Prognostic Value of NT-proBNP in Predicting Adverse In-hospital Outcomes among Patients of STEMI getting Thrombolytic therapy without Clinical Manifestation of Heart Failure

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Abstract:

Background: *Risk stratification is extremely important in ACS patients especially acute STEMI. We studied in-hospital outcomes of acute STEMI according to their NT-proBNP level as a new prognostic marker.*

Methods: *This observational prospective study was conducted to evaluate the significance of raised plasma NT-proBNP level on in-hospital outcomes in patients with STEMI, without clinical manifestation of heart failure. A total 88 patients of STEMI were included in the study. Among them 10 Patients have normal levels of NT-proBNP (<110 pg/ml) and were included in Group-A (n = 10). Patients with increased proBNP level (e"110 pg/ml) were included in Group-B (n = 78). Patients were followed to see worse in-hospital outcomes (Heart failure, cardiogenic shock, significant arrhythmia and death) during index hospitalization period.*

Results: *Plasma NT-proBNP level was observed to be significantly higher among patients who developed heart failure, cardiogenic shock and death than the patients who did not developed these outcome ($p < 0.001$). The binary logistic regression analysis of Odds Ratios for characteristics of the patients likely to cause worse in-hospital outcome shows that NT-ProBNP and smoking habit were found to be the independent predictors of worse in-hospital outcome with ORs being 5.0 and 4.7 respectively.*

Conclusion: *On admission plasma NT-pro BNP level in patients with STEMI is a strong independent predictor of adverse in-hospital outcome.*

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Introduction:

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in western society and is increasing in developing countries. In 2001, worldwide death due to ischaemic heart disease (IHD) was 11.8% in low income countries and 17.3% in high income countries.[1]

Myocardial infarction (MI) is one of the leading causes of death in Bangladesh mostly in the 4th decade of life. In a study of 2690 patients, in hospital mortality was 11.8 %. The main cause of death was pump failure and ventricular fibrillation.[2] By 2020, it is predicted that CVD will claim 20 million lives annually and coronary heart disease (CHD) will surpass infectious disease as the world's number one cause of death and disability.[3] Acute MI (AMI) can have catastrophic short and long term consequences and the affected person need to be treated on an urgent basis. The resultant myocardial injury depends on the duration of insult, rapidity and completeness of reperfusion, presence and extent of collaterals and destruction of microvasculature.[4] Many factors have been shown to have prognostic value in STEMI. Demographic variables, symptoms severity, physical signs, echocardiographic and radiological measurements, hemodynamic and neuro-hormonal parameters, high TIMI and Mayo risk score, reduced exercise capacity have been shown to be associated with poor outcome.[5]

BNP is synthesized as a 108-amino acid-long prohormone termed pro BNP, which is released from the ventricular myocyte in response to stretch and hypoxia. On secretion this pro-peptide splits into its biologically active moiety BNP (32- amino acid) and the76- amino acid containing inactive polypeptide N-Terminal-pro BNP (NT-pro BNP).[6] The diagnostic and prognostic value of BNP and NT-pro BNP is well validated in suspected and established heart failure respectively.[7] Recently, it

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has been found that in the setting of acute coronary syndrome NT-pro BNP is an extremely powerful prognostic indicator including patients with STEMI at higher risk.[8] To define prognosis in patients with AMI several methods have been developed for risk stratification. But most of these are complex, difficult to perform and time consuming. On the contrary, testing of NT-pro BNP is relatively easy, less time consuming and highly cost-effective.[9]

This study was done to assess the prognostic value of NT-pro BNP regarding short term in hospital outcome among STEMI patients without clinical manifestation of heart failure on admission.

Methods:

This observational prospective study was conducted in NICVD, Dhaka during the period of June 2009 to December 2009. We studied 88 patients of STEMI admitted in NICVD within 12 hours of onset of chest pain and receiving IV Thrombolytic (Streptokinase) therapy and who did not develop heart failure on admission. Patients with old MI, re-infarction, valvular heart diseases, congenital heart diseases, chronic renal failure, and chronic heart failure were excluded. Baseline data including demographic profile, clinical history and risk factors were recorded. Physical examination was done. 12 lead ECG was recorded to see the location of MI. Echocardiography was done in all patients for determination of LVEF, Valvular diseases & other structural abnormalities. Blood was collected within 24 hours of onset of chest pain and sent to the Biochemistry department of NICVD for analysis of plasma NT-pro BNP, Serum creatinine, blood sugar, Fasting lipid profile, troponin I and CK-MB. Patients with normal levels of NT-pro BNP (<110 pg/ml) were included in Group-A (n = 10) and patients with increased pro BNP level (e"110 pg/ml) were included in Group-B (n = 78). All patients were observed meticulously during their hospital stay to see the clinical course and development of heart-failure, arrhythmia, cardiogenic shock and death. Ethical clearance was taken from ethical committee. Collected data was analyzed with the help of software SPSS.

p -value <0.05 was considered to be significant. The binary logistic regression analysis of Odds Ratios for characteristics of the patients likely to cause in-hospital worse outcome was done. The variables revealed to be significantly associated or nearly significantly associated with worse outcome in univariate analyses were all entered into the analysis directly.

Results:

Among the studied 88 patients with STEMI 78 patients had increase NT-proBNP (e"110 pg/ml) and 47 patients had worse in-hospital outcome. Male to female ratio was 6.3:1. The mean age was 50.7±11.5 years. The comparison of clinical data and ECG characteristics are showed in table I. Plasma NT-pro BNP level was observed to be significantly higher among patients who developed heart failure, cardiogenic shock and death than the patients who did not developed these outcome ($p < 0.001$). Significant arrhythmia was also found to be associated with higher plasma NT- pro BNP level ($p = 0.435$) table II. Out of the significant 4 variables of univariate analysis, NT-Pro BNP and smoking habit were found to be the independent predictors of worse in-hospital outcome with ORs being 5.0 and 4.7 respectively in multivariate analysis. Patients with NT-Pro BNP ≥110 pg/ml were 5 times more prone to develop worse in-hospital outcome than those with NT-ProBNP < 110 pg/ml ($p = 0.037$). The Odds Ratio for smoking habit indicates that smokers are at 4.7 times higher risk of developing worse outcome than the non-smokers ($p = 0.039$) table III.

Table-I

Clinical and ECG data according to NT- proBNP (n=88).

Characteristics	Group- A (<110 pg/ml) (n=10)	Group- B (≥110pg/ml) (n=78)	p value
Mean Age (Years)	41.8 ±13.6	51.8±10.7	0.047
Sex-Male (%)	90%	85.9%	0.72
Diabetes mellitus	2(20.0)	32(41.0)	0.042
Hypertension	2(20.0)	39(50.0)	0.037
Smoking	4(40.0)	58(74.4)	0.018
Dyslipidemia	1(10.0)	15(19.2)	0.594
F/H of IHD	4(40.0)	29(37.2)	0.772
Location of AMI (Anterior)	40%	53.85%	0.572

Table-II

Comparison of NT-pro BNP level with worse in-hospital outcome

Variables	NT-proBNP (pg/ml)		p-value
	Median	SEM	
Heart failure			
Developed	5675	1312.1	< 0.001
Not developed	784.3	714	
Significant arrhythmia			
Developed	1348.0	1082.2	0.435
Not developed	1241.0	1206	
Cardiogenic shock			
Developed	10315.0	2061.5	< 0.001
Not developed	2389.1	449.9	
Death			
Developed	16415.5	3069.6	< 0.001
Not developed	1105	593.7	

Table-III

Factors related to worse in-hospital outcome

Variables of interest	Univariate analysis	Multivariate analysis	
		Odds Ratio (95% CI of OR)	p- value
Age (> 50 years)	0.011	0.3(0.1-0.9)	0.065
Smoking habit	0.050	4.7(0.9 - 24.5)	0.039
Hypertension	0.049	2.0(0.6 - 6.6)	0.233
NT-Pro BNP (pg/ml)	0.014	5.0(1.0-22.6)	0.037

Discussion:

Sudoh et al.[10] working in Matsuo's research group demonstrated an ANP-like natriuretic peptide from porcine brain, named brain natriuretic peptide (BNP). Subsequent experiments showed that BNP was produced in cardiac myocytes. A third homologous natriuretic peptide, termed CNP, is produced in brain and endothelium, but apparently not in cardiac myocyte. In the circulation the biologically active 32 amino acid BNP hormone is separated from the n-terminal part of the pro-hormone termed NT-pro BNP (76 amino acid).[11] BNP is often called the ventricular hormone, but this represents an oversimplification. Nevertheless, it seems clear that when atrial tissue is taken as a reference, ventricular BNP production is higher than that of ANP, especially in heart failure. Similarly, after myocardial infarction ventricular BNP production seems to be up regulated to a greater degree than ANP production, possibly secondary to local stretch mechanisms in the area surrounding the infarcted area.[12]

Total 88 patients with diagnosis of acute ST-elevation myocardial infarction who were admitted in CCU in NICVD, were selected for the study after considering inclusion and exclusion criteria.

The mean age of study population was 41.8 ± 13.6 in Group-A and 51.8 ± 10.7 in Group-B, p = 0.047. Raymond et al.[13] showed the mean concentration of plasma NT-proBNP almost doubled per age decade regardless of sex or normality status that consistent with this study.

Among the patients the most common risk factor was smoking, which was present in 62 patients (70.5 %). Among other risk factors, history of hypertension was present in 41 patients (46.6 %), diabetes mellitus was present in 34 patients (38.6 %) and family history of IHD was present in 33patients(42.3%). Prevalence of smoking, hypertension and diabetes mellitus were significantly higher in patients of Group-B than Group-A (p = 0.018, p = 0.037 and p = 0.042 respectively).

A study done by Siddiqui in NICVD, Dhaka showed similar prevalence of risk factors in patients with STEMI.[14]

ECG revealed that 53.8% of the patients in Group-B had anterior wall MI, 43.6% had inferior wall MI, while 50% of Group-A had inferior MI, 40% had anterior MI. Extensive anterior myocardial infarction had the highest median NT-pro BNP level which was 2713.0 pg/ml , SEM=1668.3 and inferior myocardial infarction had the lowest median NT-pro BNP level which was 713.0 pg/ml , SEM=203.50.This findings correlates well with the study of Verges B et al. that showed Plasma NT-pro-BNP was signiûcantly increased in patients with anterior wall necrosis.[15]

During the follow up period worse outcome (such as heart failure, cardiogenic shock, arrhythmia and high degree AV block requiring pacing and death) occurred in 47 patients. Most common complication was heart failure, occurred in 32 patients (36.4%). Among the patients who suffered heart failure had median NT-pro BNP level 5675 1312.1(SEM) pg/ml and those not suffered from heart failure had NT-pro BNP level 784.3 ± 714(SEM) pg/ml. The difference was statistically significant (p value <0.001).

Cardiogenic shock developed in 26 patients (29.5%).This percentage was higher than previous study done by Siddiqui.[14] The explanation, may be delay in thrombolysis, predominance of elderly people and more patients of anterior infarction group. Those suffered from cardiogenic shock had median NT-pro BNP level 10315.0 ±2061.5 (SEM) pg/ml and those not suffered had NT-pro BNP level 2389.1± 449.9 (SEM) pg/ml (p value <0.001). Significant arrhythmia developed in 37 patients (42%). A study done by Aziz M in NICVD, Dhaka showed 23.5% of the patients developed significant arrhythmia.[16] Those suffered from significant arrhythmia had NT-pro BNP level 1348.0 ± 1082.2(SEM) pg/ml and those not suffered had NT-pro BNP level 1241.0 ±1206(SEM) pg/ml (p=0.435). Arrhythmia requiring DC shock or i.v drug administrations for their control were in 7 patients. High degree AV block requiring pacing were in 9 patients.

Total 12 patients died (13.6%) during hospital stay. Most of the patients died who had highest median NT-pro BNP level than of those who survived (16415.5 ± 3069.6(SEM) vs. 1105.0 ± 593.7(SEM) pg/ml respectively, p value <0.001). Majority (95.7%) of the patients with worse outcome had significantly higher NT-ProBNP (e" 110) level (p = 0.014). The chance of having worse outcome in patients with raised plasma NT-ProBNP was 5.5 (1.3 – 21.1) times higher than that in patients with normal level of NT-ProBNP.

Conclusion:

On admission NT-Pro BNP in patients of acute STEMI is an independent predictor of adverse in hospital outcome. It may serve as a simple marker to identify patients at higher risk.

Conflict of Interest - None.

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