratification and prognostic information.

Identification of high risk patients with high NT proBNP on admission in STEMI may be helpful for selection of more intense interventional or pharmacological treatment strategies. Early tissue level reperfusion is especially important in patients with raised NT pro BNP concentration and can alter the adverse outcome for this high risk group.

Methods:

This prospective study was carried out in the Department of Cardiology, University Cardiac Centre, BSMMU, from January 2014 to October 2014.We evaluated 115 patients of STEMI admitted within 12 hours onset of chest pain which lasted for at least 30 minutes and receiving thrombolytic therapy. STEMI was diagnosed when ECG showing ST elevation of 1 mm or more in two or more contiguous leads except v2-v3 where 2 or > 2 mm of ST elevation in men with age more than 40 years, >2.5 mm with age <40 years and > 1.5 mm in women. Patients with STEMI with delayed arrival more than twelve hours, preexisting Heart Failure, NYHA III and IV functional classes, serum Creatinine > 2.5mg/dl were excluded from the study. Informed consent was obtained prior to any study-related procedures. Demographic data and

prevalence of risk factors was obtained from all patients. Detailed clinical history and physical examination was done. Venous blood sample was collected for NT pro BNP before starting fibrinolytic therapy. NT pro BNP was determined by sandwich immunoassay on an Elecsys 1010 (Roche Diagnostics).Additional clinical data was recorded include a detailed description of complications encountered during hospital stay such as ventricular arrhythmia, complete heart block, cardiac failure, cardiogenic shock, other complications of STEMI and death.

Statistical Analysis:

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). A descriptive analysis was performed for all data. The quantitative and qualitative observations were indicated by frequencies and percentages. Chi-Square test was used to analyze the categorical variables was shown with cross tabulation and unpaired t-test was used to analyze the continuous variable was expressed as mean (±SD). Receiver operating characteristic (ROC) curves was generated to determine the cutoff values for the best sensitivity, specificity for prediction of mortality and complication. A P-value will considered to be statistically significant if ≤0.05.

Results and observations:

A total number 115 patients with STEMI, out of them 93 patients were male and male to female ratio was 4.2:1. Majority 52(45.2%) patients were in 5th decade. Mean age was found 58.7±11.0 years in adverse outcome group and 50.04±8.9 years in no adverse outcome group. There were statistically significant ($p<0.05$) between two groups except result of smoking and Diabetes mellitus which was not statistically significant ($p>0.05$) between two groups (Table-1).Regarding in hospital outcome, patient with adverse outcome group had high N-terminal pro BNP level than no adverse outcome group (Table-2). Based on the receiver-operator characteristic (ROC) curves in this series it was observed that N-Terminal Pro BNP level had area under curve 1.000, which gave a cut off value e"480.0 pg/ml, with 88.5% sensitivity and 100.0% specificity for prediction of complications. Similarly based on the receiver-operator characteristic (ROC) curves N-Terminal Pro BNP level had area under curve 0.963, which gave a cut off value ≥725 pg/ml, with 72.7% sensitivity and 93.3% specificity for prediction of mortality.

Table-I

Association of demographic data and CVD risk factors with outcome among the study population (n=115)

Characteristics		Adverse outcome (n=37)		No adverse outcome (n=78)		P value
Age (years) Mean±SD		58.7±11.0		50.04±8.9		[a]0.001[s]
	Total	n	%	n	%	
Sex						
Male	93	34	91.9	59	75.6	[b]0.038[s]
Female	22	3	8.1	19	24.4	
Smoking	61(53%)	21	56.8	40	51.3	[b]0.582[ns]
Hypertension	63(54%)	28	75.7	35	44.9	[b]0.001[s]
Diabetes mellitus	53(46%)	21	56.8	32	41.0	[b]0.113[ns]
Dyslipidemia	67(58%)	37	100.0	30	38.4	[b]0.001[s]
Family history of premature CAD	23(20%)	13	35.1	10	12.8	[b]0.005[s]

s=significant; n=not significant

[a]P value reached from unpaired t-test

[b]P value reached from chi square test

Table-II

Association of hospital outcome with N-terminal Pro BNP level (n=115).

Hospital outcome	N-terminal pro BNP level (pg/ml)		
	N	Mean SD	Min - max
Heart failure	15	526.0±51.8	430 - 570
Cardiogenic shock	9	723.0±90.3	610 - 870
VT&VF	6	770.0±56.4	720 - 880
Acute MR	3	736.7±40.4	690 - 760
VSR	1	715.0± -	715 - 715
CHB	3	760.0±26.09	731 -780
Death	11	779.3±67.8	720 -880
No adverse outcome	78	201.1±86.2	49 -395

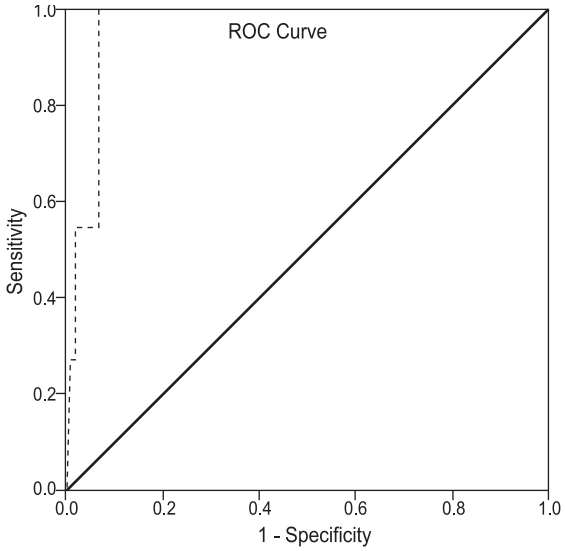

Fig.-1: *Receiver-operator characteristic curve of N-Terminal Pro BNP level for prediction of mortality*

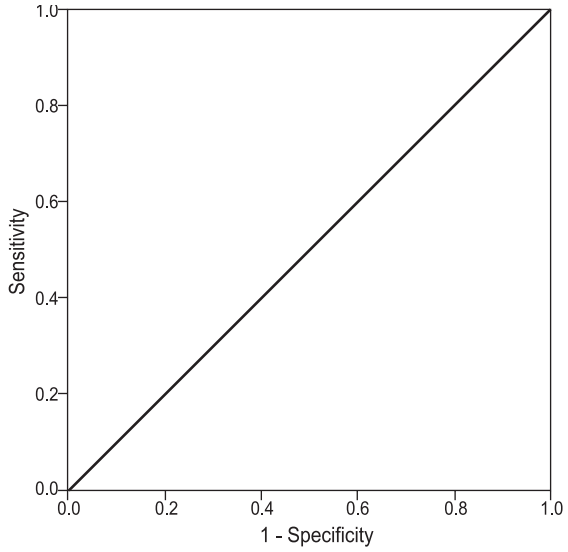

Fig.-2: *Receiver-operator characteristic curve of N-Terminal Pro BNP level for prediction of complication*

Table-III

Receiver-operator characteristic (ROC) curve of N-Terminal Pro BNP level for prediction of mortality (n=115).

	Cut of value	Sensitivity	Specificity	Area under the ROC curve	95% Confidence interval (CI)	
					Lower bound	Upper bound
N-Terminal Pro BNP level	≥725.5	72.7	93.3	0.963	0.930	0.996

Table-IV

Receiver-operator characteristic (ROC) curve of N-Terminal Pro BNP level for prediction of complications (n=115).

	Cut of value	Sensitivity	Specificity	Area under the ROC curve	95% Confidence interval (CI)	
					Lower bound	Upper bound
N-Terminal Pro BNP level	≥480.0	88.5	100.0	1.000	1.000	1.000

Table I shows association of characteristics and outcome of the patients. Mean age was found 58.7±11.0 years in adverse outcome group. All other result was statistically significant ($p<0.05$) between two groups except result of smoking and Diabetes mellitus which was not statistically significant ($p>0.05$).

Table II shows association of hospital outcome with N-terminal pro BNP level. It was observed that patient with adverse outcome group had high N-terminal pro BNP level than no adverse outcome group.

Discussion:

In this present series it was observed that out of one hundred fifteen patients 32.2% patient had adverse outcome among them 9.6% patients died, heart failure 13.0%, cardiogenic shock 7.8%, VT & VF 5.2%, acute MR 2.6%, VSR 0.9%, CHB 2.6% and 67.8% patient had no adverse outcome. Galvani et al. (2004) mentioned in their report that out of one hundred thirteen patients 6.4% died within 30 days.[3] In another study Ezekowitz et al. (2006) found 6.0% deaths, 6.3% with cardiogenic shock, 0.3% stroke and 6.6% with new-onset heart failure. In our study mortality was a bit more than other relevant study.[4]

According to association between hospital outcomes with N-terminal pro BNP level, it was observed in this present series that the mean N-terminal pro BNP level was higher in adverse outcome group. Similarly patients who had an event had a significantly higher median NT-pro BNP compared with those who remained event-free ($P<0.05$) reported by previous several authors such as Galvani et al. 2004; Bjorklund et al. 2006; Ezekowitz et al. 2006; Michael Weber at al. 2008. [3-6]

The mechanisms potentially responsible for the strong association between NT-pro BNP elevations and short-term mortality cannot be ascertained by the present study. However, BNP and NT-pro BNP release may be triggered by transient or permanent ventricular dysfunction induced by myocardial ischemia.[7] Moreover, the magnitude of the increase may reflect the extent of the ischemic injury, elevations being detected soon after the onset of myocardial ischemia.[8-9] We measured NT-pro BNP after the onset of ischemic symptoms. Such early increases may reflect the amount of the ischemic insult to the myocardium rather than the of actual extent myocardial necrosis. Accordingly the prognostic accuracy of NT-pro BNP was suggesting that NT-pro BNP may be considered as an early ischemic marker.

In this present study it was observed that based on the receiver-operator characteristic (ROC) curves N-Terminal Pro BNP level had area under curve 0.963, which gave a cut off value ≥725 pg/ml, with 72.7% sensitivity and 93.3% specificity for prediction of mortality. Similarly, Based on the receiver-operator characteristic (ROC) curves in this series it was observed that N-Terminal Pro BNP level had area under curve 1.000, which gave a cut off value ≥480.0 pg/ml, with 88.5% sensitivity and 100.0% specificity for prediction of complications. Michael Weber et al. (2008) obtained in their study that receiver-operating characteristics curve analysis yielded an optimal cutoff value of 474 pg/ml for NT-pro BNP that was able to discriminate patients at higher risk.[6] In receiver operating characteristic analysis Bjorklund et al. (2006) showed NT pro BNP strongly associated with mortality(area under the curve 0.81, 95% confidence interval (CI) 0.72 to 0.9, 0.67, 95% CI 0.56 to 0.79, and 0.66, 95% CI 0.56 to 0.77, respectively), which is closely resembled with the present study.[5]

The present study is the first one to demonstrate that a single measurement of NT-pro BNP, obtained on admission, provides important prognostic information of STEMI patients. In this study, we have demonstrated that the early measurement of NT-pro BNP provides important information for risk stratification of STEMI. To the best of our knowledge, this is the first time that elevations of NT-pro BNP early after symptom onset are shown to have a profound and independent impact on short-term mortality in STEMI patients. Such findings may have important implications for immediate management of high-risk patients with STEMI. Our results, obtained at the earliest time from symptom onset. In particular, they confirm the prognostic value of natriuretic peptides even in patients without heart failure as detected by patient history or at initial evaluation.

Conclusion:

N-Terminal Pro BNP level was highly sensitive and very much effective in the evaluation of adverse outcome of fibrinolytic treated ST elevation myocardial infarction (STEMI).We have demonstrated that higher N-Terminal Pro BNP level is associated with not only higher complication but also mortality in STEMI patients. So it can be concluded that N-Terminal Pro BNP level is a useful prognostic value to detect the hospital outcome of ST elevation myocardial infarction (STEMI) patients.

Limitations:

Although the result of this study supports the hypothesis there are some facts to be considered which might affect

the results. Results were not correlated with other confounding variables. Further required long term follow up.

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