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A Clinical Study of N-Terminal Pro- Brain Natriuretic Peptide as A Predictor of Prognosis in Acute St Segment Elevation Myocardial Infarction in Comparison with Left Ventricular Ejection Fraction

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ABSTRACT

Background: The study aims to determine the relationship between N-terminal pro brain natriuretic peptide(NT-proBNP) levels and short term complications of ST segment elevation myocardial infarction(STEMI) and the role of NT-proBNP in predicting the short term outcome of acute STEMI. Moreover, to compare the effectiveness of NT-proBNP and left ventricular ejection fraction(LVEF) in predicting prognosis of STEMI.

Materials and Methods: In this observational, single-centre study, 44 STEMI patients were enrolled. NT-proBNP at time of admission and Echocardiography within 1 day of admission were assessed in all patients. Included patients were followed upto 30 days for development of any short term complications.

Results: Mean NT-proBNP was 460.1pmol/L. NT-proBNP concentration correlated with cardiac failure(p=0.016), conduction blocks(p=0.001), and LVEF(p=0.04). ROC curve analysis showed that NT-proBNP cut off value was at 187pmol/L; analyte had a sensitivity 94.1% and specificity of 70.4% in predicting occurrence of complications.

Conclusion: NT-proBNP is a strong predictor of short term outcome in STEMI. It is better short term prognostic indicator than LVEF. Moreover, NT-proBNP can be utilized as a good tool for risk stratification of acute MI patients so that appropriate treatment strategies could be planned.

KEYWORDS brain natriuretic peptide, left ventricular ejection fraction, myocardial infarction, prognosis

INTRODUCTION

Ischemic heart diseases (IHD) are the prominent cause of death accounting for 12.2% of the total annual deaths worldwide(Mathers, Boerma, & Fat, 2009). Myocardial infarction (MI) is one of the most prevalent and fatal presentations of IHD. The MI is followed by myocardial necrosis and then consequently leading to heart failure, myocardial rupture or arrhythmias(Chan & Ng, 2010). This insinuates early and apt treatment of MI which would lead to improved outcomes. For appropriate treatment, optimal risk stratification of patients is necessary. However, the risk prognostication in regards to clinical, electrocardiography (ECG), and biochemical (i.e., cardiac troponin, creatinine kinase-MB, etc.) markers has been quite imprecise(Galvani et al., 2004).

Brain natriuretic peptide (BNP) is a vasoactive hormone secreted by the heart, mainly from ventricles, as part of a systemic response to cardiac stress, myocyte stretch and ventricular dysfunction(Galvani et al., 2004; Radwan, Selem, & Ghazal, 2014). On release BNP is cleaved into N-terminal pro brain natriuretic peptide (NT-proBNP), which is more stable in serum than BNP and can be easily measured(Mueller, Gegenhuber, Dieplinger, Poelz, & Haltmayer, 2004). NT-proBNP measurement as a prognostic tool has an apparent advantage over many other parameters as it is a quantitative test and is operator-independent(Puri et al., 2004). BNP or NT-proBNP have been illustrated to be effective in diagnosing LV dysfunction, in risk stratification across the whole spectrum of acute coronary syndrome (ACS) and providing valuable prognostic information on short and long term mortality in such patients(Szadkowska et al., 2009). Elevated NT-proBNP concentrations between 14 and 40 h after an ischemic event have found to be associated with poor prognosis, including higher mortality, development of congestive heart failure, and recurrent ischemic events(Hall, 2004; Morita et al., 1993; Morrow et al., 2005).

Thus, this study intends to determine the relationship between NT-proBNP levels and short term complications of ST segment elevation myocardial infarction (STEMI) and the role of NT-proBNP in predicting the short term outcome of acute STEMI. Moreover, to compare the effectiveness of NT-proBNP and left ventricular ejection fraction (LVEF) in predicting prognosis of STEMI.

MATERIALS AND METHODS

Study design and patient population

This was an observational study in which a total of 44 patients, of different ages, who presented with acute ST elevation myocardial infarction, were included in this study. Patients

were enrolled from August, 2014 to February, 2016 at a tertiary care hospital in India. The study was conducted in accordance with the Declaration of Helsinki. All patients signed informed consent form which was reviewed and approved by the Institutional Ethics Committee of the centre.

The inclusion criteria were patients with: 1) typical ischemic symptoms and ST segment elevation of at least 1 mm in 2 or more consecutive ECG leads; 2) admitted within 12 hours of symptoms onset; 3) the age > 21 years. The patients were excluded if: 1) STEMI patients with previous chronic heart failure; 2) STEMI patients with previous chronic kidney disease; 3) STEMI patients with cardiogenic shock at presentation; 4) STEMI patients who present 12 hours after the onset of symptoms; 5) Patients with NSTEMI and unstable angina.

Study procedure

The patients were evaluated as per the history, general physical examination, systemic examination, ECG, NT-proBNP at the time of admission and Echocardiography within 1 day of admission. The included patients were followed up over a period of 30 days for development of various short term complications of acute STEMI.

Sample volumes of 150 µl of venous blood were collected in heparinised vials and assayed using the Roche cardiac pro BNP test kits in Cobas h 232 instrument. This test is an immuno-assay. It contains one monoclonal and one polyclonal antibody directed against NT-proBNP and has a measuring range of 30 – 4000 pmol/L.

All patients were subjected to a detailed echocardiography and Doppler evaluation. Qualitative and quantitative assessment of segmental and global LV function was done in all patients with Philips Echocardiography machine. Modified Simpson's technique was used to determine the ejection fraction (EF). The EF of <55% was taken as abnormal.

Statistical analysis

Continuous variables were presented as mean ± standard deviation and categorical variables as counts and percentages. Chi-square test was applied for analysing categorical variables. All data were analysed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 17.0.

RESULTS

Table 1 demonstrates the baseline parameters of the patients. The mean age group in the study population was 52.3 years. Of total, 77.3% patients were males. It was observed that 75% patients had smoking as risk factor followed by 47.7% cases had hypertension and 95.5% patients had chest pain. Of the 44 patients studies 45.5% cases had anterior wall MI, 31.8% patients had inferior wall MI, and 9.1% patients had both inferior wall MI and posterior wall MI. The mean NT-proBNP was 460.1pmol/L and median was 223pmol/L. The values of NT-proBNP in 44 patients are represented in Figure 1.

Table 1: Baseline parameters of the patients

Parameters	Patients (N=44)
Age (mean ± SD, years)	52.3 ± 13.3
Male, n (%)	34 (77.3%)
Hypertension, n (%)	21 (47.7%)
Diabetes mellitus, n (%)	8 (18.2%)
Smoking, n (%)	33 (75%)
Family history of ischemic heart disease, n (%)	8 (18.2%)
Hyperlipidaemia, n (%)	14 (31.8%)
Symptoms	
Chest pain and sweating, n (%)	42 (95.5%)
Shortness of breath, n (%)	22 (50%)
Syncope/giddiness, n (%)	11 (25%)
Palpitations, n (%)	4 (9.1%)
Clinical presentation	
Anterior wall MI, n (%)	20 (45.5%)
Anteroseptal MI, n (%)	1 (2.3%)
Inferior wall MI, n (%)	14 (31.8%)
Posterior wall MI, n (%)	1 (2.3%)
Inferior wall + posterior wall MI, n (%)	4 (9.1%)
Inferior wall + lateral wall MI, n (%)	1 (2.3%)
Inferior wall + right ventricular MI, n (%)	2 (4.5%)
Inferior wall + posterior wall + right ventricular MI, n (%)	1 (2.3%)
Duration of symptoms (mean ± SD, hrs)	5.8 ± 0.6
NT- proBNP (mean ± SD, pmol/L)	460.1 ± 94.9
Left ventricular ejection fraction (mean ± SD, %)	48.9 ± 10.1
Thrombolysis, n (%)	34 (77.3%)

NT- proBNP – N-terminal pro-brain natriuretic peptide; MI – myocardial infarction

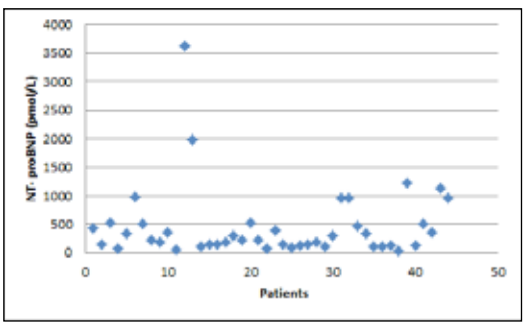

Figure 1: Levels of NT- proBNP in the patients

Over a period of 30 days, it was observed that 22.7% patients had conduction blocks as complication followed by 15.9 % deaths and 13.6 % cardiac failure (Table 2).

Table 2: Complications/outcomes in the patients

Complications/outcomes	Patients (N=44)
Cardiac failure	6 (13.6%)
Conduction blocks	10 (22.7%)
Tachyarrythmia	0 (0%)
MR/VSD/ free wall rupture	0 (0%)
LV aneurysm/ thrombus	0 (0%)
Death	7 (15.9%)

MR – mitral regurgitation; VSD – ventricular septal defect; LV – left ventricle

The level of NT-proBNP was found to be correlated with cardiac failure (p =0.016), conduction blocks (p =0.001), mortality (p =0.07), and left ventricular ejection fraction (p =0.04) (Table 3). The left ventricular ejection fraction was not statistically correlated with the complications and mortality (Table 4).

Table 3: Correlation between NT- proBNP and several variables

Parameters	NT- proBNP (pmol/L)		p-value
	<187 (n = 20)	≥187 (n = 24)	
Smoking, n	14	19	X^2 = 0.489, p = 0.484
Cardiac failure, n	0	6	X^2 = 5.8, p = 0.016
Conduction blocks, n	0	10	X^2 = 10.7, p = 0.001
Mortality, n	1	6	X^2 = 3.26, p = 0.07
Complications/ outcomes, n	1	16	X^2 = 17.5, p <0.001
LVEF ≥55, n	10	5	X^2 = 4.13, p = 0.04
LVEF <55, n	10	19	

LVEF – left ventricular ejection fraction; NT- proBNP – N-terminal pro-brain natriuretic peptide

Table 4: Correlation between left ventricular ejection fraction and outcomes

Parameters	LVEF (%)		p-value
	≥55 (n = 15)	<55 (n = 29)	
Complications, n	4	13	$X^2 = 1.37$, P = 0.241
Mortality, n	1	6	$X^2 = 1.45$, p = 0.228

ROC curve analysis (Figure 2) showed that NT-proBNP cut off value is at 187pmol/L, the analyte had a sensitivity 94.1% and specificity of 70.4% (AUC – 0.88) in predicting the occurrence of complications.

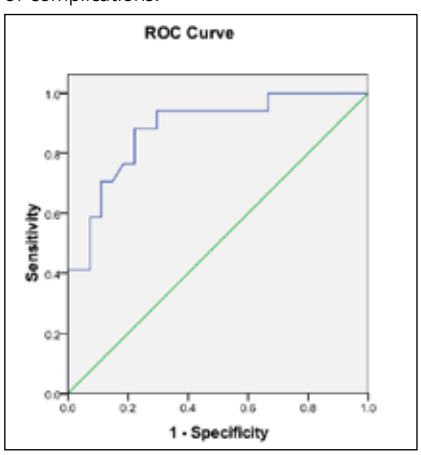

Figure 2: ROC curve analysis of NT- proBNP

DISCUSSION

The major challenge in treatment of patients with STEMI is identifying the high risk patients, such that treatment strategies can be aimed at limiting the further myocardial injury and preventing complications. Despite the advent of chest pain center with routine ECG, Echocardiography and sensitive biomarkers of myocardial necrosis, a number of patients presenting with STEMI are not properly managed(Chowdhury, Khan, & Hoque, 2014). NT-proBNP has been emerging to be preferred as a prognostic tool in STEMI patients.

Increased baseline concentrations of NT-proBNP are inferred to be predictive of adverse events at 30 and 90 days(Radwan et al., 2014). Therefore in present study, we had intended to determine the role of NT-proBNP and relationship between NT-proBNP levels and short term complications (upto 30 days) of STEMI. ROC curve analysis showed that at a NT-proBNP cut off value at 187pmol/L, the analyte has a sensitivity of 94.1 % and specificity of 70.4 % of predicting the occurrence of complications. It was found that there was a significantly higher incidence of conduction blocks (p =0.001), cardiac failure (p =0.016), lower LVEF (p =0.04), complications (p <0.001) and deaths (p =0.07) in the group who had a NT-proBNP values above the cut-off. There was a no statistical significance between abnormal LVEF and occurrence of complication (p >0.05). All the same, in some previous studies (Ranjith, Pegoraro, Naidoo, & Esterhuizen, 2005; Wang et al., 2004), concentration of NT-proBNP was found to be superior prognostic marker than the LVEF. Moreover, the mortality was compared with EF and NT-proBNP, both showed to be statistically insignificant (p >0.05). The cause for this insignificance in mortality could be because of small sample size, less number of events and because serial measurements of NT-proBNP were not taken.

The concentration of NT-proBNP has been measured in various studies for predicting the risk of outcomes in patients with ACS (Ang, Kong, Kao, & Struthers, 2009; Galvani et al., 2004; Međedović et al., 2009; Narain et al., 2007; Ranjith et al., 2005), AMI (Mayr et al., 2011; Pasupathi, Rao, Farook, Saravanan, & Bakthavathsalam, 2009; Puri et al., 2004), stable coronary heart disease(Kragelund, Grønning, Køber, Hildebrandt, & Steffensen, 2005), heart failure(Taylor, Roalfe, Iles, & Hobbs, 2014), atrial fibrillation, stroke or transient ischemic attack and CAD(Wang et al., 2004) . Several studies have also utilized NT-proBNP in predicting risk in STEMI patients. In a study by Kwon et al. patients with NT-proBNP > 991pg/ml (approx. >116.9pmol/L) had lower LVEF (p < 0.001), needed longer intensive care (p < 0.001) and had higher in- hospital mortality (p < 0.001) than those with, NT-proBNP level ≤ 991pg/ml(Kwon et al., 2009). Similarly, a sub-study of ASSENT-2 and ASSENT PLUS trials by Bjorklund et al revealed that NT-proBNP, on admission, is a strong independent predictor of long term mortality in STEMI patients managed with fibrinolytics. The amalgamation of NT-proBNP and ST resolution at one hour provides complementary information indicating the prognosis in such patients(Björklund et al., 2006). However, Ben-Dor et al. conducted a study on 55 STEMI patients and found that there was no significant correlation between NT-proBNP and systolic function early after STEMI (p=0.49)(Ben-Dor et al., 2007). Our study deduced that elevated NT-proBNP is associated with increased complications, thus indicating its strong correlation with the risk prediction. However, the combination of NT-proBNP with LVEF considerably upgrades risk stratification beyond that provided by either alone.

Limitations of the study

The present study suffers limitation that sample size was small; there was a lack of precise decisional cut off values for NT-proBNP.

CONCLUSION

The study concludes that NT-proBNP is a strong predictor of short term outcome in STEMI. It is a better short term prognostic indicator than LVEF. Moreover, NT-proBNP can be utilized as a good tool for risk stratification of acute MI patients so that appropriate treatment strategies could be planned.

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